TYPE 2 DIABETES PATIENTS AND THEIR BODY WEIGHT: A MIXED METHODS STUDY INVESTIGATING BELIEFS, ATTITUDES, AND ADHERENCE TO THEIR MEDICINES OVER TIME

PSAROU, A.

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INDEX

Contents

ACKNOWLEDGEMENTS 12
ABSTRACT 13
LIST OF TABLES 14
LIST OF FIGURES 15
LIST OF APPENDICES 21
LIST OF ABBREVIATIONS 23
INTRODUCTORY CHAPTER 25
I. Introduction 26
II. Purpose- Aims and Objectives 27
III. Thesis Structure 28
CHAPTER ONE: TYPE 2 DIABETES 30
1.1 What is type 2 diabetes? 31
1.2 Causes and complications of T2D 31
1.3 Impact and cost to NHS and patients 33
1.4 Management of T2D in UK 35
1.5 Lifestyle Interventions for T2D 35
1.6 Pharamacotherapy 36
1.6.1. Biguanides 40
1.6.2 Sulphonylureas 40
1.6.3 Thiazolidinediones (or Glitazones) 41
1.6.4. Meglitinides 41
1.6.5 α-Glucosidase Inhibitors [AGI] 41
1.6.6 Gliptins (DPP-4 inhibitors) 42
1.6.7 Incretin mimetics GLP-1 42
1.6.8 Sodium-Glucose Co-Transporter 2 [SGLT-2] Inhibitors 43
1.6.9 Insulin 43
1.6.10 Orlistat 44
1.7 Summary and Future Medication and Management of T2D 45
CHAPTER TWO: SYSTEMATIC REVIEW OF QUALITATIVE RESEARCH 47
2.1 Background 48
2.2 Methods 55
2.2.1 Design 55
2.2.2 Search Strategy 57

2.2.3 Selection and eligibility of studies 58
2.2.4 Quality Assessment 61
2.2.5 Data abstraction and synthesis 65
2.2.6 Determining how the studies are related 66
2.2.7 Translating studies into one another and synthesising translations 67
2.3 Results 68
2.3.1 Research Design and Methodology 68
2.3.2 Participants' characteristics 69
2.3.3 Types of medicines 70
2.3.3.1. Oral glucose lowering drugs 70
2.3.3.2 Insulin 70
2.3.3.3 Weight Loss Medicines and Weight related Issues 71
2.3.4. Conceptual Framework 72
2.4 Synthesis results 88
2.4.1 Oral Glucose Lowering Drugs and Insulin Maps 88
2.4.1.1 Negative Feelings 91
2.4.1.2 My diabetes is serious 92
2.4.1.3 My diabetes is not serious 93
2.4.1.4 Expectations of Treatment 96
2.4.1.5 Expectations of Care 96
2.4.1.6 Negative Perceptions of medicines 97
2.4.1.7 Negative Experiences with medicines 100
2.4.1.8 Positive Experiences with medicines 100
2.4.1.9 Positive Perceptions of medicines 101
2.4.1.10 Self-Regulation 102
2.4.1.11 Patterns of Medicine Taking Behaviour 103
2.4.1.12 Strategies to overcome negative aspects of insulin (Figure 2.3) 106
2.4.1.13 Lifestyle behaviour (Lifestyle Adherence and Non-Adherence) 107
2.4.2 Line of Argument Synthesis: Patient's journey - the impact of diabetes medicines on re-evaluating oneself 109
2.4.2.1 Severity 111
2.4.2.2 Difficulties 112
2.4.2.3 Passive- Active Patient Role 112
2.4.2.4 Adherence or Non- Adherence 113
2.4.2.5 Grief Reaction 113
2.4.2.6 Diabetes and medication related beliefs 114

2.4.2.7 Re-evaluation of one self 115
2.4.2.8 Acceptance-Denial 115
2.4.2.9 Strategies to regain control 116
2.5 Summary 117
2.5.1 Application of theory in medicine taking behaviour for T2D 118
2.5.2 Strengths and limitations of review 119
2.5.3 Research gaps 121
CHAPTER THREE: GENERAL METHODOLOGY AND RECRUITMENT STRATEGY 122
3.1 Introduction 123
3.2 Mixed Methods Research 123
3.2.1. Justification for methodology 126
3.3 Research Questions 127
3.4 Study design 128
3.4.1 Justification of study design 130
3.4.2 Study population (inclusion and exclusion criteria) 131
3.4.3 Justification of sample size 133
3.5 Recruitment strategy 134
3.5.1 Recruitment for Questionnaire (Quantitative) Data 135
3.5.2 Recruitment for Interview (Qualitative) Data 137
3.6. Ethical considerations and Ethical Approval 137
CHAPTER FOUR: DATA COLLECTION TOOLS AND 140
DATA ANALYSIS METHODS 140
4.1 Introduction 141
4.2 Quantitative Data Collection Tools 141
4.2.1. Questionnaires 141
4.2.1.1. Expectations About and Experiences with Insulin Treatment 145
4.2.1.2. Beliefs and Attitudes about Medicines 146
4.2.1.3. Medication Adherence 147
4.2.1.4 Satisfaction with Medication Information 148
4.2.1.5. Satisfaction about Diabetes/ Weight Loss Medicines 149
4.2.1.6. Self–Efficacy for Appropriate Medication Use 151
4.2.1.7. Obesity and Weight Loss Quality of Life Measure 152
4.2.2. Additional demographic and clinical data 153
4.2.3 Piloting of Questionnaire 154
4.2.4 Data management and statistical analysis 154
4.3. Qualitative Data Collection Tools 161

4.3.1 Interviews 161
4.3.1.1 Purpose of Interviews 162
4.3.1.2 Development of interview guides 163
4.3.1.3 Sampling techniques and sample size 164
4.3.1.5 Data management and analysis 166
4.3.1.6 Presentation of Findings 168
4.3.2 Mixed Method Data Management and Analysis 168
CHAPTER FIVE: QUESTIONNAIRE RESULTS 170
5.1 Introduction 171
5.2 Recruitment, Survey Response and Data Screening 171
5.3 Internal Reliability 174
5.4 Participants 174
5.4.1. Whole Group 174
5.4.2 Groups according to effect of new medicine on body weight 179
5.5 Changes in expectations, beliefs and attitudes overtime 186
5.5.1 Expectations and perceptions of new medicine (EITQ, PITQ) 186
5.5.1.1 Whole Group- Baseline versus Follow-up 186
5.5.1.2 Weight-Effect Groups – Baseline versus Follow-up 187
5.5.1.3 Weight-Effect Groups – Comparison between groups 191
5.5.2 Satisfaction with information about medicines (SIMS) 191
5.5.2.1 Whole Group- Baseline Versus Follow-up 191
5.5.2.2 Weight-Effect Groups – Baseline Versus Follow-up 194
5.5.2.3 Weight-Effect Groups – Comparison between groups 196
5.5.3 Beliefs about Medicines (BMQ)- General and Specific 198
5.5.3.1 Whole Group- Baseline Versus Follow-up 198
5.5.3.2 Weight-Effect Groups – Baseline versus Follow-up 203
5.5.3.3 Weight-Effect Groups – Comparison between groups 205
5.5.4 Satisfaction with Diabetes Medicines -DiabMedSat 207
5.5.4.1 Whole Group- Baseline Vs Follow-up 207
5.5.4.2 Weight-Effect Groups – Baseline Versus Follow-up 211
5.5.4.3 Weight-Effect Groups – Comparison between groups 215
5.5.5 Satisfaction with Diabetes Medicines -TRIM-Weight 217
5.5.5.1 Whole Group- Baseline Versus Follow-up 217
5.5.5.2 Weight-Effect Groups – Baseline Versus Follow-up 220
5.5.5.3 Weight-Effect Groups – Comparison between groups 223
5.5.6 Medication adherence (MMAS-8) 224

5.5.6.1 Whole Group- Baseline Versus Follow-up 224
5.5.6.2 Weight-Effect Groups – Baseline Versus Follow-up 225
5.5.6.3 Weight-Effect Groups – Comparison between groups 226
5.5.7 Self-Efficacy with Medication (SEAMS) 227
5.5.7.1 Whole Group- Baseline Versus Follow-up 227
5.5.7.2 Weight-Effect Groups – Baseline Versus Follow-up 229
5.5.7.3 Weight-Effect Groups – Comparison between groups 231
5.5.8. Weight Related Quality of Life (OWLQOL) 233
5.5.8.1 Whole Group- Baseline Versus Follow-up 233
5.5.8.2 Weight-Effect Groups – Baseline Versus Follow-up 234
5.5.8.3 Weight-Effect Groups – Comparison between groups 235
5.6 Impact of expectations, beliefs and attitudes on adherence 237
5.6.1 Whole Group 244
5.6.1.1 Predicting medication adherence at 3-month follow-up from baseline and change values 244
5.6.1.2 Predicting a change in medication adherence from baseline and change values 252
5.6.2 Weight-Effect Groups 258
5.6.2.1 Weight Reducing Group 258
5.6.2.2 Weight Neutral Group 260
5.6.2.3 Weight Increasing Group 262
5.7. Summary 266
CHAPTER SIX: INTERVIEW RESULTS 268
6.1 Introduction 269
6.2 Interview Participants 269
6.3 Central Themes 274
6.3.1 My Type 2 Diabetes and my medicines 275
6.3.1.1 Diabetes understanding 275
6.3.1.2. Perceptions of Blood Glucose and Self-monitoring 275
6.3.1.3 Diabetes Treatment 280
6.3.1.4 Acceptance to new medicine 283
6.3.1.5 Perceptions of Seriousness 287
6.3.2 My Body Weight 291
6.3.2.1 Weight Worry 291
6.3.2.2 Medicines and effects of body weight 292
6.3.2.3 My diabetes matters Vs my body weight matters 293

6.3.3 Beliefs and Perceptions about medicines 295
6.3.3.1 Trust in Doctors to Prescribe Medicines 295
6.3.3.2 Necessity and Benefits of Prescribed Medicines 296
6.3.3.3 Effectiveness of Prescribed Medicines 297
6.3.3.4 Concerns about Prescribed Medicines 301
6.3.3.5 Trial and Error when taking Medicines 304
6.3.3.6 Tablets versus Injections 304
6.3.4 Experiences of taking medicines 307
6.3.4.1 Inconvenience and Forgetting to take Prescribed Medicines 307
6.3.4.2 Experience of side effects 311
6.3.5 Emotional Impact of taking Diabetes medicines 312
6.3.6 Routine and Coping Mechanisms 316
6.3.6.1 Medication Routine 316
6.3.6.2 Self-Regulation 327
6.3.6.3 Negotiation 329
6.3.6.4 Seeking information 330
6.3.7 Compromise and Perseverance 331
6.3.8 Helpful and Unhelpful Support 333
6.3.8.1 Unhelpful Support 336
6.3.8.2 Helpful Support 338
6.4 Summary 348
CHAPTER SEVEN: DISCUSSION 350
7.1 Introduction 351
7.2 Key Findings 351
7.2.1 Setting the context 352
7.2.2: Perceptions and beliefs of diabetes and diabetes medicines 354
7.2.3: Expectations and experiences of new diabetes medicines 357
7.2.3.1 Effectiveness 358
7.2.3.2 Side effects and hypoglycaemia 359
7.2.3.3 Body weight 360
7.2.3.4: Burden and Convenience 362
7.2.4: Adherence 363
7.2.5 Self-efficacy (Routine practices and Self-regulation) 366
7.2.6 Impact of medicines' concerns and self-efficacy on adherence 369
7.2.7: Expectations of Care: Helpful and Unhelpful Support 373
7.2.8 Emotional impact of taking diabetes (and other) medicines 375

7.2.9 Potential Future Intervention(s) 377
7.3 Theory review 378
7. 4 Strengths and Limitations 380
7.5 Implications for policy and practice 385
7.6 Future Research 388
7.7 Conclusion 389
REFERENCES 391
APPENDICES 424

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ABSTRACT

Background: Type 2 diabetes [T2D] is a chronic, debilitating condition often associated with obesity. People with T2D rarely fully comply with their medication regime whether it is tablets or injections. Yet, weight gain is a common side effect of most diabetes medicines and, therefore, can be problematic for patients already overweight.

Study Aim: To measure how expectations, beliefs and attitudes towards different diabetes treatments change over time focusing on medicines which cause weight loss, weight gain or are weight neutral. To investigate the impact of this belief/attitude change on adherence, and explore ideas for future interventions which improve both diabetes management and adherence.

Methods: A mixed methods observational study was conducted in parallel with a systematic review. Individuals self-completed validated questionnaires (n=190) and selected purposively to be interviewed (n=24/190) before and three months after a change in treatment. A change was defined as the addition of, or a change to, a new glucose-lowering or anti-obesity drug to the patient's current therapy.

Results: The systematic review identified that T2D patients go through a constant self-evaluation as a result of daily emotional and cognitive experiences with their condition and medicines. However, weight loss was not perceived as strategy in managing diabetes. The questionnaires and interviews revealed that patients' views of their medicines and the severity of their condition changes over time. Overall they were ambivalent about the effectiveness of their diabetes treatment, whilst most were concerned about their body weight. Although there was evidence of reluctance to make treatment changes and a desire to stop them, most patients appeared to accept new medicines if they portray a dual purpose, particularly if they help weight loss and/or in reduction medication number or doses. Nevertheless, despite significantly positive appraisals at 3-month follow-up from participants prescribed medicines promoting weight loss, 70% of the whole group had suboptimal adherence levels. Adherence was influenced by perceptions of medicine's effectiveness, concerns and convenience, experience of side effects and self-efficacy levels. Interviewees who had an established routine and took their medicines in conjunction with other events, such as self-monitoring of blood glucose, were classified as highly adherent. Yet, perceptions of blood glucose and lack/excessive self-monitoring could hinder appropriate management of diabetes and weight loss. Whilst health professionals, family and other people with T2D can have both a positive and negative impact on individual's perceptions and treatment adherence, interviewees valued most the support they received from their health care team, particularly if this was intensive, diverse and timely.

Conclusion: Study findings demonstrate that the needs and desired outcomes of T2D patients change over time after a treatment change, but the new medicine's weight-effect does not influence adherence. Instead, patients could benefit from NHS services that give support in increasing confidence levels in taking medicines as well as exploring medicines concerns and adherence, through the use of the visual models developed in this study.

LIST OF TABLES

Table 1.1: Overview of Medicines Prescribed for Type 2 Diabetes 38
Table 2.1 Seven Steps for conducting meta-ethnography (Adapted from Noblit & Hare, 1988 and Campebell et al., 2011) 56
Table 2.2: Engine Search and number of articles screened 58
Table 2.3: Inclusion and Exclusion Criteria 58
Table 2.4: Reasons for exclusion of articles screened 59
Table 2.5: Eligible papers examined and quality appraisal outcome 63
Table 2.6: Research focus of review papers based on types of medicines 66
Table 2.7: Summary of key characteristics of studies included in meta-ethnography 77
Table 3.1: List of diabetes and anti-obesity medications for eligibility criteria 132
Table 3.2: Rationale for Minor and Substantial Ethics Amendments 138
Table 4.1: Validated scales used in the questionnaires 143
Table 4.2: Participant characteristics for the development of sampling framework 165
Table 5.1: Sample Characteristics (n=190) - Demographic 175
Table 5.2: Sample Characteristics (n=190)-Clinical 177
Table 5.3: Proportions of types of new medicine prescribed 180
Table 5.4: Study participant characteristics at baseline and follow-up for each weight-effect group 182
Table 5.5: Baseline and Follow-up scores for all scales for the whole group and each weight-effect group 184
Table 5.6: Baseline and Follow-up scores for low, medium and high adherents (MMAS-8) 240
Table 5.7: Baseline and Follow-up scores for those who improved, decreased or remained stable in adherence levels 242
Table 5.8: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the whole group 245
Table 5.9: Multivariate Ordinal Analysis predicting adherence at follow-up 246
Table 5.10: Separate binary logistic regressions for high adherents and, medium and high adherents for key explanatory variables from ordinal regression 248
Table 5.11: Predicted probability for Follow-up adherence levels with various baseline scores and age for key variables from multivariate analysis 251
Table 5.12: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the whole group 252
Table 5.13: Multinomial Analysis predicting change in adherence over time following initiation of new diabetes medicine 255

Table 5.14: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the WR group 258
Table 5.15: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the WR group 259
Table 5.16: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the WN group 260
Table 5.17: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the WN group 262
Table 5.18: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the WI group.....263
Table 5.19: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the WI group 265
Table 6.1: Key Characteristics of interview participants (baseline and change data) 271
Table 6.2: Routine and coping mechanisms/ strategies 318

LIST OF FIGURES

Figure 2.1: Adapted PRISMA Flowchart 61
Figure 2.3: Synthesis of Insulin Treatment 90
Figure 2.4: Line of Argument Synthesis 110
Figure 3.1: Visual Representation of Mixed Methods Study Design 129
Figure 3.2: Research Study Flowchart.....135
Figure 4.1: Sampling Framework 165
Figure 5.1: Number of potential participants approached and recruited in in primary and secondary care NHS Trusts 172
Figure 5.2: Recruitment Flowchart 173
Figure 5.3: Number of participants completing questionnaires in each weight-effect group. 179
Figure 5.4: Expectations (EITQ) and Perceptions (PITQ) about new medicine at baseline and follow-up 186
Figure 5.5: Percentage of participants whose expectations of new medicine were unmet, met or exceeded by experience 187

Figure 5.6: Percent agreement to EITQ/PITQ item “taking this new medicine (will/makes) it easier to control my blood sugars” at baseline and follow-up for WR group. 188
Figure 5.7: Percent agreement to EITQ/PITQ item “taking this new medicine (will/makes) me feel better” at baseline and follow-up for WR group..... 188
Figure 5.8: Percent agreement to EITQ/PITQ item “taking this new medicine (will/makes) it easier to control my blood sugars” at baseline and follow-up for WN group. 189
Figure 5.10: Percent agreement to EITQ/PITQ item “taking this new medicine (will/makes) me feel better” at baseline and follow-up for WI group..... 190
Figure 5.12: Overall satisfaction with amount of information about new medicine (SIMS) at baseline and follow-up. +Indicates significant difference between baseline and follow-up for the whole group, * Indicates significant difference between baseline and follow-up in the WR group..... 191
Figure 5.13: Satisfaction with amount of information related to action and usage of new medicine (SIMS-AU) at baseline and follow-up. 192
Figure 5.14: Satisfaction with amount of information related to potential problems with new medicine (SIMS-PPM) at baseline and follow-up. 192
Figure 5.15: Percentage of participants who showed improvement, no change or reduction in satisfaction with information received about new medicine (SIMS)..... 193
Figure 5.16: Percentage of participants who showed improvement, no change or reduction in satisfaction with information received about new medicine related to action and usage (SIM-AU) 194
Figure 5.17: Percentage of participants who showed improvement, no change or reduction in satisfaction with information received about new medicine related to potential problems with medicine (SIM-PPM) 194
Figure 5.18: Percent agreement to SIMS item “Have received enough information about what you should do if you forget a dose” at baseline and follow-up for WR group. 195
Figure 5.19: Differences in satisfaction with amount of information related to action and usage of new medicine (SIMS-AU) at baseline and follow-up. 197

Figure 5.20: Beliefs about necessity of new medicine (BMQ-Necessity) at baseline and follow-up. 198
Figure 5.21: Beliefs about Concerns of new medicine (BMQ-Concerns) at baseline and follow-up. 198
Figure 5.22: Diabetes Medicines Belief Groups at baseline and follow-up. 199
Figure 5.23: Beliefs about Harm of medicines in general (BMQ-Harm) at baseline and follow-up. 200
Figure 5.24: Beliefs about Benefits of medicines in general (BMQ-Benefits) at baseline and follow-up. 200
Figure 5.25: Beliefs about Overuse of medicines in general (BMQ-overuse) at baseline and follow-up. 201
Figure 5.27: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about concerns over the new medicine (BMQ-Concerns) 202
Figure 5.28: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about overuse of prescribed medicines (BMQ-Overuse) 202
Figure 5.29: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about benefits of prescribed medicines (BMQ-Benefits) 203
Figure 5.30: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about harm of prescribed medicines (BMQ-Harm).... 203
Figure 5.31: Percent agreement to BMQ item “I worry that taking these medicines will cause me to gain weight” at baseline and follow-up for WR group. ... 204
Figure 5.32: Differences in beliefs about Necessity of new medicine (BMQ-Necessity) at baseline and follow-up. 205
Figure 5.33: Total Satisfaction about diabetes medicines (DiabMedSat) at baseline and follow-up. 207
Figure 5.34: Total Satisfaction, burden scale, about diabetes medicines (DiabMedSat-Burden) at baseline and follow-up. 208
Figure 5.35: Total Satisfaction, efficacy scale, about diabetes medicines (DiabMedSat-Efficacy) at baseline and follow-up. 208

Figure 5.36: Total Satisfaction, symptom scale, about diabetes medicines (DiabMedSat-Symptom) at baseline and follow-up. 209
Figure 5.37: Percentage of participants who showed improvement, no change or reduction in satisfaction of new medicine (DiabMedSat) 210
Figure 5.38: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the efficacy of new medicine (DiabMedSat-Efficacy) 210
Figure 5.39: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the burden of new medicine (DiabMedSat-Burden) 211
Figure 5.40: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the symptoms of new medicine (DiabMedSat-Symptom) 211
Figure 5.41: Percent agreement to DiabMedSat item “How satisfied or dissatisfied have you been with your diabetes medicine(s) ability to help you from feeling tired and lacking energy” at baseline and follow-up for WR group. 212
Figure 5.42: Percent agreement to DiabMedSat item “How satisfied or dissatisfied have you been with the impact of your diabetes medicine(s) on your physical well-being” at baseline and follow-up for WR group. 213
Figure 5.43: Percent agreement to DiabMedSat item “How satisfied or dissatisfied have you been with your diabetes medicine(s) ability to keep your blood sugars stable (avoid highs and lows” at baseline and follow-up for WI group. 214
Figure 5.44: Percent agreement to DiabMedSat item “How satisfied or dissatisfied have you been with your diabetes medicine(s) ability to help you from feeling tired and lacking energy” at baseline and follow-up for WI group. 215
Figure 5.45: Differences in satisfaction about burden (DiabeMedSat-Burden) and efficacy (DiabeMedSat-Efficacy) of diabetes medicines at baseline and follow-up. 216
Figure 5.46: Satisfaction with the impact of new medicine on daily life (TRIM-Wt-DL) at baseline and follow-up. 217

Figure 5.47: Satisfaction with the impact of new medicine on weight management (TRIM- Wt-WM) at baseline and follow-up. 217
Figure 5.48: Satisfaction with the impact of new medicine on psychological health (TRIM- Wt-PH) at baseline and follow-up.....218
Figure 5.49: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the impact of new medicine on daily life (TRIM-Wt-DL) 219
Figure 5.51: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the impact of new medicine on psychological health (TRIM-Wt- PH) 220
Figure 5.52: Percent agreement to TRIM-Weight item “How bothered or not bothered are you by being tired or drowsy during the day because of your medicine(s)” at baseline and follow-up for WR group. 221
Figure 5.54: Percent agreement to TRIM-Weight item “How satisfied or dissatisfied are you with your medicine’s ability to control your appetite” at baseline and follow-up for WR group. 222
Figure 5.55: Differences in satisfaction about impact of new medicine on weight management (TRIM-Wt-WM) at baseline and follow-up.....223
Figure 5.56: Medication adherence (MMAS-8) at baseline and follow-up. 224
Figure 5.57: Level of adherence with diabetes medicines prior and 3 months after new medicine prescription for the whole group 224
Figure 5.58: Percentage of participants whose levels of medication adherence (MMAS-8) increased, remained stable or decreased over time 225
Figure 5.60: Percentage of baseline and follow-up medication adherence levels (MMAS-8) for each weight-effect group 226
Figure 5.61: Self efficacy with taking medication scale (SEAMS) at baseline and follow-up. 227
Figure 5.62: Self efficacy with taking medication under conditions of uncertainty (SEAMS-UCU) at baseline and follow-up. 227
Figure 5.63: Self efficacy with taking medication under difficult circumstances (SEAMS-UDC) scale at baseline and follow-up. 228

Figure 5.64: Percentage of participants who showed improvement, no change or reduction in self-efficacy of appropriate use of new medicine (SEAMS)... 228
Figure 5.65: Percentage of participants who showed improvement, no change or reduction in self-efficacy under difficult circumstances (SEAMS-UDC) of appropriate use of new medicine..... 229
Figure 5.66: Percentage of participants who showed improvement, no change or reduction in self-efficacy under conditions of uncertainty (SEAMS-UCU) of appropriate use of new medicine..... 229
Figure 5.67: Percent agreement to SEAMS item “How confident are you that you could take your new medicine correctly when you are feeling unwell (you know like having a cold or the flu)” at baseline and follow-up for WR group. 230
Figure 5.68: Percent agreement to SEAMS item “How confident are you that you could take your new medicine correctly when you get a refill of your old medicine and some of the pills look different than usual” at baseline and follow-up for WR group. 231
Figure 5.69: Differences in self-efficacy of taking new medicine under difficult circumstances (SEAMS-UDC) at baseline and follow-up. 231
Figure 5.70: Obesity and weight loss quality of life (OWLQOL) scale at baseline and follow-up. 233
Figure 5.71: Percentage of participants who showed improvement, no change or reduction in weight related quality of life (OWLQOL)..... 233
Figure 5.72: Percent agreement to OWLQOL item “Because of my weight, I try to wear clothes that hide my shape” at baseline and follow-up for WR group. 234
Figure 5.73: Percent agreement to OWLQOL item “I worry about physical stress that my weight puts on my body” at baseline and follow-up for WR group..... 234
Figure 5.74: Percent agreement to OWLQOL item “I feel depressed because of my weight” at baseline and follow-up for WR group. 235
Figure 5.75: Differences in obesity and weight loss quality of life (OWLQOL) at baseline and follow-up. 236

Figure 5.76: Baseline and follow-up adherence levels for the four diabetes medicines belief groups. 238
Figure 6.1: Number of participants completing both interviews in each NHS Trust in primary and secondary care 270
Figure 6.2: Participants' perceptions of factors affecting blood glucose 277
Figure 6.3: Perceptions of Seriousness of Type 2 Diabetes 287
Figure 6.4: Conceptual Model of Participants' Beliefs and Perceptions about their Diabetes Medicines....297
Figure 6.6: Participants' Medicines Concerns and Polypharmacy 302
Figure 6.7: Patterns of Adherence 328
Figure 7.1: Conceptual Model on key factors influencing beliefs and adherence to medicines over time 355
Figure 7.2: Adherence Spectrum 366

LIST OF APPENDICES

Appendix 2.1 Systematic Review Search Terms 425
Appendix 2.2 Adapted CASP Tool 427
Appendix 2.3 Translational Synthesis: key components of perceptions of T2D and T2D medicine taking, including illustrative quotes (1st and 2nd order constructs) from primary studies....430
Appendix 3.1 Research Flyer 433
Appendix 3.2 Potential Participant Research Invitation Letter 434
Appendix 3.3 Study Consent Form....435
Appendix 3.4 Participant Information Sheet 436
Appendix 3.5 – Questionnaire 1 and 2....439
Appendix 3.6 Interview Consent From 458
Appendix 4.1 Clinical Data Form 459
Appendix 4.2 Interview Guide 1 and 2....460
Appendix 4.3: Thematic Framework - Node Hierarchy 466
Appendix 5.1: Internal reliability of adapted questionnaire scales 467
Appendix 5.2: Demographic characteristics of whole group, participants returned questionnaire 1 and participants returned both questionnaires. 468
Appendix 5.3: Clinical characteristics of whole group, participants returned questionnaire 1 and participants returned both questionnaires. 469
Appendix 5.4: Cronbach's alpha, baseline standard deviation and Standard Error of Measurement for each scale 471

Appendix 5.5: Proportion of patients whose expectations were unmet, met, or exceeded by experience (EITQ-PITQ) 472
Appendix 5.6: Proportion of patients whose satisfaction with information received about new medicine had improved, did not change or decreased 472
Appendix 5.7: Proportion of patients whose beliefs about the new medicine had improved, did not change or decreased 473
Appendix 5.8: Proportion of patients whose treatment satisfaction of new medicine had improved, did not change or decreased 474
Appendix 5.9: Proportion of patients whose impact of new medicine related to daily life, weight management and Psychological Health had improved, did not change or decreased 475
Appendix 5.10: Proportion of patients whose medication adherence levels had improved, did not change or decreased 475
Appendix 5.11: Proportion of patients whose self-efficacy with appropriate use of new medicine had improved, did not change or decreased 476
Appendix 5.12: Proportion of patients whose weight related quality of life had improved, did not change or decreased 476
Appendix 5.13 Ordinal Regression – Single Baseline (non-significant) Predictors for follow-up medication adherence 477
Appendix 5.14: Ordinal Regression – Single Change (non-significant) Predictors for follow-up medication adherence 478
Appendix 5.15: Correlation Matrix (Pearson Correlation) 480
Appendix 5.16: Multinomial Regression – Single Baseline Predictors for change in medication adherence based on SEM 481
Appendix 5.17: Multinomial Regression – Single Change Predictors for change in medication adherence based on SEM 482
Appendix Figures Chapter 5 484
Appendix 6.1: Interview Sample Characteristics and Scale scores 491
Appendix 6.2: Key aspects showed change or not change for the duration of the study per participant 493

LIST OF ABBREVIATIONS

ACR	Microalbuminuria (or albumin to creatinine ratio)
ADA	American Diabetes Association
BD	Twice a day
BME	Black and Ethnic Minority
BMI	Body Mass Index
BMQ	Beliefs about Medicines Questionnaire
CASP	Critical Appraisal Skills Programme
CHD	Coronary Heart Disease
CHO	Carbohydrates
COPD	Chronic Obstructive Pulmonary Disease
CP	Community Pharmacy
CRD	Centre for Reviews and Dissemination
CVD	Cardiovascular Disease/Coronary vascular disease
DARE	The Database for Abstracts of Reviews of Effects
DPP-4	Dipeptidyl Peptidase-4
DOH	Department of Health
DSN	Diabetes specialist Nurse
DUK	Diabetes UK
DiabMedSat	Diabetes Medication Satisfaction
EITQ (or EAITQ)	Expectations About Insulin Therapy Questionnaire
GLP-1	Glucagon-like Peptide -1
GP	General Practitioner
HbA1c	Glycated Haemoglobin
HBM	Health Belief Model
HCD	Health Care Delivery
HCT	Health Care Team
HP	Health Professional
HRQOL	Health Related Quality of Life
HSCIC	Health and Social Care Information Centre
IDF	International Diabetes Federation
IMD	Index of Multiple Deprivation
IQR	Interquartile Range
IWQOL-Lite	Impact of Weight on Quality of Life-Lite
MDT	Multidisciplinary team
MID	Minimal Important Difference
MMAS	Morisky Medication Adherence Scale
MRC	Medical Research Council
NHS	National Health Service
NICE	The National Institute for Health and Clinical Excellence

NSF	National Service Framework
OD	Once a day
OGD	Oral Glucose-lowering Drug
OWLQOL	Obesity and Weight Loss Quality-of-Life.
PCRN	Primary Care Research Network
PCT	Primary Care Trust
PITQ	Perceptions With Insulin Therapy Questionnaire
(or EWITQ)	(Experiences with Insulin Therapy Questionnaire)
PIS	Participant Information Sheet
PRISMA	Preferred Reporting Items for Systematic Reviews & Meta-Analysis
QDS	Four times a day
QOF	Quality and Outcomes Framework
RT	Research Team
SCDC	Secondary Care Diabetes Centre
SD	Standard Deviation
SGLT-2	Sodium-Glucose Co-Transporter 2
SE	Side effects
SEAMS	Self-Efficacy for Appropriate Medication Use Scale
SEAMS-UCU	SEAMS for Under Conditions of Uncertainty
SEAMS-UDC	SEAMS for Under Difficult Circumstances
SEM	Standard Error of Measurement
SIMS	Satisfaction with Information about Medicines Scale
SIMS-AU	SIMS- Action and Usage
SIMS-PPM	SIMS- Potential Problems of Medication
SMBG	Self-Monitoring of Blood Glucose
SPSS	Statistical Package for the Social Sciences
T1D	Type 1 Diabetes
T2D	Type 2 Diabetes
TDS	Three times a day
TRIM-Weight	Treatment Related Impact Measure of Weight
TRIM-Wt-DL	Treatment Related Impact Measure of Weight-Daily Life
TRIM-Wt-WM	Treatment Related Impact Measure of Weight-Weight Management
TRIM-Wt-PH	Treatment Related Impact Measure of Weight-Psychological Health
TZD	Thiazolidinedione
UK	United Kingdom
UKPDS	UK Prospective Diabetes Study
VIF	Variance Inflation Factor
WHO	World Health Organisation
WI	Weight Increasing
WN	Weight Neutral
WR	Weight Reducing

INTRODUCTORY CHAPTER

I. Introduction

Prevalence of Type 2 Diabetes [T2D] is increasing alarmingly and regarded as a major public health concern. In the United Kingdom [UK], currently, there are 3 million individuals who have been diagnosed with T2D. However, it is projected that by 2025 there will be 5 million in total with this condition (Diabetes UK [DUK], 2012). T2D is a complex heterogeneous and progressive disease associated with insulin resistance and obesity. Failure to control diabetes can lead to serious macrovascular and microvascular complications leading to great disability and premature mortality (DUK, 2012). Therefore, T2D requires management of a range of factors including blood glucose, blood lipids, blood pressure and body weight (Philippe & Raccah, 2009; Aicher et al., 2010; Lau, 2010).

In the UK, T2D is managed at both primary and secondary care level. Its treatment consists of lifestyle interventions and subsequently addition of glucose-lowering drugs (National Institute for Health and Clinical Excellence [NICE], 2009a). Although there are a number of medication treatments for T2D, many promote weight gain, which then adversely affects diabetes control. Hence, health care providers face a challenge in maintaining the balance between achieving normoglycaemia while simultaneously minimising hypoglycaemia and weight gain (Lau, 2010). Despite the effectiveness of glucose-lowering drugs in controlling hyperglycaemia (Turner et al., 1999; Inzucchi et al., 2012), there is limited information about patients' experiences and expectations of these drugs.

It is already known that T2D patients rarely fully comply with their medication regime (Cramer, 2004). A number of factors have been identified to explain lack of adherence to the medication regime, including; polypharmacy, complex dosing regimens, routines (or lack of) in medication behaviour, safety concerns, experiences with medications and complications, patient education and beliefs, social support, information about the prescribed medication, socioeconomic issues and ethnicity (Borgsteede, 2011; Bailey & Kodack, 2011). However, recent studies have suggested that fear of weight gain may also contribute to low adherence levels (Farmer et al.,

2006; Peyrot et al., 2009; Pi-Sunyer, 2009). To date, there have been few studies of T2D patients' expectations, beliefs and attitudes towards their diabetes medication, and their medication taking behaviour as a result of their medications' effects on their body weight. In addition, previous studies have not explicitly addressed how patients' beliefs and attitudes change over time as a result of taking their diabetes medications. Furthermore, there is little evidence of patients' experiences with medications through qualitative studies.

II. Purpose- Aims and Objectives

This study involves a mixed methodology and aims to address the following questions:

1. How do the expectations, beliefs and attitudes of people with T2D towards different diabetes treatments that either promote weight loss, are weight neutral or result in weight gain, change over time?
2. What is the impact of the change on patients' adherence to their medicine(s)?
3. What type(s) of intervention(s) promoting treatment options, focusing on effects on body weight, are acceptable to patients in order to increase their understanding of their diabetes treatment and improve adherence?

The subsequent objectives were formulated to consider the above research questions:

- Measure the change in patients' expectations, beliefs and attitudes towards glucose-lowering (and/or anti-obesity) drugs (including those with different body weight effects) prior to, during and after taking medicine(s) (where appropriate), within primary and secondary care using self-completed validated questionnaires. (Question 1)
- Explore in depth, using semi-structured interviews, the expectations, beliefs and attitudes towards these drugs (including those with different body weight effects) and associated lifestyle advice in a subsample of patients, and verify and compare the findings with the data from the above questionnaires. (Question 1)

- Investigate the relationship of these changes with patients' diabetes management (adherence) using self-completed validated questionnaires. (Question 2)
- Utilise integrated findings from the above questionnaires and interviews and the systematic review in chapter 2 to explore ideas for intervention(s) which promote understanding of diabetes treatment and adherence in patients with T2D. (Question 3)

Understanding patients' experiences, and how these change over time should help inform guidance on how to improve health care services for overweight and obese T2D patients in the National Health Service [NHS] and make the experiences of patients more positive. The development of this research programme is in line with the Medical Research Council [MRC] framework for developing complex interventions (MRC, 2008).

III. Thesis Structure

In *chapter 1*, T2D is outlined, focusing on the impact on people's health and the National Health Service. This chapter gives an overview of diabetes management interventions providing more detail on current pharmacological agents used for the treatment of T2D, their effectiveness on glycaemic control and their effects on body weight. This chapter also summarises current guidance on using glucose-lowering (and anti-obesity) drugs in the UK and outcomes of studies in primary care. In *chapter 2*, the central theme of the study, presents information from a limited area of research studies on patients' perspectives of drug use in long term conditions, with a focus particularly on T2D through a systematic review and identifies potential theoretical models in investigating such perspectives.

Chapter 3 describes the general methodology of this research programme starting with the aims and justification of the thesis. Detailed description of the study design, and information about group selection and sample size are also provided in this chapter. Also, this chapter provides a detailed account of the recruitment strategy, as well as ethical considerations and an outline of ethical approval and amendments.

Chapter 4 presents the validity and reliability of all data collection tools, as well as relevant pilot procedures and statistical and qualitative analysis conducted.

Chapter 5 provides the first results chapter based on questionnaire analysis and *Chapter 6* provides the second results chapter based on qualitative interviews analysis. The scope of the two result chapters is to answer the research questions as set out in chapter three.

Finally, in *chapter 7* all the data are brought together, informing the audience about the key issues emerged from the study in terms of expectations and experiences of patients taking glucose-lowering and/or anti-obesity drugs, as well as patterns of adherence. This chapter provides a discussion of key findings, underpinning theory, and recommendations. The strengths and limitations of the research study are covered here too. This *final chapter* concludes of the findings of this research and implications for health care services (primary and secondary care), and direction for future research.

CHAPTER ONE: TYPE 2 DIABETES

1.1 What is type 2 diabetes?

Type 2 Diabetes is a complex heterogeneous and progressive disease associated with insulin resistance and failure of the pancreas to produce sufficient insulin due to a gradual loss of beta-cell function resulting in chronic hyperglycaemia[1]. Insulin is a hormone that helps absorb glucose from the bloodstream, which then provides energy to the cells and body organs. Individuals with T2D can be undiagnosed for many years, and subsequently when they are diagnosed they have already lost 50% of their beta-cell function. Due to the progressive nature of T2D, individuals may only have 25% of their normal beta-cell function 6 years following diagnosis (UK prospective diabetes study [UKPDS], 1995).

Although hyperglycaemia in diabetes is associated with various symptoms, these often can be mild or ignored by individuals which leads to delayed diagnosis (Singh et al, 1992). Common symptoms include polydipsia (excessive thirst), polyuria, particularly at night, lethargy, weight loss, visual disturbance and genital irritation or thrush.

1.2 Causes and complications of T2D

Prevalence of T2D is increasing alarmingly and regarded as a major public health concern worldwide (International Diabetes Federation [IDF], 2013). In the UK, currently, there are 3 million people who have been diagnosed with T2D. However, it is projected that by 2025 there will be 5 million in total with this condition (DUK, 2012). In Merseyside, the prevalence of diabetes is close (3.87-4.99%) to the average prevalence for England (4.75%) (Health and Social Care Information Centre [HSCIC], 2013), and even higher in some areas. Type 2 diabetes is closely related to obesity[2] and it is estimated that up to 85% of individuals with T2D are either overweight or obese (DUK, 2012). In addition, obese people are more likely to develop T2D than those who maintain a healthy weight (DUK, 2005).

[1] Increased/excess plasma/blood glucose levels

[2] Overweight and obesity is a condition of excess body fat; where overweight is defined as a Body Mass Index [BMI] of 25.0kg/m² to 29.9kg/m² and obesity as a BMI of greater than 30.0kg/m² (WHO, 2000).

People with T2D are usually over the age of 40, although increasingly younger people are also being affected (Wilmot et al., 2010; IDF, 2013). Other determinants include family history and ethnicity (IDF, 2013). Failure to control diabetes can lead to serious macro and microvascular complications, such as heart disease, stroke, renal disease, retinopathy and neuropathy leading to great disability and premature mortality (DUK, 2012; IDF, 2013). Diabetes is also the leading cause of blindness and lower extremity amputations. Therefore, it requires the management of a range of factors including blood glucose, blood lipids and blood pressure (Philippe & Raccah, 2009).

Long term glycaemic control is monitored by measurements of glycated haemoglobin [HbA1c]; a gold standard measurement which provides a biological marker over a 2-3 month period (Hanas & John, 2010). Diabetes is regarded well controlled if HbA1c is below 6.5% (48mmol/mol) but for certain individuals a range between 7.0-7.5% (53-59mmol/mol) can be acceptable (NICE, 2009a; Inzucchi et al., 2012), particularly for those who find it difficult to achieve the target despite intensive self-management, education and glucose-lowering therapy.

A fundamental aspect of T2D management is to control not only hyperglycaemia in general but also pay attention to pre-prandial (before a meal) and post-prandial (after a meal) glucose levels. Evidence suggests that failure to control either of these will result in long term hyperglycaemia (HbA1c>8.0%, 64mmol/mol) and may directly increase the risk of cardiovascular events (Haffner, 1998; Stratton et al., 2000).

In addition, an increase in body weight in patients with T2D can have major adverse effects in the management of their condition leading to an increased risk of the aforementioned micro and macrovascular complications (Daousi et al., 2006; Dhaliwal & Welborn, 2009). Therefore, weight is considered as an important outcome for the management and delayed progression of diabetes (Aicher et al., 2010; Lau, 2010)

Evidence shows that a reduction in HbA1c by 10mmol/mol (1%) reduces the risk of microvascular complications by 37% and diabetes related deaths by 21% (Stratton et

al., 2000). In addition, a decrease of 5-10% of body weight is associated with significant reduction in diabetes, cardiovascular risk and mortality rates (Lau, 2010; Ross et al., 2011).

1.3 Impact and cost to NHS and patients

In recent years, there has been a shift in the management of T2D from secondary care to primary care, to potentially improve patient outcomes by encouraging patients to self-manage their condition (Liebl, Rutten & Abraira, 2010). The aim is to improve patients' quality of life and to reduce service costs (Department of Health [DOH], 1999).

However, the increasing prevalence of obesity and diabetes is generating additional cost and time pressures in primary care (Counterweight Project Team, 2005). This has implications for the NHS, as the cost of obesity and diabetes is escalating (DUK, 2012; NICE, 2009a), reaching almost £10 billion in 2011 for all aspects of diabetes care and projected to increase to £16.9 billion by 2035 (Hex et al., 2012). Over a 10 year period (1997-2007) primary care treatment costs for T2D increased considerably without an improvement in HbA1c (Currie, Gale, & Poole, 2010). The cost of prescribing glucose-lowering drugs alone has increased by £30 million from 2011 to 2012 (HSCIC, 2012). Evidence demonstrates that direct medical costs associated with the treatment of T2D are significantly higher for individuals with poor glycaemic control than those with optimal control (Gilmer et al., 1997) and such individuals are more likely to have increased hospital admissions further impacting the health service (Wagner et al., 2001; Jiang et al., 2003). It is apparent that after nine years since diagnosis of T2D, only a quarter of patients are able to control their diabetes with a single drug. Hence, most patients require combination therapy (oral glucose lowering drugs [OGDs] and/or insulin) within 5-10 years of diagnosis (Turner et al., 1999).

Self-management is the cornerstone of diabetes treatment, and is defined as the behaviours and skills that an individual employs on a daily basis to manage their diabetes (DUK, 2009; Shrivastava et al., 2013). Such behaviours include following a

healthy diet, participating in physical activity, quitting smoking, monitoring their blood glucose, screening of their eyes, looking after their feet, and body weight on a regular basis and adhering to their medicines' regime in order to prevent hyper- and where relevant hypoglycaemia[3] (Ismail, Winkley, & Rabe-Hesketh, 2004; Shrivastava et al., 2013). The behaviours and decisions employed are based on their knowledge, beliefs, attitudes, resources and support systems available to them (Longo et al., 2010; Nam et al., 2011).

These everyday tasks described above can be seen by patients as a burden (Vijan et al., 2005a; Vijan et al., 2005b), as T2D patients have to follow them for the duration of their life. This may lead to low self-efficacy and subsequently to suboptimal adherence to any or all of the above tasks (Grant et al., 2003; Agborsangaya et al., 2013) which then impacts on patients' well-being (Sacco et al., 2007).

Often individuals with T2D suffer from other comorbidities such dyslipidaemia, hypertension, depression and thyroid dysfunction, which requires them to take more medicines to control these conditions (Rubin, 2005; Huang et al, 2009). A suboptimal adherence to any of these tasks will have detrimental effects to their health and progression of diabetes and micro- and macrovascular complications (Kuo et al., 2003; Shrivastava et al., 2013), further impacting patients' physical and mental health well-being. Diabetes diagnosis, lifestyle adjustment, incidence of hypoglycaemia and onset of complications are associated with psychosocial problems (Cox & Gonder-Frederick, 1992). The presence of diabetes and obesity in an individual also significantly reduces health related quality of life [HRQOL] (Gough et al., 2009), in fact self-perception of weight gain without evidence of weight gain also impacts on HRQOL (Grandy, Fox, & Bazata, 2013). It is believed also that hypoglycaemia can cause psychological and physiological morbidity (Davis et al., 2005; Marrett et al., 2009).

[3] Hypoglycaemia is a state when the blood glucose levels fall below normal range (< 3.9mmol/l) (Bonds et al, 2010). Symptoms can be relatively minor such as sweating, hunger and anxiety or very severe such as behavioural changes, cognitive impairment, seizures and coma. Other symptoms include shakiness, dizziness, headache, pale skin colour, confusion/ feeling disoriented, clumsy/jerky movements, tingling sensations around the mouth and difficulty concentrating.

1.4 Management of T2D in UK

In the UK, NHS primary and secondary care are key providers of medical support and appropriate treatment for people with T2D. The UK government has made efforts to improve the quality of NHS services for patients with diabetes (DOH, 2004a). Diabetes has been identified as a priority for action with the National Service Framework [NSF] for Diabetes (DOH, 2001a). Furthermore, since 2004, primary care teams are financially rewarded to undertake specified clinical activities and achieve tight glycaemic and metabolic targets in patients under their care through the Quality and Outcomes Framework [QOF] (Campbell et al., 2007; Khunti et al., 2007). Such targets and standards have been recently emphasized within the document about quality standards for diabetes in adults by NICE (NICE, 2011[4]).

1.5 Lifestyle Interventions for T2D

The foundation of the management of T2D incorporates lifestyle modification including dietary and exercise strategies which are of most importance in order to maintain a healthy body weight and aid glycaemic control, as an integral component of diabetes self-management education (American Diabetes Association [ADA], 2008).

Dietary advice for people with T2D includes a healthy balanced diet. Although, specifically for diabetes, there is no certain advice on macronutrients or micronutrients, an emphasis on fibre rich foods (fruits, vegetables, whole grains, and legumes) and a reduction of foods high in saturated and trans fats is recommended for blood lipid lowering and reduction of cardiovascular risk (Van Horn et al., 2008). Guidelines also recommend to monitor carbohydrate intake through carbohydrate counting, exchanges, or estimation, as there is evidence that carbohydrate is the primary determinant of post-prandial blood glucose response (ADA, 2008; Franz et al., 2010). Furthermore, the glycaemic index, which measures how quickly a carbohydrate-containing food raises blood glucose levels, may be a helpful addition

[4] This NICE Quality Standard was updated in August 2016, however the PhD study was conducted between years 2011-2014, so the thesis is referring to the guidelines that were available at the time for health professionals and people with Type 2 Diabetes.

to carbohydrate counting. However, when the focus is on weight management, then a reduction of total energy intake is required rather than changing the source of energy in the diet (ADA, 2008; DUK, 2011).

Lifestyle interventions that entail diet, physical activity and behavioural interventions help with reductions in body weight by up to 1.7kg after one year (Norris et al., 2005). Physical activity interventions also have clear benefits on cardiovascular risk reduction and glycaemic control in people with T2D, showing an improvement of HbA1c by 0.6% (Thomas, Elliott, & Naughton, 2006).

1.6 Pharamacotherapy

Although lifestyle interventions are the first line of treatment of this condition, most people subsequently need sequential addition of glucose-lowering drugs (NICE, 2009a[5]). There are a number of medication treatments for T2D (see 1.6.1-1.6.10), however many promote weight gain, which then adversely affects diabetes control. Hence, one of the main challenges facing health care providers in diabetes management is maintaining the balance between achieving normoglycaemia while simultaneously minimising hypoglycaemia and weight gain that may negatively affect adherence to therapy and subsequent health outcomes (Lau, 2010).

There is clear guidance (NICE, 2006[6]; 2009a) for the pharmacotherapy management of obesity and T2D, using various algorithms following lifestyle interventions (diet, physical activity and behaviour modification), emphasising that when a drug is being recommended, health professionals [HPs] must offer advice and support to alter lifestyle and make lifelong changes (Nunes et al., 2009). In summary, NICE guidelines recommend a combination of metformin and insulin secretagogues (and/or Dipeptidyl peptidase-4 [DPP-4] or Sodium-Glucose Co-Transporter 2 [SGLT-2] inhibitors) in those who have inadequate blood glucose control with monotherapy

[5] The NICE guidance for newer agents for blood glucose control in T2D was replaced in July 2016 by the new NICE guidance NG28 titled "Type 2 diabetes in adults: management", however this PhD thesis refers to the old guidelines as explained in footnote 4.

[6] The NICE guidance about Obesity was last updated in March 2015 and as explained in footnote 4, the thesis refers to the old guidance.

(i.e. HbA1c≥6.5%, 48mmol/mol) (NICE, 2009a). Furthermore, a glucagon-like peptide -1 [GLP-1] analogue may be added to dual therapy to help with glucose control in the most severely obese patients with a Body Mass Index [BMI] greater than 35.0kg/m^2 with some exceptions if it is considered that weight loss will benefit other comorbidities. However, for those whom dual or triple therapy has been unsuccessful in terms of both glucose control (i.e. HbA1c≥7.5%, 59mmol/mol) and weight loss (i.e. <3% at 6 months), will move on to insulin.

Due to the progressive nature of T2D, treatment may include increasing the dose of OGDs and introduction of additional medicines either in oral or injectable form in order to achieve treatment goals (Turner et al., 1999; Nathan et al., 2009). Numerous studies have shown glucose-lowering drugs to be effective in controlling hyperglycaemia. Sections 1.6.1-1.6.10 describe the various available drugs for diabetes and their effects on glycaemic control and body weight including common side effects [SE]. Table 1.1 also gives an overview of each class of medicine for T2D that were available at the time of the PhD study.

Table 1.1: Overview of Medicines Prescribed for Type 2 Diabetes

Drug Class/ medicine	Regime	Taken	Impact on HbA1c %	Weight change (+ gain, - loss)	Side Effects
Biguanides (tablets)	Metformin: 500mg/850mg OD-TDS, 1000mg OD-BD Metformin ER: 500mg/ 1000mg/ 1500mg/ 2000mg OD	Up to three times a day, with meals	↓0.14% - 1%	Neutral	diarrhoea abdominal cramping, rare lactic acidosis
Sulphonylureas (tablets)	Glimepiride : 1-8mg OD Glipizide: 5-20mg OD-BD, Glipizide ER: 5mg/20mg OD Gliclazide: 40-160mg OD-BD Gliclazide ER: 30-120mg OD	Glimepiride: once daily shortly before or during breakfast or main meal Glipizide: Once or twice a day, shortly before a meal Gliclazide: Once or twice a day with main meals	↓1%	+3kg	hypoglycaemia
Glitazone (tablets)	Pioglitazone: 15-45mg OD	Once daily with or without food	↓1%	+3.9kg	oedema, bone fractures
Metiglinides (tablets)	Repaglinide: 0.5-4mg TDS Nateglinde: 60-120mg TDS	Three times per day, 10 - 30 minutes before meals	↓0.1%- 2.1%	+3kg	hypoglycaemia diarrhoea
AGI (tablets)	Acarbose: 50mg TDS	Three times per day, should be chewed with first mouthful of food, or swallowed whole with little liquid directly before the meal	↓0.14% -1%	Neutral	flatulence, stomach ache, diarrhoea
DPP-4 inhibitor (tablets)	Sitagliptin 100mg OD Saxagliptin 2.5-5mg OD Linagliptin 5mg OD Vildagliptin 50mg BD	Once daily, taken with or without a meal at any time of the day	↓0.6-0.7%	Neutral	Raised blood lipids raised, all cause infections (see 1.6.6), pancreatitis

GLP-1 agonists (injectables)	Liraglutide: 0.6/1.2/1.8mcg OD Exenatide: 5-10mcg BD Exenatide ER: 2mg Once weekly	Liraglutide: once daily at any time, independent of meals, but recommended to be injected around the same time each day Exenatide: Twice a day, at any time within the 60-minute period before the morning and evening meal, or two main meals of the day, approximately 6 hours or more apart Exenatide ER: Once weekly on the same day each week, at any time of day, with or without meals	↓~1%	-(2.3–5.5 kg)	nausea, diarrhoea, vomiting, pancreatitis
SGLT-2 inhibitor (tablets)	Dapagliflozin 10mg OD	once daily, at any time of day, with or without food	↓0.5-1%	- 4.5kg	Urinary, genital infections
Insulin (injectables)	Human Insulin and Insulin Analogues No dose limit	Varies from once daily at the same time each day with or without a meal (Detemir/ Glargine), up to three times a day immediately before a meal (rapid acting insulin aspart/intermediate acting isophane insulin) or twice daily immediately before a meal (rapid and intermediate acting insulin aspart/ soluble and isophane insulin)	↓1.5-2.5% (as additional therapy)	+6.5kg	hypoglycaemia
GI Lipase Inhibitor (Tablets)	Orlistat 120mg TDS	Three times a day, with water immediately before, during or up to one hour after each main meal. Dose should be omitted if a meal contains no fat	↓0.74%	-3kg	fatty/ oily stool, ↑defecation, faecal incontinence

Details taken from a) Summary of Product Characteristics for individual drugs retrieved June 2013 from http://emc.medicines.org.uk and b) references in sections 1.6.1- 1.6.10. Regime: OD/BD/TDS/QDS refers to “once”/“twice”/ “three”/“four” times per day as a direction for prescriptions.

1.6.1. Biguanides

Metformin is a highly effective first line glucose lowering drug for managing T2D. It is a biguanide that reduces hepatic glucose output, increases insulin sensitivity and uptake, and utilises glucose by peripheral tissues (Saenz et al, 2005). Its effectiveness was established through the UKPDS trial (UKPDS, 1998), where intensive treatment over a median duration of 10.7 years significantly reduced diabetes related outcomes and all-cause mortality. When metformin is compared with other glucose-lowering medicines and dietary interventions, the reductions in HbA1c range from as little as 0.14% up to 1% (Saenz et al., 2005; Qaseem et al., 2012). Exceptions to this are drugs like metiglinides, alpha-glucosidase inhibitors and insulin. However metformin has an advantage over these drugs due to its neutral effect on body weight (UKPDS, 1998; Saenz et al., 2005); an important consideration for T2D individuals who are overweight or obese. In addition, metformin has less risk of hypoglycaemia (Saenz et al, 2005). Yet, metformin is associated with gastrointestinal side effects such as diarrhoea, and abdominal cramping, which can lead to discontinuation of the drug for a small percentage of individuals (Chacra, 2014). On the other hand, newer drug formulations such as Extended Release Metformin (Metformin MR), appear to be better tolerated and dose frequency is reduced to once a day compared with standard metformin [up to 3 times per day] (Chacra, 2014).

1.6.2 Sulphonylureas

Sulphonylureas are the oldest drugs in the treatment of T2D but second (gliclazide, glipizide) and third (glimepiride, gliclazide MR) generations of this class of medicines are now more commonly used (Hemmingsen et al., 2013). They are very effective at reducing HbA1c levels by up to 1% as monotherapy (Hemmingsen et al., 2013) or in combination with other medications (Bennett et al, 2012). They stimulate insulin secretion from beta-cells in pancreas and, therefore, there is an increased risk of hypoglycaemia with this treatment (Hemmingsen et al., 2013). Intensive treatment with this class of medicines has been associated with weight gain by about 3kg at 10 years (UKPDS, 1998). However third generations of sulphonylureas appear to be associated with less weight gain than second generations (Mitri & Hamdy, 2009) and there is significantly lower incidence of hypoglycaemia (Wang et al., 2011). Similarly

with biguanides, the extended release forms of sulphonylureas daily dose is reduced to once a day instead of twice a day.

1.6.3 Thiazolidinediones (or Glitazones)

Thiazolidinediones [TZDs] are peroxisome proliferator activated receptor γ (PPAR-γ) activators that improve insulin sensitivity in skeletal muscle and reduce hepatic glucose production (Inzucchi et al., 2012). Pioglitazone is the only drug in this category available for prescription for T2D. This drug is associated with increase in body weight (up to 3.9kg) as monotherapy or in combination with other glucose-lowering drugs (Richter et al., 2006; Mitri & Hamdy, 2009) and increased risk of oedema and bone fractures, but does not increase the risk of hypoglycaemia (Richter et al., 2006, Inzucchi et al., 2012). Its effect on HbA1c is similar to those other OGDs (~1%) (Richter et al., 2006; Qaseem et al., 2012), with an advantage that it requires a single daily dose.

1.6.4. Meglitinides

Meglitinides are short-acting insulin secretagogues that enhance insulin synthesis and release. Two analogues are currently available for clinical use: repaglinide and nateglinide and both are used as monotherapy or in combination with metformin, TZDs or long-acting insulin (Landgraf, 2000; Black et al., 2007). The range of HbA1c reductions from these drugs is between 0.1-2.1% depending on the brand (Black et al., 2007). Meglitinides generally cause weight gain by up to approximately 3kg either as monotherapy or in combination with metformin or insulin and most common adverse events include hypoglycaemia and diarrhoea (Black et al., 2007). The dose for this class of medicine is taken typically three times per day.

1.6.5 α-Glucosidase Inhibitors [AGI]

In most guidelines, this type of drug is rarely frequently used for T2D patients (Innunchi et al., 2012; NICE, 2009a). Acarbose is the most common drug in this category that is prescribed (Van de Laar et al., 2005) and it is used as an addition to other drugs when treatment goals are not met, or in case of contra-indications for

other medications. Its main action is to inhibit the alpha-glucosidase enzyme in the small intestine and therefore delay gut carbohydrate absorption (Inzucchi et al., 2012). This inhibits postprandial glucose peaks thereby leading to decreased postprandial insulin levels (Van de Laar et al., 2005). Due to its mode of action, abdominal discomfort like flatulence, diarrhoea and stomach ache are the most frequently occurring adverse effects but it does not cause hypoglycaemia (Van de Laar et al., 2005; Inzucchi et al., 2012). Alpha-Glucosidase Inhibitors reduce HbA1c by up to 0.8% but they have no significant body weight effects (Van de Laar et al., 2005). Acarbose has a single dose which is taken three times per day.

1.6.6 Gliptins (DPP-4 inhibitors)

Dipeptidyl peptidase-4 inhibitors improve glycaemic control by preventing rapid degradation of the incretin hormones, gastric inhibitory polypeptide [GIP] and in particular glucagon-like peptide -1 [GLP-1] by the enzyme DPP-4 (Inzucchi et al., 2012; Deacon, 2011). There are four approved DPP-4 inhibitors in the global market, sitagliptin, vildagliptin, linagliptin and saxagliptin (Deacon, 2011; Traynor, 2011). Alogliptin was the latest drug in this class to be approved after the completion of this PhD study. Gliptins are available in the form of oral tablets and are taken once a day in a single dose, with the exception of Vildagliptin which is taken twice per day. They are very effective in reducing HbA1c between 0.6-0.7% similarly to other glucose lowering drugs (Deacon, 2011; Inzucchi et al., 2012), although there is evidence that metformin is more effective than DPP-4 in reducing HbA1c by up to 0.5% more than DPP-4 inhibitors (Bennett et al., 2012). On the whole, these drugs are well tolerated with some of the drugs associated with all cause infections (e.g. nasopharyngitis, gastroenteritis, upper respiratory tract infection, urinary tract infection), but their effect on body weight is neutral and there is no risk of hypoglycaemia (Richter et al., 2008; Goke et al., 2010; Gallwitz et al., 2012).

1.6.7 Incretin mimetics GLP-1

The GLP-1 receptor agonists mimic the action of endogenous GLP-1 (a gut hormone that is secreted from the intestine in response to food ingestion), in stimulating glucose-dependent insulin secretion and by suppressing glucagon secretion, thereby

improving glucose homoeostasis. Gastric emptying is delayed, especially in the early weeks of therapy, resulting in appetite suppression and thus loss of body weight (Inzucchi et al., 2012). These drugs are injectable and there are three drugs available on prescription; Exenatide (twice daily injection), Liraglutide (one daily injection) and Exenatide extended release (once weekly injection). These drugs are associated with nausea, diarrhoea, and vomiting, which appear to subside after the first weeks of treatment in most cases (Shyangdan et al., 2010; Vilsbøll et al., 2012). Nevertheless, GLP-1 drugs have favourable outcomes in regards to weight loss (around 2.3–5.5kg in bodyweight), they lower HbA1c by up to 1%. (Shyangdan et al., 2010, 2011) and they do not increase the risk of hypoglycaemia (Vilsbøll et al., 2012). After the PhD study was completed, three further drugs became available; lixisenatide, dulaglutide and albiglutide.

1.6.8 Sodium-Glucose Co-Transporter 2 [SGLT-2] Inhibitors

Dapagliflozin is a SGLT-2 inhibitor that blocks the reabsorption of glucose in the kidneys and promotes excretion of excess glucose in the urine. At the time of conducting this PhD study, it was the only drug in this class available on the NHS (NICE, 2013), but canagliflozin and empagliflozin have subsequently also been approved. It comes in the form of a tablet and it is taken once a day. Dapagliflozin reduces HbA1c by about 0.5-1% and contributes to weight loss of up to 4.5kg (Clar et al., 2012). Although there appears to be a slight increase in urinary and genital tract infections with this treatment, there is no risk of hypoglycaemia (Clar et al., 2012).

1.6.9 Insulin

Insulin therapy is the most effective treatment in T2D when all other glucose-lowering agents begin to fail, achieving 1.5-2.5% reduction in HbA1c as an additional therapy to OGDs (Nathan et al., 2006; Goudswaard et al., 2004). Compared with human insulin (NPH), insulin analogues have either delayed and prolonged absorption called long acting or basal insulin (insulin glargine and insulin detemir), or act relatively faster and absorbed rapidly after injection called short acting insulin (insulin lispro, insulin aspart, and insulin glulisine). These analogues can be used either alone (basal insulin) or in combination (basal bolus – injection up to 4 times

per day or premixed insulin- injection twice per day) to mimic a relatively normal physiological insulin profile of low constant secretion of insulin (basal) as well as short bursts of insulin release in response to meals (bolus) (Hermansen & Mortensen, 2007). The choice of insulin in T2D depends on the individual; generally is related to HbA1c values, the pre and post prandial glycaemic control, the age of the individual and the risk of hypoglycaemia as well as the risk of weight gain and adverse outcomes associated with these (Lavernia, 2011). Evidence suggests there is no difference between human insulin and long–acting analogues in relation to metabolic control (i.e. HbA1c), however long acting insulin analogues have significantly lower rate of overall and nocturnal hypoglycaemia (Horvath et al., 2007). Although most individuals start with low doses of insulin, these can considerably increase if hyperglycaemia persists (Inzucchi et al., 2012). Insulin has long been associated with increased risk of hypoglycaemia and most preparations induce weight gain of 6.5kg on average (Holman et al., 2008).

1.6.10 Orlistat

Orlistat is the only anti-obesity drug currently for the treatment of obesity on the NHS (NICE, 2006). Orlistat frequently is used in patients with T2D to help with weight loss. Orlistat is a gastrointestinal lipase inhibitor that reduces the absorption of dietary fat by about 30%. In combination with a hypocaloric diet, it has shown to produce a 3kg weight loss greater than placebo, therefore it is an important aid in losing and maintaining weight (Torgerson et al., 2004). Moreover, it can improve glycaemic control by decreasing HbA1c by 0.74% in patients with T2D with or without weight loss (Hollander et al, 1998, Jacob et al, 2009). However, its widespread use is limited by adverse effects such as fatty/oily stool, increased defecation and occasional faecal incontinence (Wittert, Caterson & Finer, 2007; Padwal & Majumdar, 2007), which generally are associated with increased dietary fat. Also after the discontinuation of this medicine weight gain could be expected (Halpern & Mancini, 2003). Orlistat comes in the form of a tablet which is taken three times per day with meals.

1.7 Summary and Future Medication and Management of T2D

In summary, changes to medications take place often in T2D and could therefore affect adherence levels, beliefs, attitudes and quality of life. On average, any second agent added to an individual's diabetes therapy is typically associated with an approximate further reduction in HbA1c of 1% (11mmol/mol) (Inzucchi et al., 2012). However, the effects of current glucose-lowering drug treatments on body weight vary markedly between classes (Campbell, 2010), with sulphonlyureas, pioglitazone and insulin causing weight gain; biguanides, DPP-4 inhibitors and acarbose being weight neutral and only incretin mimetics, SGLT-2 inhibitors and orlistat having favourable outcomes on body weight. An increase in our understanding of the physiological control of energy balance and the pathophysiology of obesity and diabetes will hopefully lead to the development of newer drugs that are better tolerated and more efficacious in diabetes and weight management (Salem & Bloom, 2010). As more drugs become available, a more complex combination of pharmacotherapy is likely to be adopted, possibly alongside shifting dosing schedules, to overcome adverse effects and promote weight loss and blood glucose control in patients with diabetes (Wilding, 2007; Aicher et al., 2010; Salem & Bloom, 2010).

Despite the emphasis on the long term control of diabetes, evidence shows that in 2008/2009, 67% of people with T2D achieved a recommended HbA1c of less than 7.5% (IFCC HbA1c 58mmol/mol) (NICE, 2009a). Generally, one in ten of the population has glycaemic control over 10% (≥86mmol/mol) (Khan et al., 2011). Furthermore, the National Diabetes Audit (HSCIC, 2016) showed that large proportions of patients with diabetes continue to have poor glycaemic (34%), blood pressure (26%), and cholesterol (23%) control, with only 41% of patients achieving all the above targets.

It is well known that T2D patients rarely fully comply with their medication regime whether it is with oral tablets or insulin injections (Cramer, 2004). Patients are generally reluctant to take medicines and would prefer to take as few as possible (Pound et al., 2005). Although a number of factors have been explored related to

non-adherence and very poor glycaemic control (Khan et al., 2011), little is known about individuals' expectations, beliefs and attitudes towards their blood glucose-lowering drugs, particularly in relation to body weight effects.

Non-adherence amongst patients with diabetes has been associated with concern about weight gain (Peyrot et al., 2009). Since weight gain is a common side effect of most diabetes medicines, it can be problematic for individuals with T2D as most of them will be overweight prior to starting glucose-lowering drugs. Also, it is unknown how individuals' past experiences with glucose-lowering treatments and body weight effects may affect adherence with current and newer drugs on the market. Therefore, it is imperative that HPs understand patients' experiences with their diabetes medications in order to provide responsive health care services within the NHS to meet patients' needs, improve quality of life and minimise costs.

CHAPTER TWO: SYSTEMATIC REVIEW OF QUALITATIVE RESEARCH

2.1 Background

As described in the previous chapter; T2D is now considered a major global public health problem with over 80% of patients with this condition in the UK being either overweight or obese (DUK, 2005). Long term hyperglycaemia (HbA1c>8.0%, 64mmol/mol) and weight gain above a healthy weight can increase the risk of disabling secondary complications such as retinopathy, neuropathy, coronary vascular disease, and cerebrovascular accident. Weight management is, therefore, important in managing T2D along with managing blood glucose control, blood lipids and blood pressure (Philippe & Raccah, 2009).

Despite the availability and effectiveness of a number of glucose-lowering drugs for the management of diabetes, systematic reviews have shown that patients with T2D rarely adhere to their medication (Cramer, 2004; Krass et al., 2015) and currently, there are no effective interventions that consistently support and improve adherence in this group of patients (Haynes et al., 2008; Vermeire et al., 2009; Sapkota et al., 2015).

Compliance and adherence are often synonymously used in the literature with apparently little consensus of meaning and appropriate usage. However, 'adherence' describes the extent to which a person's behaviour, in this case taking medication, corresponds with agreed recommendations from a health care provider (WHO, 2003). This term is used as it suggests that patients are actively participating in their care and agree to recommendations provided. The consultation process that results in agreement between the patient and the health provider (shared-decision making) is termed concordance (Hearnshaw & Lindenmeyer, 2005). Both adherence and concordance terms are in line with the increase in patient autonomy and self-management of diabetes and their active involvement in decision making processes. However, the term adherence is specifically focused on patient behaviour. In recent years, two additional terms emerged in the literature which describe the extent which patients intentionally or unintentionally adhere to their medication regimens (Hearnsahw & Lindenmeyer, 2005). That is when a patient makes a specific decision not to take the prescribed medication (intentional) or when a patient does not take

the medicine as a result of forgetting, misunderstanding the medication regime or other psychosocial factors (unintentional). Nevertheless, patterns of adherence can be determined as early as at the point of prescription. It has been suggested that the first year of medication therapy is critical as up to 50% of patients will fail to take at least 80% of their medication doses; hence "new users" will almost certainly have lower levels of adherence than "experienced users" (Blackburn et al., 2013). Blackburn et al (2013), defines three types of non-adherence levels that appear in the first year of therapy; primary non-adherence (receives prescription but fails to obtain medication); non-persistence (begins to take medication but later stops taking it altogether) and poor execution (continues to take medication but fails to take the recommended quantity consistently). Regardless of types of adherence, this medicine taking behaviour is complex and multifactorial (Vermeire et al., 2001) particularly in diabetes (Hearnshaw & Lindenmeyer, 2005; Blackburn et al., 2013). It has implications for patients as it may mean a lost opportunity for health gain (Horne & Weinman, 1999) or more rapid disease progression which risks further more intensive medical intervention, alongside the financial burdens this can impose on health care budgets.

Many systematic reviews have been conducted which have explored patients' views of their medicines or medication adherence. These are either based solely on qualitative or quantitative research or have a mixed methods approach. A qualitative synthesis of Pound et al. (2005) explored patients' views of medicines in general showing that patients are usually reluctant to take medicines and would prefer to take as few as possible. This review did not include any papers with individuals on T2D medicines.

However, other reviews are specific to diabetes. Campbell et al. (2003) used a qualitative synthesis through a meta-ethnographic approach about individuals' experiences of diabetes and diabetes care. They argued that people have to go through critical stages and overcome obstacles to managing their diabetes effectively and to achieving a degree of balance and control. Most importantly it appeared that the approach to life balance was characterised by a "strategic non-compliance" which

involved monitoring of symptoms and manipulating diet and medication regimes in order to live life as fully as possible rather than restricting social and work activities. This review included patients with both Type 1 Diabetes [T1D] and T2D. It also included only the first 7 papers (10 original) that met their criteria due to time limitations and therefore, this synthesis may not fully represent diabetes patients' experiences of their condition, nor does it assess any changes in experiences with diabetes care over time.

Gomersall et al. (2011) attempted to synthesise qualitative and mixed methods research on patient perspectives on self-management of T2D in the first 10 years of the 21st Century. The synthesis uncovered multiple, complex and competing factors that influence self-management of diabetes including interpersonal relations, gender and sociocultural context. Similarly, a systematic review by Nam et al. (2011) identified several barriers to T2D management including adherence, beliefs, attitudes, knowledge, ethnicity/culture, financial resources, comorbidities, and social support. These two reviews did not focus only on medication taking behaviour but on all other aspects of self-management including self-monitoring of blood glucose [SMBG], physical activity, healthy eating, and regular foot examination.

A meta-analysis by Gherman et al. (2011) investigating the association between diabetes related beliefs and adherence to diabetes regimens, revealed that people who are more adherent to self-care behaviours are more confident that they can perform these behaviours as recommended (e.g. taking medication), they expect to achieve relevant and meaningful benefits, and they intend to engage in such behaviours. The opposite is true for those individuals who are less adherent, they are more likely to perceive barriers to adherence, are less confident in dealing with these barriers, worry about medication side effects and have negative attitudes towards insulin. However, this review included studies of both T1D and T2D as well as one study in gestational diabetes. Furthermore, many of the papers included in the analysis did not report type of diabetes treatment, for example whether on diet alone, OGDs, or injectable medication.

Two systematic reviews were also undertaken in relation to diabetes medication adherence. Odegard and Capoccia (2007) identified common barriers to medication adherence for both oral and injectable (insulin) glucose-lowering drugs such as regimen complexity (more than 1 diabetes drug/frequency of daily dosing), remembering doses, obtaining refills and depression. Peeters et al. (2011) identified factors that may influence adherence to OGDs such as demographic, disease-related, treatment-related, socio-economic and cultural factors. However, these reviews were combined for people with T1D and T2D (Odegard & Capoccia, 2007), or for people with T2D but from different ethnic groups other than those of Caucasian background (Peeters et al., 2011). The latter review also indicated that there is an unclear picture of medication adherence in different ethnic groups in part due to: measurements of ethnicity and adherence, diversity of settings, study designs, and drugs used in the studies they reviewed. Furthermore, neither of these systematic reviews explored patients' views on their perceptions of their adherence levels to their medicines.

Majeet-Ariss et al. (2013) employed a mixed-method systematic review (but mostly qualitative research) on self-management of black and ethnic minority [BME] patients with T2D. The review identified specific themes on medication adherence and insulin use. They described that most patients recognised the importance of taking medication correctly but motivation varied and some would reduce doses if they felt well. This particular BME group also appeared to worry about western medicines' side effects, long-term health implications and often discussed alternative remedies. Furthermore, there appeared negative perceptions and stigmatisation with use of insulin, particularly due to its injectable form. Participants viewed insulin as symbol of severity and further complications of their diabetes. However, there were participants for whom, following experiences of taking insulin, they felt that it helped control their symptoms and had better quality of life and that insulin worked faster than oral medicines. Nevertheless, the review was limited to papers published between 1986 and 2008, it excluded those of Caucasian background, and included participants from a wide range of backgrounds and countries thereby synthesising factors that might not be relevant or appropriate for all countries.

A mixed methods systematic review by Wang and Yeh (2012), focused on T2D insulin therapy. It suggested that there is a psychological resistance to insulin involving both processes of cognitive appraisal and negative emotional reactions for individuals. Due to the approach of this review, a small number of papers were included which were assessing or developing a tool around resistance to insulin or willingness to take insulin. From these studies, one paper included both T1D and T2D patients, another did not specify in their methodology whether patients had T1D or T2D and the third included participants with T2D treated with diet only.

A systematic review by Polinski et al. (2013) specifically looked at barriers to insulin initiation and intensification for patients with T2D and explored whether barriers differ from those individuals who were insulin-naïve or insulin-experienced. Seven articles in total were identified in this review; however these were all cross-sectional surveys using self-report questionnaires (with validated and non-validated scales) or discrete choice experiments (Jendle et al., 2010). The review showed that those individuals with prior experience in taking insulin had less barriers related to injections and the burden of insulin progression than those who were insulin-naïve. Those who were insulin-experienced were more concerned with side effects, glycaemic control, weight gain, and hypoglycaemic events of insulin treatment than with the need for injections. However, this review included three studies which recruited both T1D and T2D patients and one study which excluded anyone below 30yrs of age with the assumption that they will have T1D. Furthermore, the authors reported that the methodological rigor of the studies included was low.

Another systematic review by Purnell et al. (2014) synthesised evidence of T2D patients' preferences for non-insulin diabetes medications (oral and injectable). The review revealed that patients' preferences are driven by their medications' ability to support weight loss or control, as well as blood glucose control when compared with treatment burden and side effects. Additionally, gastrointestinal effects were also ranked by patients in this review as more important than hypoglycaemia. The review included ten cross-sectional studies using methods of discrete choice experiments, trade off exercises (Jendle et al., 2010), standard gamble (Boye et al., 2011) and

surveys, for which most of them did not focus on specific medications, or used hypothetical scenarios. Only one study compared patient preferences between liraglutide and exenatide (GLP-1 agonists), drugs which both result in weight loss but can have unpleasant gastrointestinal side effects (Shyangdan et al., 2010; Vilsbøll et al., 2012). The authors also reported their exclusion criteria but did not report whether they excluded studies with T1D patients, neither did they report the treatments patients were prescribed (diet therapy, oral or injectable glucose-lowering drugs) and whether their analysis considered patients' prior experiences with diabetes medications.

One more recent qualitative meta-synthesis by Brundiisini et al. (2015) focused on T2D patients' and HPs' perspectives on medication non-adherence. They identified seven categories that influence adherence: (1) emotional experiences as positive and negative motivators to adherence, (2) intentional non-compliance, (3) patient-provider relationship and communication, (4) information and knowledge, (5) medication administration, (6) social and cultural beliefs, and (7) financial issues. However, the authors did include all the data from three papers with both T1D and T2D patients as they could not distinguish which data came from T2D patients only.

In summary, this critical review has shown that although there are many reviews that describe diabetes patients' barriers to medication adherence and self-management, many of them are focused on both types of diabetes, despite some of them claiming that their review was on T2D only. While, Brundiisini et al.'s (2015) meta-synthesis focused on patients' perspectives of medication non-adherence, they included all articles that met their criteria without carefully appraising the research prior to inclusion. Many of the studies in these reviews; whether qualitative or quantitative, did not explore patients' barriers to medication adherence over time and how their views or attitudes are changed by their experiences of taking medication for diabetes. Qualitative research focuses on the person and their lived experiences as well as exploring the meanings people attach to these experiences. Yet, this critical review found a limited number of qualitative syntheses with focus on T2D individuals and their experiences with their diabetes medications.

Furthermore, the latest literature search was conducted up to August 2013 (Brundiisini et al., 2015). Medication adherence and particularly non-adherence is a timeless topic that concerns everyone; both patients and HPs, due to its implications to health and health care. Research on medication non-adherence is on-going, especially as the array of medications for treating T2D is increasing. Therefore, since 2013, there are more published research papers that have the potential to illuminate further on T2D patients' experiences and views of their medications. In addition, of those reviews which focus on diabetes medicines, only one review (Purnell, et al., 2014) considered studies with injectable treatments other than insulin, but this focused on patients' preferences to these treatments looking at specific pre-defined attributes and did not describe patients' experiences with these kinds of treatments. The experience of receiving insulin, a drug that results in weight gain, compared to other injectable treatments, such as GLP-1 agonists which promote weight loss, can be fundamentally very different despite similar clinical outcomes (Reaney et al., 2013; Ostenson et al., 2013). It is unclear how acceptable are to patients treatments such as GLP-1 agonists or other diabetes treatments that either promote weight loss or are weight neutral when considering the associated side effects with each treatment. Therefore an up-to-date search is justified given that there is a gap in relation to a systematic review qualitatively investigating only T2D patients' lived experiences and individual perspectives of their diabetes medicines including oral medicines, as well as all forms of injectable medicines.

This systematic review aims to fill this gap by addressing the following research questions:

1. How do people with T2D view their glucose-lowering and/or weight loss medicines?
2. How do people's views towards their diabetes/weight loss medicines affect their adherence levels or medicine taking behaviour?
3. Do the effects of these drugs on glucose control and body weight affect peoples' perceptions and adherence levels or medicine taking behaviour?
4. What theoretical perspectives have been used to study beliefs, attitudes and behaviour towards these medicines?

To answer these questions, the review focuses on the following aspects:

- Beliefs and attitudes about relevant medications for diabetes and overweight/obesity.
- Expectations and perceptions about relevant medications prior to, during and after taking these medicine(s) in relation to their diabetes management
- Adherence behaviours including intentional or unintentional non-adherence to medications and reasons why
- Types of research designs and theoretical perspectives used to study the above

The purpose of this review is to identify areas for future research and practice including informing empirical research exploring the personal experiences of adults with T2D; and identifying appropriate interventions to improve adherence to treatment for T2D patients self-managing their condition. This systematic review forms the basis of the development of this PhD study which is in line with the Medical Research Council [MRC] framework for developing complex interventions (MRC, 2008)

2.2 Methods

2.2.1 Design

As the focus was to identify only qualitative empirical research, a meta-synthesis review of the literature was undertaken based on the meta-ethnographic approach as described by Noblit and Hare (1988) which was later adopted by Britten et al. (2002), Campbell et al. (2003) and Pound et al. (2005). The subsequent adaptations to this approach were all related to medicine taking and/or diabetes management and are therefore highly relevant to this review. Meta-ethnography involves induction and interpretation, and translating individual studies into one another, whilst allowing the researcher to use metaphors or concepts across the studies in a way that illuminates understanding of the phenomenon under review. The aim is to develop a new interpretation and conceptual insight (Noblit & Hare, 1988). The translations can be literal or idiomatic, and the meaning(s) of the text can be preserved. Therefore the original interpretations and explanations in the studies can

be used as data in the synthesis and studies included can relate to one another in three ways: (i) directly comparable as reciprocal translations; (ii) oppositional to one another as refutational translations, or (iii) taken together to represent a line of argument. Noblit and Hare (1988) outlined a seven step process for conducting a meta-ethnography as shown in Table 2.1.

Table 2.1 Seven Steps for conducting meta-ethnography (Adapted from Noblit & Hare, 1988 and Campebell et al., 2011)

Seven steps of Meta-ethnography		Description of each step	Reference to sections
1	Getting started	Identifying topic that qualitative research will inform	Research Questions of Systematic Review and Section 2.2.2
2	Deciding what is relevant	Selecting research relevant to the topic of interest, Set inclusion and exclusion criteria	Section 2.2.3, Tables 2.3-2.4
3	Reading the studies	Critical appraisal of retrieved studies, Repeated reading of studies and noting metaphors and initial extraction of data from papers	Sections 2.2.4-2.2.5, Table 2.5
4	Determining how studies are related	organising papers into medicine groups, creating a list of metaphors, key phrases, concepts for each account	Table 2.6, Section 2.2.6
5	Translating the studies into one another (reciprocal or refutational)	The metaphors and/or concepts in each account are compared with other accounts (one-level synthesis), first within medicine groups and then across groups, initial production of medicine maps	Section 2.2.7, Figures 2.2-2.3
6	Synthesising translations (line of argument synthesis)	Analysing competing interpretations to produce a new interpretation/ conceptual development (second-level of synthesis), initial production of final model	Section 2.2.7, Figure 2.4
7	Expressing synthesis	Communicating and presenting synthesis taking into account intended audience-use concepts and language understood	Section 2.4, Figures 2.2-2.4

2.2.2 Search Strategy

An effective combination of search terms was defined based on the research questions and included: *Type 2 Diabetes, Medication Taking, Treatment, Medication, Oral Hypoglycaemic Drugs/Agents, Insulin, Adherence, Compliance, Beliefs, Attitudes*, and *Weight*. A broad and specific approach was used to identify appropriate qualitative studies. Pound et al. (2005) suggested that either method can be used, indicating that the broad search they used was as efficient as the detailed one, with a higher sensitivity in some of the databases such as CINAHL. Electronic databases were searched for relevant articles until February 2016. Databases included Cochrane Library (via Cochrane Library 1985 to 12/February/16), DARE/CRD/NHS[7] (via www.crd.york.ac.uk/ all dates to 12/February/16), PROSPERO (via www.crd.york.ac.uk/PROSPERO all dates to 12/February/16), Web of Science (via Web of Knowledge 1900 to 12/February/16), Scopus (via SCOPUS and Science Direct all years to 12/February/16), PsychINFO/ Articles (via EBSCO 1924 to 12/February/16), CINAHL Plus (via EBSCO 1937 to 12/February/16), MEDLINE (via Ovid 1946 to 12/February/16), EMBASE (via Ovid 1946 to 12/February/16), AMED (via EBSCO 1924 to 12/February/16). References of all retrieved articles were checked for relevant studies, and experts/authors were contacted for advice, and to collect further information that may have not been provided in the original published article. Appendix 2.1 shows a detailed description of the search terms and combinations. Table 2.2 shows the number of articles retrieved from each search engine as well as the number of titles and abstracts screened. Additionally, articles already known by the researcher which were potentially relevant for this synthesis were included in the list of articles to be screened, even though they were not identified by the above search. It is well known that there are still deficiencies in the indexing of studies and in the study filters of search engines, therefore additional techniques are required to ensure a comprehensive search for identification of relevant articles for a systematic review (CRD, 2008).

[7] DARE stands for The Database of Abstracts of Reviews of Effects and CRD stands for Centre for Reviews and Dissemination. PROSPERO is an international prospective register of systematic reviews.

Table 2.2: Engine Search and number of articles screened

	Articles Retrieved (excluding duplicates) February 2016	**Titles/Abstracts screened February 2016**
Cochrane Library	235	99
DARE/NHS/CRD	199	195
PROSPERO	75	75
Web of Science	965	608
Scopus	2262	1971
PsychINFO/Articles, CINAHL Plus, AMED (via EBSCO)	803	735
MEDLINE, EMBASE (via Ovid)	3017	1454
Researchers list of articles	12	12
Total	7556 +12	5137 + 12

NB: When all databases combined in EndNote X5 there were 2419 duplicates.

2.2.3 Selection and eligibility of studies

Studies were selected if the population was adult (>18yrs) living with T2D and using pharmacological therapy to manage their diabetes and weight. All types of study designs were included if they reported qualitatively medication taking behaviour or, beliefs or attitudes towards diabetes and weight loss medicines. Qualitative data reported in mixed methods studies were also included. Only literature published in the English language from inception to February 2016 was included. Table 2.3 shows in detail the inclusion and exclusion criteria for this review and Table 2.4 shows the reasons for exclusion of the articles retrieved.

Table 2.3: Inclusion and Exclusion Criteria

	Inclusion Criteria	**Exclusion Criteria**
Population	Adults with T2D over 18 years of age	Studies based on T1D and T2D participants unless sub-group analysis presented by type of diabetes Gestational diabetes
	Treated with glucose-lowering drugs and/or anti-obesity drugs	Treated with: - Diet therapy only - Bariatric surgery
Setting	Managed by primary care or community or outpatient clinics in a secondary care setting (hospital)	Inpatients/patients admitted to hospital

	UK based studies	Other countries unless multinational and sub-group analysis was done by country
Focus	Participants' medication taking personal perspectives and/or behaviour (adherence)	- Health professionals (or other than patients) beliefs or attitudes - Reporting prevalence of non-adherence
Study Design	Qualitative Mixed Method Studies (including only qualitative data) Existing systematic reviews/ qualitative syntheses	RCTs Observational Studies Cross-sectional Studies Cohort Studies
Publication Type	English language Articles with available full text	Other language Abstracts/Theses, Grey literature

Table 2.4: Reasons for exclusion of articles screened

- Clinical Recommendations/Expert opinions/ algorithms and guidelines
- T2D patients not on pharmacological treatment/ studies related to non-diabetes patients or patients at high risk of T2D
- Clinical trials on efficacy, safety and cost-effectiveness of diabetes medicines or insulin regimes
- Effectiveness of: dietary interventions, SMBG, psychological/behavioural interventions not related to medication adherence/medication taking, HP interventions on glycaemic control not related to medication adherence or medication taking, educational interventions/computerised systems
- Focus on: dietary patterns and eating habits, postprandial glycaemia, cardiovascular and microvascular events, GLP-1 levels, neuroscience, treatment adherence in mental illness, physiological aspects of diabetes medicines, diabetes medicines prescription rates, mobile health applications, adherence to guidelines for hospital inpatient treatment, dental care
- Family physicians/Specialist diabetologists' perceptions of diabetes care and attitudes/beliefs towards diabetes medicines, HPs' perceptions of patients' barriers to insulin
- Articles relates to a research/review protocol
- Association of weight change with incidence of diabetes/prevalence of T2D
- Research study in rats or other animals
- Conference abstracts/poster presentations

Figure 2.1 shows the flowchart of number of articles identified, screened and finally included in the final list of articles for critical appraisal based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidance (Liberati et al., 2009).

According to the meta-synthesis by Brundiisini et al. (2015), countries such as Canada, United States, Australia, Netherlands, Romania, Sweden, UK and other countries (multi-country studies that include Croatia, Norway, Germany, and Belgium) have similar health care systems for T2D management. However, the UK is the only country which has a fully paid NHS through taxes, where people with diabetes are exempt from all prescription charges (Garrofe et al., 2014). Many of the countries mentioned above use private or government insurance which is partly reimbursed when it comes to medication prescriptions. In addition, health care systems related to delivery of diabetes care are varied across countries; particularly with guidelines to medication treatment, HbA1c targets, and availability and/or licences of prescribed drugs. Therefore, due to the timeframe and to ensure that studies appraised are in context with current PhD study, the final number of articles was further reduced to focus on UK based studies or multinational papers where UK data were shown separately. This enabled us to produce an in-depth understanding of the unique culture and health care system in the UK.

Five articles that appeared in Brundiisini et al. (2015) synthesis were based in UK and these were selected and screened for potential eligibility in this review (not shown in Figure 2.1). These included: Courtenay et al. (2010), Hinder and Greenhalgh (2012), Mc Sharry et al. (2013), Bissell et al. (2004) and Parry et al. (2006). The first three articles included patients with both types of diabetes, however they were screened to ensure that data could be distinguished between the two types. Likewise, Majeed-Ariss et al. (2013) also identified a further five potentially relevant qualitative research articles with UK participants. These included: Lawton et al. (2006a), Lawton et al. (2006b), Macaden et al. (2006), Scott (1997), and Stone et al. (2005). These were also screened for potential eligibility in this review.

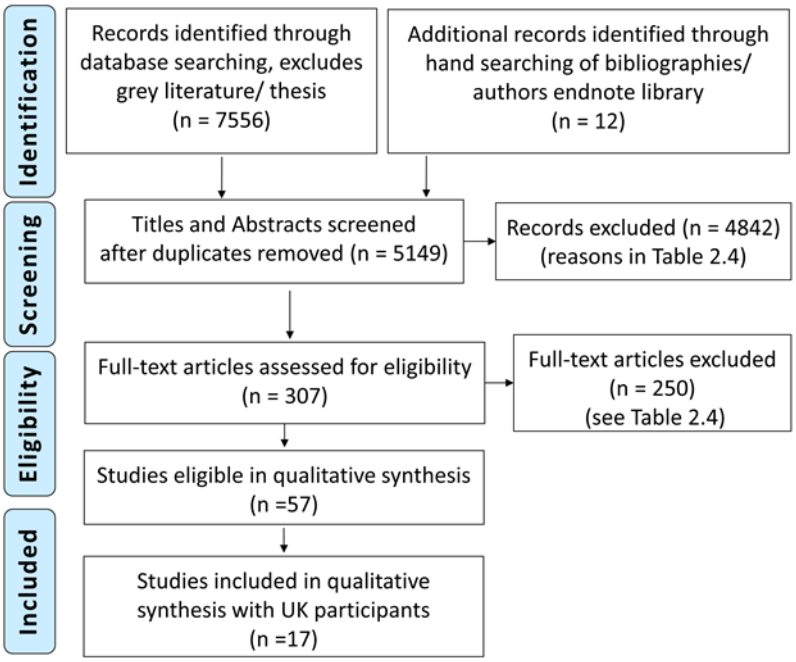

Figure 2.1: Adapted PRISMA Flowchart

2.2.4 Quality Assessment

Titles and abstracts checked by one reviewer (AP) and a sample was verified by a second reviewer (HC, PhD supervisor). Full texts of selected studies were critically appraised for synthesis by one reviewer (AP) and a sub-sample checked by the second reviewer (HC) followed by a discussion meeting to examine those papers that scored low during critical appraisal in order to reach a consensus. There is currently no agreement on the best method to appraise the quality of qualitative studies (Campbell et al., 2011) and the value of appraisal remains controversial. In this review the quality of included studies was assessed in accordance with the Critical Appraisal Skills Programme [CASP] criteria for quality appraisal for qualitative research (CASP, 2010), using version 31.05.13. The CASP tool for qualitative research included an additional question in relation to whether the studies described their theoretical perspective as illustrated in the adapted version of the CASP tool by Campbell et al. (2011). The final adapted CASP tool for qualitative research that was used can be found in Appendix 2.2. Only articles with a score of seven and above (maximum score 11) were included in this review. A score of seven meant that only rigorous studies that provided sufficient information on recruitment strategy, data collection and

analysis and participants quotes to support study findings were included in this review.

Of the ten additional studies identified through the systematic review of Marjeet-Ariss et al. (2013) and the qualitative synthesis of Brundiisini et al. (2015), only three articles were considered eligible and added to the list of articles to be critically appraised. These three articles were: Parry et al., 2006; Stone et al., 2005 and Bissell et al., 2004. Reasons for excluding the other articles were due to: inability to distinguish data of T2D patients from T1D patients, from HPs or health development workers, from those who were on diet therapy only, and when the focus was not on participants' medication taking personal perspectives.

Table 2.5 shows all papers underwent critical appraisal (17+3=20) with their individual CASP scores. The appraisal process identified areas that papers either failed to report clearly or did not report at all. In descending order, these included: i) the relationship between researcher and participants, ii) a theoretical perspective, iii) justification for data collection methods, and iv) ethical considerations. In addition, the paper from Frandsen and Kristensen (2002) was a mixed methods research study, reporting both qualitative and quantitative research within the paper but failed to report many of the areas in qualitative assessment so was excluded from this review. All of the above are similar issues identified by other researchers undertaking critical appraisal for reviews of qualitative research (Atkins et al., 2008; Newton et al., 2012).

Table 2.5: Eligible papers examined and quality appraisal outcome

Author	Date	Title	Type of study	CASP Score
Bissell et al	2004	From compliance to concordance: barriers to accomplishing a re-framed model of health care interactions	Qualitative	9
Bower et al	2012	Illness representations in patients with multimorbid long-term conditions: Qualitative study.	Qualitative- part of mixed methods programme	8
Brod et al	2014	Barriers to initiating insulin in type 2 diabetes patients: development of a new patient education tool to address myths, misconceptions and clinical realities	Mixed Methods	9
Brown et al	2007	Health beliefs of African-Caribbean people with type 2 diabetes: a qualitative study.	Qualitative	9
Frandsen and Kristensen	2002	Diet and lifestyle in type 2 diabetes: the patient's perspective	Mixed Methods	5- Excluded
Hood et al	2009	'With age comes wisdom almost always too late': Older adults' experiences of T2DM.	Qualitative	8
Jenkins et al	2010	Initiating Insulin as Part of the Treating To Target in Type 2 Diabetes (4-T) Trial An interview study of patients' and health professionals' experiences.	Qualitative- part of Research Trial	8
Jenkins et al	2011	Participants' experiences of intensifying insulin therapy during the Treating to Target in Type 2 Diabetes (4-T) trial: qualitative interview study.	Qualitative- part of Research Trial	11
Khan et al	2008	Prevalence and reasons for insulin refusal in Bangladeshi patients with poorly controlled Type 2 diabetes in East London.	Mixed Methods	7
Lawton et al	2005a	Perceptions and experiences of taking oral hypoglycaemic agents among people of Pakistani and Indian origin: qualitative study.	Qualitative	11

Lawton et al	2005b	Lay perceptions of type 2 diabetes in Scotland: bringing health services back in.	Qualitative	9
Lawton et al	2008	Patients' perceptions and experiences of taking oral glucose-lowering agents: a longitudinal qualitative study.	Qualitative	8
Morris et al	2005	Experiences of people with type 2 diabetes who have changed from oral medication to self-administered insulin injections: a qualitative study	Qualitative	9
Noakes	2010	Perceptions of black African and African-Caribbean people regarding insulin.	Qualitative	9
Parry et al	2006	Issues of cause and control in patient accounts of Type 2 diabetes	Qualitative	8
Patel et al	2015	Concerns and perceptions about necessity in relation to insulin therapy in an ethnically diverse UK population with type 2 diabetes: a qualitative study focusing mainly on people of south Asian origin.	Qualitative	9
Phillips	2007	Experiences of patients with type 2 diabetes starting insulin therapy	Qualitative	10
Stack et al	2008	A qualitative exploration of multiple medicines beliefs in co-morbid diabetes and cardiovascular disease	Qualitative	10
Stone et al	2005	Empowering patients with diabetes: a qualitative primary care study focusing on South Asians in Leicester, UK	Qualitative	8
Vermeire et al	2007	Obstacles to adherence in living with type 2 diabetes: An international qualitative study using meta-ethnography (EUROBSTACLE)	Qualitative	8

2.2.5 Data abstraction and synthesis

A data abstraction tool was created to collect a broad range of information including: year of publication, research design, theoretical perspectives and other methodological aspects (sampling, data collection method, location, setting of study), participant characteristics, type of diabetes/weight loss medicine(s) and duration of experience, any details about BMI or weight, and theoretical models or conceptual frameworks used to analyse or interpret the data relating to self-management of diabetes and adherence behaviour. Papers that reported data from the same research study were collated as one.

All eligible papers (n=19) were separated into groups according to their research focus which was either according to type of diabetes medicines reviewed or multimorbidity/polypharmacy (Table 2.6), following the meta-synthesis approach adopted by Pound et al. (2005). For example, articles which only described participants' experiences with OGDs was part of the first group, these articles were then reviewed based on chronological order. The chronological approach was used to form the synthesis rather than an "index paper" that other reviewers have used in the past (Campbell et al., 2003). The timeframe of the published studies spanned over 10 years and there was not enough citation tracking to consider any one of these papers as an "index paper". Table 2.6 describes the four research focus groups as well as the order in which each article was reviewed.

Table 2.6: Research focus of review papers based on types of medicines

Research Focus Groups	Papers in Order of Synthesis
Oral glucose-lowering drugs [OGDs]	Lawton et al., 2005a Lawton et al., 2005b, 2008 Parry et al., 2006 (related to Lawton 2005b, 2008)
Insulin	Morris et al., 2005 Phillips, 2007 Khan et al., 2008 Noakes, 2010 Jenkins et al., 2010, 2011 Brod et al., 2014 Patel et al., 2015
Diabetes Medicines (includes both OGDs and insulin)	Bissell et al., 2004 Stone et al., 2005 Vermeire et al., 2007 Brown et al., 2007 Hood et al., 2009
Polypharmacy/multimorbidity	Stack et al., 2008 Bower et al., 2012

2.2.6 Determining how the studies are related

The initial approach to synthesis included reading and re-reading the articles from each research focus group, and identifying relevant passages and themes. To manage the synthesis process a Microsoft Excel spreadsheet was used to collate extracts from the papers that included both first and second order constructs (direct participants' quotes and authors' interpretations) by inserting each passage under a column which was assigned a theme. Each paper was entered into a separate row and passages were extracted in the same words as the published work of the authors. The themes included passages relating to participants' views about their diabetes/weight loss medicines *prior* to starting their treatment and their views of these *after* initiation of the treatment. This was done purposefully to identify changes in their views about their medicines and changes in medication-taking behaviour over time. These two categories of *Prior* and *After,* were a way of organising a large amount of data and they do not represent themselves third order constructs. Themes also included passages related to quality of care and weight to identify if these aspects influenced medicine taking behaviour.

2.2.7 Translating studies into one another and synthesising translations

Following data extraction for each paper, the studies were translated into each other, one by one, following a systematic approach as described by Campbell et al. (2011). Briefly, the synthesis of the first two papers was compared with the third paper, and the subsequent synthesis was compared with fourth paper and so on, until all the studies were translated into each other. For example, first paper had findings X, Y and Z, whilst second paper had findings x and y (similar to paper 1) and finding w (something new not in paper 1), but nothing like Z as in first paper. This was an attempt to "match" themes/concepts from one paper to another in order to capture a central theme, as well as adding or incorporating new separate themes (Britten et al., 2002; Munro et al., 2007). This process was done separately for the "oral glucose-lowering drugs" and "insulin" groups. The findings from the "diabetes medicines" group were then compared with each of the first two groups where relevant. Finally the "polypharmacy/ multimorbidity" group was compared with each of the "oral glucose-lowering drugs" and "insulin" groups. Noblit and Hare (1988) identified this process of translating studies into each other as either "reciprocal" or "refutational" translation, where the findings from studies when compared had similar issues, or refuted each other. In the process of comparing the studies against each other, explicit differences between the studies in relation to a range of factors including their geographic location, socioeconomic conditions, cultural differences, participants' diabetes control, body weight, diabetes duration, diabetes treatment types, initiation and/or duration of treatment and use of primary and/or secondary care services were noted. This synthesis produced two separate "maps"; one for OGDs and one for insulin (Figures 2.2-2.3) and the two groups were then finally compared to identify how the findings related or not, across the two medicine groups, an example of the translational synthesis with the themes identified can be found in appendix 2.3. The synthesis of medicines maps in this study used the reciprocal approach, except where one paper appeared to refute (Jenkins et al., 2010), although not strongly, what other similar studies described. Finally, a "line-of-argument" synthesis (Noblit & Hare, 1988) was constructed by developing an overarching model that linked together the translations and authors interpretations

in order to address the main aims of the review. This was particularly important as papers focused on different aspects but the line of argument brought them together.

2.3 Results

In total 16 studies were reviewed (19 papers), as two papers were related to the same study by Lawton et al (2005b) and one paper was related to the study by Jenkins et al. (2010). Key features of the studies are summarised in Table 2.7 and are discussed next. Each paper included in the review was assigned a numeric identification [ID] code (and alphabetic code for related studies), which can be seen in Table 2.7. The sections below use these ID codes in superscript form to refer to the relevant papers.

2.3.1 Research Design and Methodology

Most participants were recruited from primary (n=9 [1, 2A, 2B, 2C, 9, 10, 11, 12, 14, 15, 16]) and secondary care (outpatient hospital clinic, n=7 [2A, 2B, 2C, 3, 4, 5, 6, 10, 14]); one study recruited participants from clinical trial centres[7A, 7B], one study recruited from professional organisations[8] and one study did not mention the research setting[13]. Studies were conducted in Scotland (n=2 [1, 2A, 2B, 2C]), in the North West of England (n=3[3, 10, 16]), in London (n=4 [5, 6, 8, 14]), in the West Midlands (n=1, Coventry/ Warwickshire[4]), and in the East Midlands (n=3, Leicester, Nottingham[9, 11, 12]). One was a UK wide study (n=1[7A, 7B]) therefore capturing a range of areas in the UK, but two studies did not specify region (n=2 [13, 15]).

The majority of the studies used grounded theory approach (n=8, [1, 2A, 2B, 2C, 7A, 7B, 8, 9, 10, 13, 15]) for their methodology, of which two used a modified version. Two studies used phenomenology, of which one was interpretive[3, 4]. However, six studies did not mention any methodological details[5, 6, 11, 12, 14, 16]. Qualitative data collection methods included in depth or semi-structured one-to-one interviews (n=12, [1, 2A, 2B, 2C, 3, 4, 7A, 7B, 9, 10, 11, 12, 14, 15, 16]), focus groups (n=4[5, 6, 8, 13]) and/or field notes/participant observation notes (n=2,[2A, 2B, 2C, 3, 4]). Data was collected at participants' own homes (n=9[1, 2A, 2B, 2C, 4, 9, 10, 11, 12, 14, 15]), in a Hospital or GP Practice (n=6[3, 4, 5, 6, 11, 12]), at a university (n=2[9, 15]) and/or at a professional research organisation[8]. Three studies did not specify where the interviews took place[(7A, 7B, 13, 16)], although Jenkins et al. (2010, 2011)[(7A,7B)],

mentioned it was at a location convenient to participants. Most studies were cross-sectional in study design, where interviews or focus groups were conducted at one point in time, but there were two studies which employed a longitudinal approach to identify changes in participants' views[2B,3]. Despite the longitudinal approach of these studies, only Lawton et al. (2008)[2B] were able to analyse data longitudinally. All studies used purposive sampling techniques except Brown et al. (2007)[12] where theoretical sampling was used. Lawton et al. (2005a)[1] and Bissell et al. (2004)[10] used snowballing sampling in addition to their purposive sampling.

2.3.2 Participants' characteristics

There were 173 men and 151 women, but there were another 36 participants for whom their gender was not reported (n=360). Participants were from a range of ethnic backgrounds, with the majority being Caucasians (n=133), followed by those of South Asian Origin (Indian, Pakistani, Bangladeshi, n=122), African-Caribbean (n=29), Black-African (n=5), White European (n=1), and 70 for whom ethnicity was not described. The age range of participants across all studies was 21-89 and they were either recently diagnosed with T2D or had diabetes for a maximum of 35 years (range 0-35). Three studies reported participants had diabetes related complications including: neuropathy, retinopathy and Cardiovascular Disease [CVD][3, 5, 12, 14]. Three studies reported socioeconomic status[1, 2A, 2B, 2C, 12]. Two studies reported glycaemic control[7A, 7B, 5], although one study reported the glycaemic control of participants following their completion of a clinical trial[7A, 7B]. None of the studies in this review reported either participants' BMI or weight; however one study was part of a clinical trial[7A, 7B] for insulin initiation and therefore inclusion criteria to the trial indicated that participants had a BMI of less than 40.0kg/m^2 (Holman et al., 2009). The original 4-T trial paper (Holman et al., 2009) indicated that all participants had gained weight by the end of the trial (3 years later; average weight gain ranged from 3.6-6.4kg).

The two multimorbidity studies reported the number of medicines participants were taking which ranged from 2-12, combined medicines for diabetes and other co-morbidities such as hypertension, hyperlipidaemia and others[16, 15]. Although other studies did not specifically report the mean number of medicines or the range, many

participants' quotes indicated that they were on multiple diabetes and non-diabetes medicines.

2.3.3 Types of medicines

Broadly the studies can be separated in examining issues around two types of diabetes medicines; OGDs and insulin. None of the studies examined specifically other injectable medications for diabetes such as GLP-1 agonists or weight loss medicines (i.e. orlistat). In most studies, no specific diabetes medication was mentioned as part of the inclusion criteria.

2.3.3.1. Oral glucose lowering drugs

Of those studies specific to OGDs, some mentioned specific names such as metformin, gliclazide (or sulphonylurea) and pioglitazone usually through participants' quotes; whereas others reported whether they were on monotherapy or combination therapy or on maximum oral therapy. None of the studies mentioned DPP-4 inhibitors, or SGLT-2 inhibitors, or other diabetes medicines described in Chapter 1. Patel et al. (2015)[9] described one interviewee who was on insulin therapy as well as exenatide, a GLP-1 analogue, however the focus was solely on insulin. Only two studies specified the length of OGD treatment, which ranged from 4 months to 10 years[2A, 2B, 2C, 6].

2.3.3.2 Insulin

Of those studies specific to insulin, few described whether patients were on basal insulin (once daily injection), biphasic insulin (twice daily injection) and prandial insulin (thrice daily injection)[3, 4, 7A, 7B]. Three studies mentioned participants were on both tablets and insulin[6, 8, 9]. Although Lawton et al., (2008)[2B] was specifically focused on participants' views of OGDs, at their final interview there was one patient who had started on insulin [2A, 2B, 2C].

Of the studies concerned specifically for insulin, three were related to participants' views around insulin initiation and all participants had started insulin for at least one

month[3], but others had been taking insulin for longer than two years [4, 7A, 7B]. Two more studies were related to barriers and refusal to initiate insulin, however in one study all participants had refused starting insulin in the last three months prior to the focus group[5], and in the other study half of the participants had started insulin in the last six months, whereas the other half had refused to start[8]. A further two studies were related to perceptions about insulin, and both studies included participants who either were already taking insulin (5 months-22 years) or were insulin-naïve[6, 9]. Six of the general studies looking at diabetes management and experiences, and multimorbidity or polypharmacy, did not specify the length of insulin duration [10,11, 12, 13, 14, 15].

2.3.3.3 Weight Loss Medicines and Weight related Issues

The literature search did not find any relevant studies on patients' experiences and medicine taking behaviours for weight loss medicines that met the inclusion criteria. There was one study on patients' views of anti-obesity drugs (Psarou & Brown 2010), however it was not clear whether all participants had T2D. None of the studies included in this review investigated views of weight loss medicines and associated adherence. Nonetheless, some weight related issues were found. Weight gain appeared to be a concern for patients with T2D[2A, 2C, 5, 6, 8, 10, 12, 13, 14, 15], however this was not always related to their diabetes medicines. Fear of weight gain was associated as a barrier to insulin initiation [5, 8, 12]. Patients understood that weight is related to lifestyle measures [2A, 2C,10, 14, 15], however many discussed difficulties with adhering to the diet commenting on being "*naughty*" and "*cheating*" [2A, 10], or not understanding how to cut down on calories from the foods that they eat [6], and that HPs do not understand the difficulties they face [10, 13]. Conversely, others suggested that they would lose weight if they were to avoid taking medicines [2C,15], although not all believed that it would be diabetes medicines [15], as the following quote describes:

"What diabetes is really, erm you can't really repair it, unless of course it is a weight problem. The weight loss would stop the strain on the heart, it's not going to sort your pancreas out, because that's gone isn't it? Once the damage is done it doesn't matter

if you lose the weight anyway you still have to take tablets or insulin, you probably wouldn't have to take the cholesterol, perhaps or maybe the aspirin, if you got down to a proper weight level." (White British male, aged 53, prescribed five medicines) [(15)].

It was evident from the studies that those who managed to lose weight had higher self-efficacy and coping levels [(2C, 14)] by taking control and becoming more confident over time about managing their diabetes. This review identified that people varied in their perceptions of lifestyle measures and particularly weight loss as an effective way in managing their diabetes, a finding that conflicts with current medical advice (Lau, 2010; Ross et al., 2011).

2.3.4. Conceptual Framework

Behavioural and social theories are considered important in identifying determinants of effective behaviour change. Many have been established to describe treatment behaviour, in this case medicine taking behaviour, which is either related to chronic disease or illness, or to patients' beliefs and attitudes. The models and theories used most often to inform the research studies in this systematic review were those that relate to individuals' health-related behaviour. Although studies did not provide much detail beyond stating the theory or model applied, generally they used these to inform the analysis of their data, or to validate their findings through triangulation.

Four studies described psychological insulin resistance as a phenomenon for people who refuse insulin initiation (Polonsky & Jackson, 2004), although not all applied this framework to inform analysis/validation (Khan et al., 2008[(5)]; Noakes, 2010[(6)]; Patel et al., 2015[(9)]; Brod et al., 2014[(8)]. One study (Jenkins et al., 2010)[(7A)] described psychological insulin receptiveness for their participants in the study, indicating that not all individuals are resistant to insulin initiation. Psychological insulin resistance, although not a theoretical model in itself, has links to social cognitive theory (Bandura, 1977) where individuals learn from watching what others do. Individuals' behaviour is influenced by several factors including personal beliefs and attitudes, existing behaviours, and the social and physical environment. In addition, a change in an individuals' behaviour is related to the expectations of outcomes that will result

from engaging in the behaviour, and the perceived ability to perform the behaviour i.e. self-efficacy. Although social cognitive theory predicts and explains behaviour change, it has been criticised for its emphasis on the individual behaviour as opposed to acknowledging other social, economic and political factors (Clark & Janevic, 2014). One study (Bower et al., 2012)[16] used the common sense model linking it with the ways multimorbidity can impact on individuals' illness representations. The common sense model (or illness representations model or self-regulation model) (Leventhal et al., 1980 cited in Bower et al., 2012) is a system of conscious health management containing a number of processes which influence health behaviour and its principle is directly drawn from social cognitive theory (Clark & Janevic, 2014). The processes include (1) extracting information from the environment (social network/external cues), (2) generating a representation of the illness as dangerous to oneself (owns beliefs/attitudes based on internal cues), (3) planning and acting, taking into account emotions that are generated from the potential coping strategies (e.g. to take or not to take medication), to achieve specific effects or goals, and finally (4) monitoring or appraising the success or failure of coping efforts. It is believed that in T2D these processes occur in parallel involving both cognitive representations (illness identity, cause, consequences, time-line, control/cure, perceptions of self–efficacy and coping efficacy) and emotional representations of illness (Cooper et al., 2003a). Hence, these illness representations may affect patient outcomes.

Bower et al. (2012)[16] used the common sense model with the added dimension of multimorbidity (defined as the presence of two or more conditions in the same patient) to identify whether multimorbidity impacts on patient representations of their individual conditions, or leads to representations about their relationships (i.e. as interrelated or distinct entities), or other emergent dimensions that only occur in the presence of multiple conditions. In the common sense model external factors do play a part in predicting health behaviour but it has been criticised as some external factors for example, health related policies, political dynamics, and community infrastructure are generally beyond the ability of one individual to change (Clark & Janevic, 2014).

Patel et al. (2015)[9] as well as Bower et al. (2012)[16] used the necessity-concerns framework in the analysis of their findings. This framework developed by Horne et al. (1998, 1999), is an extension to the common sense model by Leventhal et al., in that additional constructs about the beliefs of necessity and concerns related to treatment (in this case medication) can predict medication adherence. The beliefs about necessity and concerns about the treatment are specific to the condition (that is diabetes medications) rather than beliefs in general about medicines, and adherence is determined by the balance between these two constructs. Aikens et al. (2005) extended the necessity-concerns framework further to determine four individual groups based on the necessity–concerns balance and association with adherence. The groups include those who are; sceptical (low necessity, high concerns), ambivalent (high necessity, high concerns), indifferent (low necessity, low concerns) and accepting (high necessity, low concerns). Those who are accepting are more adherent to their medicines than those who are sceptical, with the other two groups having adherence levels somewhere in between. Only Patel et al. (2015)[9] used the above groups to analyse their data.

One study used the Health Belief Model [HBM] to inform data collection and analysis (Brod et al., 2014)[8], but claimed that it was not used rigidly for organising and interpreting the findings. The HBM was developed in the 1950s within the psychology discipline to predict health behaviour. It has five main constructs; perceived susceptibility, perceived severity, perceived barriers, perceived benefits and cues to action. However other related constructs from the social cognitive theory could be added to the model, such as self-efficacy (Rosenstock et al., 1988). The model has been criticised for not adequately explaining health behaviour because of: (1) other influential factors which may not relate to the constructs in the model and are not explained by individuals' beliefs or attitudes, (2) not explaining how individuals come to have certain beliefs (past experiences/habits) (Clark & Janevic, 2014), and (3) not explaining irrational behaviours (Horne & Weinman, 1998).

Other studies were influenced by sociological and anthropological perspectives. One study used the theoretical framework of chronic illness as biographical disruption

(Hood et al., 2009)[14]. In this, disruption, such as chronic illness, is key to understanding the complex relationship between an individual and society (Bury, 1982), and how individuals making sense of their illness, of themselves, and how they adapt through their experience and practices in society, and also mobilise resources. This framework is deeply rooted to medical sociology.

Another study (Bissell et al., 2004)[10] discussed in their findings that participants raised concerns that relate to the biographical model of care, where again chronic illness is represented as profoundly disruptive, and where individuals present with many sociocultural dimensions and variations of their illness (Kleinman, 1988 cited in Bissell et al., 2004). The biographical model of care is based on Kleinman's explanatory model of illness (1978), which was developed to help improve patient-provider communication. It has been suggested that low patient adherence to treatment regimens may be related to different frames of understanding of the disease between patients and providers (Cohen et al., 1994). Therefore, HPs need to understand those illness narratives and acknowledge their existence for patient meaningful outcomes (Mishler, 1984) and improved communication (Kleinman et al., 1978). This framework is deeply rooted to medical anthropology.

Stack et al. (2008)[15] mentioned in their findings that some participants exemplified "strategic non-compliance", a term situated within the model developed by Campbell et al. (2003), on reaching a balance in the management of diabetes. The model suggests that people have to pass through critical stages and overcome certain obstacles, in no particular order, to manage their diabetes effectively and to achieve a degree of balance and control. Strategic non-compliance is a key concept at the centre of this model which indicates that individuals thoughtfully and selectively use medical advice rather than blindly adhering to it. Campbell et al. (2003) argued that their findings resonate with the theoretical framework of chronic illness as a biographical disruption by Bury (1982), as people with diabetes appear to have commonalities in the ways in which they experience this disruption and, the elements described above, seem to be required in order to repair or reconstruct their biography. Stack et al. (2008)[15] also discussed terms of "intentional" and "non-

intentional" non-adherence, which derived from two key theoretical models; the necessity-concerns framework (as described above) (Clifford et al., 2008) and the construct of locus of control (Wallston & Wallston, 1978). Locus of control describes an individuals' perceived degree of control (either internal or external) in predicting an outcome behaviour including taking medication. For example, if an individual feels they have control over their illness this may positively influence adherence to medication, however if they feel their illness is outside of their control, they may not adhere to their medication.

Other key findings from studies included the notions of "contextual knowing" (Lawton et al., 2005b)[(2A)] and "down to me and up to them" (Parry et al., 2006)[(2C)]. Although not explicitly mentioned, both constructs can be related to the aforementioned behavioural and social theories. Contextual knowing – a way that individuals embody illness (Gordon, 1990), by manipulating and cultivating uncertainty so that they can dissociate themselves from the diabetic identity can be directly associated with chronic illness as a biographical disruption. Parry et al. (2006)[(2C)] compared the "down to me and up to you" constructs with known explanatory models of illness for T2D (Cohen et al., 1994). However, descriptions of how patients express the cause of their condition (within or outside of their control) with accounts of how actively (or not) they are managing their condition (adhere or not adhere to lifestyle and medication regime) resembles the health locus of control construct. Parry et al. also argued that some participants were characterised by the concept of self-conscious change through telling certain types of stories to confirm and reaffirm the new identity (Frank, 1993). Therefore, negative experiences, over time, can be shaped into new positive outcomes.

Table 2.7: Summary of key characteristics of studies included in meta-ethnography

Author Date [Study ID] Region/ Country	**Research Topic**	**Research Design**	**Methodological Perspective Data Collection Methods Sampling Technique Research Setting**	**Participant Characteristics (Sample size (n), Gender, Age (yrs), Diabetes Duration (yrs), Ethnicity, Other)**	**Medicine Type(n)**	**Weight/ BMI**	**Theoretical Model/ Conceptual Framework**
Lawton et al. (2005a) [1] Edinburgh, UK	Perception and experience of OGD	Cross Sectional	Grounded theory In depth face-to-face interviews Purposive, snowballing sampling Research Setting: 5 GP practices, Pakistani and Indian Communities. Home Interviews	N=32 (15M, 17F) **Age:** 30- ≥71 **Diabetes Duration:** 0-≥16 **Ethnicity:** Pakistani/Indian **Religion:** Muslim, Christian, Hindu, Sikh **Occupation (includes prior occupation for those retired):** Professional/ higher managerial, semiskilled , Unskilled, unknown	4 Sulphonylurea 12 Metformin 13 Sulphonylurea and Metformin 3 Diet only No details given about medication taking duration.	none mentioned	none mentioned

Lawton et al. (2005b) [2A], (2008)[2B] Parry et al. (2006) [2C] Edinburgh, UK	Perception of T2D, issues of cause and control, perception and experience of OGD	Longi-tudinal	Grounded Theory Field notes Face-to-face semi-structured interviews x 4 per participant (first 3 in year 1- baseline, 6months, 12months and 4th in yr 3) Purposive sampling Research Setting: 17 GP Practices, 3 Hospital Clinics Most home interviews	**Interviews 1-3** N=40 (22M, 18F) **Age:**21-71+ **Diabetes Duration:≤**6months **Ethnicity:** 39 Caucasians, 1 Pakistani **Socioeconomic Status:** I -V **Diabetes Care:** 5 GP Practices, 35 Hospital/ other services **Interview 4:** N=20 (11M, 9F) **Age:** 40-80 **Socioeconomic Status:** I-V **Structured education** received post diagnosis=17	**Interview 1:** 9 Diet only, 11 OGD monotherapy, 0 OGD combination therapy 0 insulin and OGDs **Interview 4:** 6 Diet only, 5 OGD monotherapy (3 increased dose), 8 OGD combination therapy 1 Insulin and OGDs Mentioned Metformin and Gliclazide. Medication taking duration: 6months - 3years depending on time of interview	none mentioned	None mentioned but key findings related to: “Contextual Knowing” (Gordon, 1990) “Down to me and up to you” (Cohen et al., 1994; Frank, 1993)

Morris et al. (2005) [3] Manchester, UK	Insulin initiation	Longi-tudinal	Interpretive Phenomenology Participant observation notes 2x interviews per participant (2 weeks after start of insulin and then 1 month after) Purposive sampling Research Setting: Manchester Diabetes Centre	N=6 (3M, 3F). **Age:** 59-73 **Diabetes Duration:** 6-31 **Ethnicity:** 1 Asian, 1 African-Caribbean, 4 Caucasian **Marital Status:** Single/Married **DM complications:** 2 erectile dysfunction, 3 neuropathy, 5 microalbuminuria	BD injections of biphasic insulin. All participants experienced with OGDs. Insulin taking duration=1 month No details given about OGD taking duration.	none mentioned	none mentioned
Phillips (2007) [4] Coventry/ Warwick-shire, UK	Insulin initiation	Cross Sectional	Phenomenology In depth face-to-face unstructured interviews, Field notes Purposive sampling Research setting: 3 Home interviews 5 Hospital interviews	N=8 (4M, 4F). **Women Age range:** 59-72 **Men age range:** 49-72	Women: 4 BD insulin Men: 3 BD insulin, 1 OD insulin Insulin taking duration: 2-4yrs No other medicines specified	none mentioned	none mentioned

Khan et al. (2008) [5] Inner City London UK	Reasons for insulin refusal	Cross Sectional	Focus groups (single -sex groups) purposive sampling Research setting: large inner-city hospital diabetes unit	N= 36 (20M, 16 F), Characteristics provided only for 43 invited to Focus Groups. Stated Age, Diabetes duration and glycaemic control did not differ significantly from those attended focus groups **Age:** 34.2- 77.2 **Diabetes Duration:**2.3-27.1 **Ethnicity:** Bangladeshi **Glycaemic control - HbA1c:** 8-13.8% or 64-127mmol/mol **Diabetes Complications**: 11 CVD, 10 Retinopathy, 20 Micro and Macroalbuminuria	No OGDs specified but inclusion criteria indicate they should be on maximum oral therapy i.e. Metformin, Sulphonylurea and glitazone where not contraindicated All participants continued to refuse insulin initiation after one-one education consultation and written material provided over a 3-month period. No details given about OGD taking duration	none mentioned	Psychological insulin resistance (Polonsky & Jackson, 2004) but does not link it with study data

Noakes (2010) [6] London-South East UK	Perception of insulin therapy	Cross Sectional	Focus groups (tablet and insulin groups) purposive sampling Research Setting: Diabetes Hospital outpatient clinics, Interviews at Education Centre NHS Trust	N=13 (5M, 8F); tablet group=5F, 2M insulin group=3F, 3M **Age:** tablet group 44-77 insulin group 53-69 **Diabetes Duration:** tablet group=4months-11yrs insulin group=4-26yrs **Ethnicity:** 5 Black Africans, 8 African-Caribbeans	OGDs and insulin None specified Treatment Duration: Tablet group= 4months-10yrs, insulin group= 5months-22yrs	none mentioned	Psychological insulin resistance but does not link it with study data (Polonsky & Jackson, 2004)
Jenkins et al. (2010) [7A] (2011) [7B] Nationwide UK	Insulin initiation and intensifi-cation	Cross Sectional	Grounded Theory In depth face-to-face interviews Purposive sampling Research setting: 11 Clinical trial centres to reflect diversity in centre size and geographical location	N=45 (29M, 16 F) **Age:** Mean 64.7 ±8.5 **Ethnicity:** majority White British **Glycaemic control HbA1c at year three of trial:** 5.3-9.9%/ 34-85mmol/mol 26 participants with HbA1c ≤7% (53mmol/mol) 19 participants with HbA1c ≤6.5% (48mmol/mol)	Insulin Initiation: Arm 1:15 Basal Insulin (OD) Arm 2: 15 Biphasic Insulin (BD) Arm 3: 15 Prandial Insulin (TDS) Metformin and/or Sulphonylurea Insulin Intensification (n=41 at year 2/3 of trial)	Inclusion criteria indicated BMI≤40.0 kg/m^2. All gained weight by end of trial: Biphasic group mean 5.7±0.5kg	Psychological insulin receptiveness (Jenkins et al., 2010)

			Interview setting location convenient to participants		Arm 1: Basal and Prandial Arm 2: 13 Biphasic and Prandial Arm 3: 14 Prandial and Basal. On Metformin if tolerated, Sulphonylurea discontinued Insulin Taking duration:>2yrs (calculated from original 4-T Trial paper) No details given about OGD taking duration	Prandial group: mean 6.4±0.5kg Basal group: mean 3.6±0.5kg (taken from original 4-T trial paper)	
Brod et al. (2014) [8] Multi-national	Barriers to insulin initiation	Cross Sectional	Modified Grounded Theory Focus groups (per country- 2 in UK) Purposive sampling	N=15 in UK Demographics given but not separated by country	Equal mix of participants initiated or refused insulin when	none mentioned	Health Belief Model (Rosenstock et al., 1988), Psychological Insulin resistance

including London, UK			Research setting: international professional research organization that recruited and hosted the focus groups at their affiliates' facilities in each country		recommended by physician All participants faced this decision 6 months prior to focus groups All taking OGDs. Insulin taking duration for those initiated: <6months No other medicines specified		(Polonsky et al., 2005)
Patel et al. (2015) [9] Leicester, UK	Concerns and perception of insulin therapy	Cross Sectional	Grounded Theory Semi-structured face-to-face interviews Purposive sampling Research setting: recruited from 4 GP practices 1 university premises interview, 17 home interviews	N=18 (9M, 9F) **Diabetes Duration:** <10years ->20years **Ethnicity:** South Asian- mainly Indian Origin=13, Caucasians=5	7 Insulin (two were taking it for >2yrs, no details given for the others) 11 Not on insulin (two on OGDs, no details given for others). No medicines specified	none mentioned	Necessity- Concerns Framework (Horne et al., 1999; Aikens et al., 2005). Psychological Insulin resistance (Polonsky et al., 2005) but does not link with data.

					No details given about diabetes medication taking duration		
Bissell et al. (2004) [10] North West England, UK	Views and experience of T2DM treatment- from compliance to concordance	Cross Sectional	Grounded Theory Face-to-face interviews Purposive and snowballing sampling Research setting: 2 primary care practices, 1 secondary care diabetes centre/ local community Home interviews	N=21 **Ethnicity:** Pakistani Origin.	Quotes from participants on metformin. No other medicines specified No details given about diabetes medication taking duration	none mentioned	Biographical model of care (Kleinman, 1988) with a link to concordance.
Stone et al. (2005) [11] Leicester, UK	Experience and attitude of T2D and its treatment	Cross Sectional	Semi-structured face-to-face interviews (one of two interviewers in either English or Gujarati or Punjabi)	N=19 with T2D **Age:**37-80 (South Asians) **Diabetes Diagnosis** <1-35 (South Asian)	1 Diet only 13 OGD 2 Insulin No details given about diabetes	none mentioned	none mentioned

			Purposive sampling Research setting: 2x GP practices Home or GP practice interviews	**Ethnicity:** 15 (6M, 9F) South Asians Indian origin, 1M Caucasian All South Asian sample T2D, 4 Caucasians T2D but only one identified taking OGDs	medication taking duration		
Brown et al. (2007) [12] Nottingham, UK	Health beliefs of T2D	Cross Sectional	Face-to-face interviews Theoretical sampling Research setting: Self -help groups and GP practices. Home or GP practice Interviews	N=16 (6M, 10F) **Age:** 40-76 **Diabetes Duration:** 0.3-29yrs **Ethnicity:** African Caribbean **Diabetes Complications:** n=10 **Mean Townsend score based on postcode residence** =4.23 (-4.08-7.32)	5 Diet only 6 Insulin 5 OGDs No medicines specified No details given about diabetes medication taking duration	none mentioned	none mentioned
Vermeire et al.(2007) [13] Multi-national including UK, no specific	Obstacles to adherence in living with T2D	Cross Sectional	Grounded Theory-individual focus groups; then meta-ethnography all groups Focus groups (per country- 5 in UK) No research setting	N=19 from UK (9M, 10F) **Age:**<50-75 **Diabetes Duration:** 1-22	Mentioned insulin No other medicines specified No details given about diabetes medication taking duration	none mentioned	Stated no theoretical framework used, which facilitated direct comparison of the focus groups

region mentioned			mentioned or sampling method				
Hood et al. (2009) [14] East End London, UK	Experience of T2D	Cross Sectional	In depth semi-structure interviews - twice per participant Purposive sampling Registered with DM centre in local hospital, but some managed by GPs Home interviews	N=28 (19M, 9F) **Age:** mean 70yrs **DM duration:** >20yrs **Ethnicity:** White British **Socio-economic status:** working class, primarily residing in council housing **DM complications:** impaired eyesight=21, heart surgery/attacks=11. **Disable/Housebound:** 3	23 Insulin 5 OGDs (1 about to commence insulin, 2 stopped insulin due to weight loss) No other medicines specified No other details given about diabetes medication taking duration	none mentioned	Theoretical framework of Chronic illness as a biographical disruption (Bury, 1982)
Stack et al. (2008) [15] UK	Multiple medicines beliefs	Cross Sectional	Modified Grounded Theory Semi-structured interviews Purposive sampling Research Setting: 2 inner city Primary Care General Practices	N=19 (9M, 10F) **Age:** 41-82 **Ethnicity:** 4 African-Caribbean 3 South Asian 11White British 1White-European **Number of Meds taken:** mean 4.8 (range 3-12).	Medicines numbers prescribed for whole group: 24 OGDs 5 Insulin Other meds: 32 anti-hypertensive, 18 Lipid-lowering, 13 anti-platelet Mentioned	none mentioned	None mentioned but commented about strategic compliance-does not link with study data.

			16 Home interviews 3 University interviews		metformin, gliclazide, pioglitazone No other details given about diabetes medication taking duration		
Bower et al. (2012) [16] Greater Manchester, UK	Illness represe-ntations with multi-morbid conditions	Cross Sectional	Face-to-face semi structured interviews Purposive sampling Research Setting: 6 GP practices; all part of local comprehensive research network No interview setting mentioned	N=28 (16M, 12F) of which 23 T2D **Age:** 39-89 **Comorbidities: (**T2D, Chronic Obstructive Pulmonary Disease [COPD], Coronary Heart Disease [CHD], arthritis, Depression, Cancer, Thyroid Disease, Hypertension) mean number =4 (range 2-10).	Various medicines for chronic conditions including diabetes medicines-none specified. No details given about diabetes medication taking duration	none mentioned	Common sense model (Leventhal et al., 1980) with presence of Multimorbidity and Necessity- Concerns Framework (Horne et al., 1999; Horne & Weinman, 2002).

2.4 Synthesis results

The synthesis starts with the description of the two medicine maps. These maps show a timeline illustrating (a) patients' emotions arising from the prospect of initiating medication for their T2D, (b) factors that influenced their acceptance (or non-acceptance) in receiving such medication, and (c) patterns of medication taking behaviour and lifestyle behaviour including their relationship with point (b) above. Finally, the line-of-argument synthesis is presented, demonstrating in a final conceptual model the key processes to understanding patients' journeys in medication management. The following sections refer to the aspects as presented in the relevant figures, and individually are discussed on how they relate to each other.

2.4.1 Oral Glucose Lowering Drugs and Insulin Maps

A visual representation of the final synthesis of all studies that described aspects related to OGDs (Figure 2.2) and insulin (Figure 2.3) can be found below. The first map portrays patients who moved on from diet therapy into taking tablets and the second map portrays patients who either moved on from tablet therapy into taking insulin, or resisted insulin and continued taking tablets.

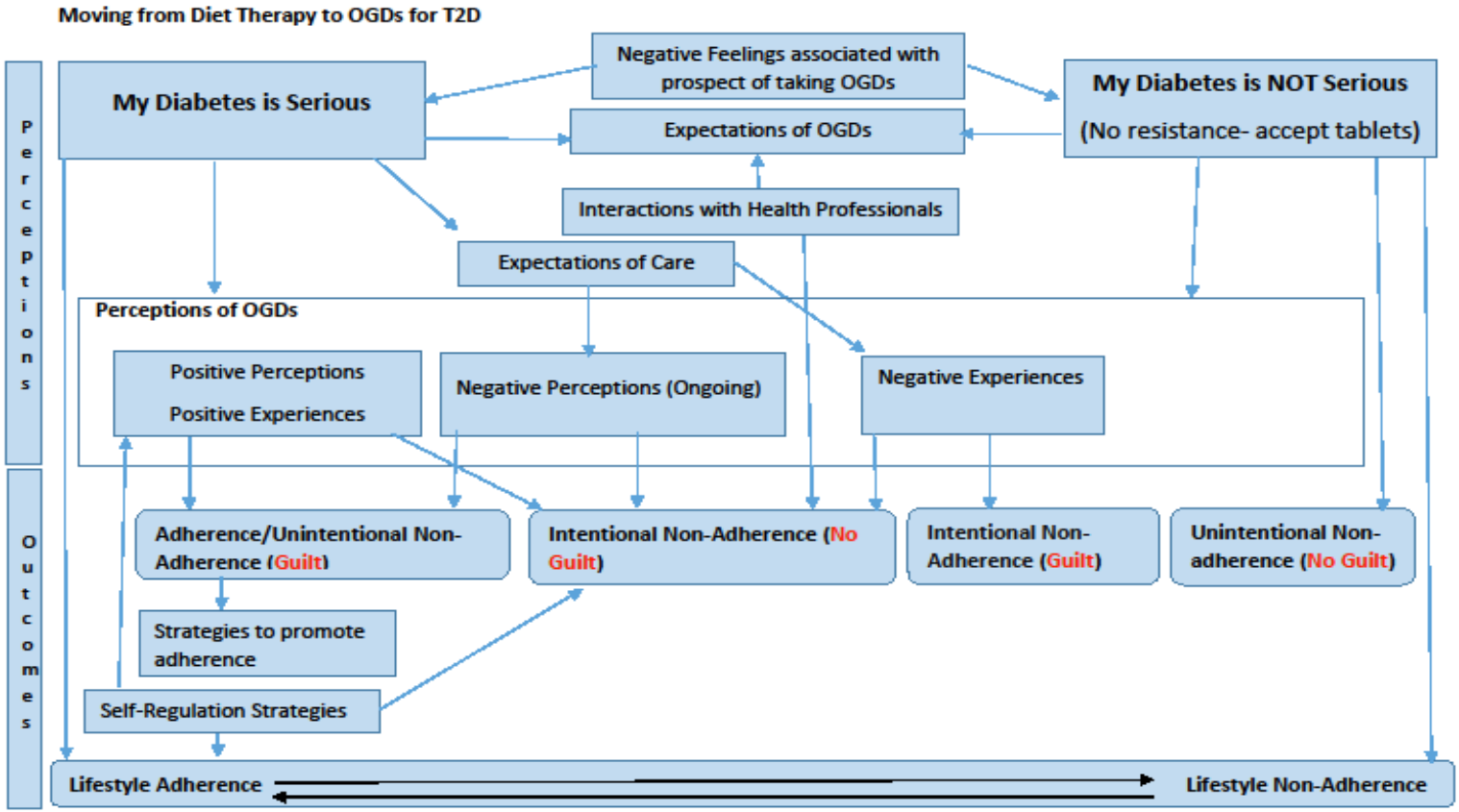

Figure 2.2: Synthesis of Oral Glucose-Lowering Drugs

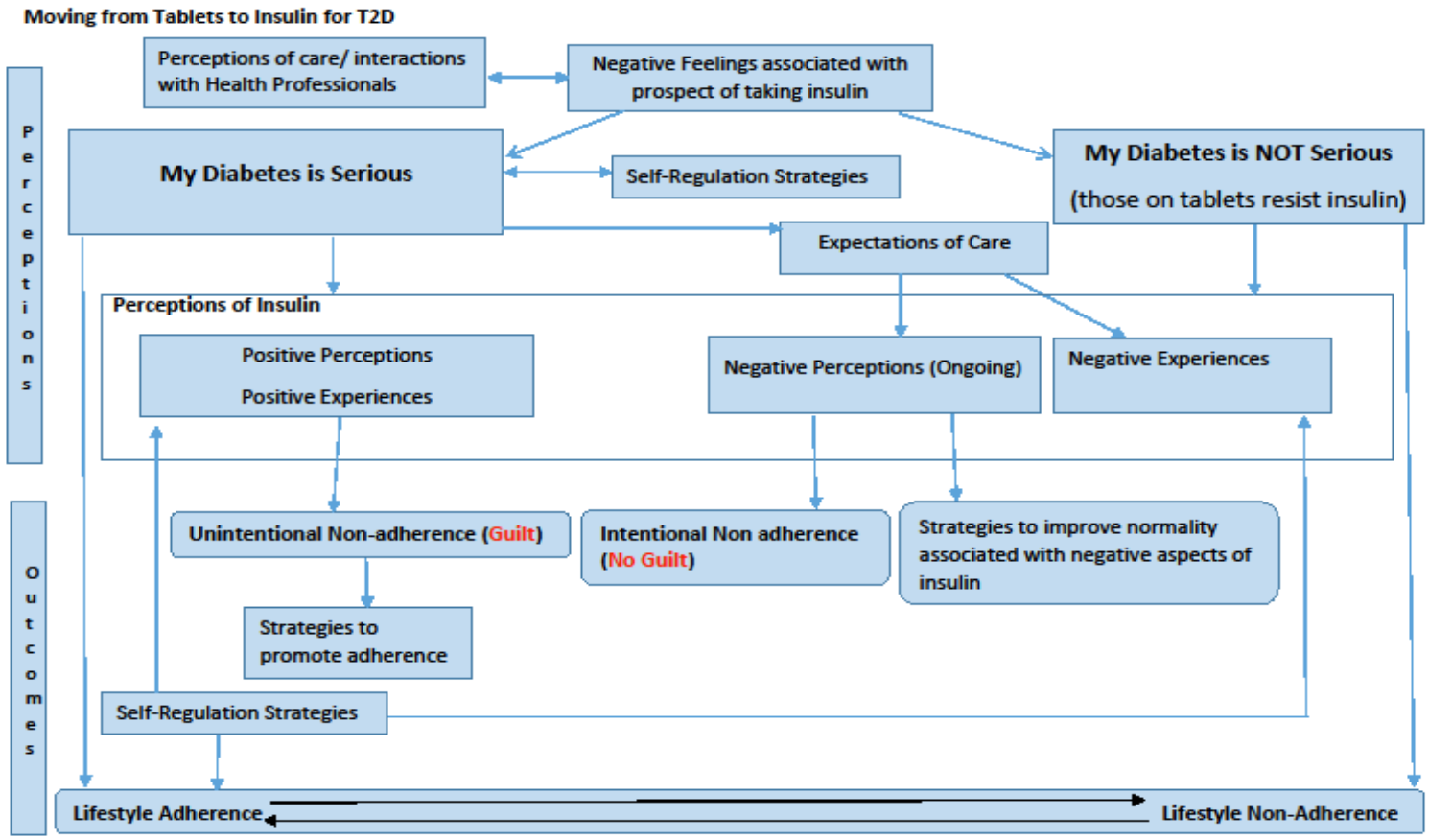

Figure 2.3: Synthesis of Insulin Treatment

2.4.1.1 Negative Feelings

For most of the patients, the prospect of taking medicines for diabetes brought feelings of devastation[1], "*trepidation*"[1, 2B], shock[3, 4, 7A, 14], anger[3, 14] and disappointment[7A]. Taking medicines was associated with becoming a "*patient*" or that their identity will change to that of a "*sick person*"[1, 2B], as the following quotes demonstrate:

"*when I was diet-controlled, I always thought just well "Am I a diabetic?" and since she's given me the tablets for it, well, you know, I thought I was ok and obviously I'm not,…*" (M20.2)[2B]

"*This is diabetes to me. Before I was just taking pills and you just didn't eat your sweet stuff, and you know. But then all of a sudden now I've got diabetes 'cause it's needles you know and that IS diabetes. That is an illness now, wasn't before.*"[3]

Patients started OGDs described it as entering "*a slippery slope*" or "*stage 2*"[2B], and "*...that's a bit closer to stage 3*" (M20.2)[2B] where once you start on taking the first medicine, then this will lead to take insulin, often associated as "*the last resort*"[5, 9, 6]. Insulin, as a symbol of severity, was also found in the review by Majeet–Ariss et al. (2013). These negative feelings towards the diabetes medicines appear, ultimately, to be related to patients' experiences in managing their diabetes with either lifestyle measures (OGDs map) or tablets (Insulin map). Patients referred to being "*defeated*" and letting themselves down for not taking advantage of all the chances they had, and failing to manage their diabetes and diabetes treatment through their own efforts[2B,4,6,8]. Feelings of personal failure also emerged at the point when patients were told they need to start insulin particularly if the initiation was imminent: [4]. Part of the self–blame was related to feelings that others with diabetes would judge them as being a "*bad diabetic*"[14]:

"*Oh yes. Some people feel very proud of themselves that not having gone on the insulin because they were clever and took their tablets*." (Mrs 07, aged 71 years, insulin)[14]

"*What you would find if you went outside and asked all the other diabetics, they think you've failed if you go onto insulin*."[3]

Feelings of personal failure about self-managing diabetes were reported to be extremely rare in the study by Jenkins et al. (2010)[7A]. However these patients were interviewed almost 2 years after they had started their insulin treatments, compared to the patients from Brod et al.'s (2014)[8] study who were initiated insulin within the last 6 months prior to focus group interviews.

Despite the negative feelings associated with starting medicines, all patients who took OGDs appeared to accept taking these medicines, in contrast to studies related to insulin (Figures 2.2-2.3). Nevertheless, as a result of exploring people's perceptions of their medicines, two distinct groups were formed; those who believed that their diabetes is serious and those who did not.

2.4.1.2 My diabetes is serious

Overtime patients rationalised that their diabetes is a progressive disease[1, 2B, 15], believing that lifestyle can cause it but cannot cure it[2C]. This rationalisation was more prominent to those who started developing symptoms[14] as this man describes:

"*…something generally happens like you know, you notice some physical symptom, the feet, pins and needles and then someone says, carry on the way you are and you will lose a limb or your circulation will cause this, that or the other and so eventually something happens that you actually do start taking it much more seriously."*(Mr 11, aged 60 years)[14].

Those taking/starting insulin justified that insulin is an integral part of managing their diabetes[3, 4, 6, 14, 15], while others conclude this after realising their tablets were not helping to control their diabetes[7A, 9]. The use of self–regulation strategies was crucial in accepting insulin as treatment for diabetes and reinforced to patients that their diabetes was serious (top box in Figure 2.3). The combination of SMBG and/or testing of blood glucose control with HbA1c tests as well as observing over-time an

increase in the number of tablets and doses for their diabetes were good indicators of poor diabetes control despite the fact that they were following the treatment[7A, 9]. However, taking insulin for this group of patients meant that they had lost their identity[3, 14] and normality[3]. There was a sense that this was now *"…final. This is the worst this can now get because now you're having to take insulin.* (London, UK)"[8], and *"… the end of things like when you go on like that, you know, there's nothing else out there for me like."*[3].

For many awareness of diabetes as a condition and its treatment came from family and relatives[11], so they were familiar with the need to control blood glucose and diabetes-associated complications [11]. This group of patients placed importance on the role of medicines in managing diabetes. They often expressed that once they start on medicines they have to be on them for the rest of their life[1, 15, 16] otherwise something is going to happen to them[15], they would be in "*danger*"[1] or "*risk dying*"[1]. Understanding diabetes better, following initiation of insulin, meant that patients were more willing to inform others (family, friends, public through the media) about the condition[4, 6]. Those who were taking insulin for a long time[6], or those who were symptomatic but found insulin relieved their symptoms[3] were suggesting that insulin has helped them to feel normal again[3], saved their life[6], or regained their health[6].

2.4.1.3 My diabetes is not serious

This group of patients consists of those prescribed OGDs but who had no experience of taking insulin, including those who had been advised to take insulin but refused to do so[5, 6, 8, 9, 10]. For some patients, there was a sense of denial towards diabetes, as for them it is largely "*invisible*",

"…You can only see diabetes in your blood. You cannot see it visually inside the human body. …it's invisible, you can't see it. Unfortunately, for everyone, what we can't see…we ignore. It's not ignorance, we just ignore it, because we can't see it." (Mr 07, aged 67 years)[14].

Fear about acknowledging that diabetes was serious was described as "*contextual knowing*" (Lawton et al., (2005b)[2A]. Patients often expressed how they wanted to push their diagnosis to the back of their minds[11, 2B], believing that their diabetes is not serious if they are taking tablets[4, 5, 8, 9, 14], perceived insulin as an indicator of the worse type of diabetes[4,5,6], or a "*pre-terminal event*"[5, 6] with more side effects than tablets[6] , denying the possibility of future complications[12], or believing these are not imminent, as described by these patients:

"…If I stop taking medicine for diabetes I'm not likely to go blind or lose my feet tomorrow, and I might get hit by a truck in the next 20 years. If I stop taking the medication to control my blood pressure I might have a stroke tomorrow and I don't want to do that." (Interview 13)[15]

"*I feel fine—why do I need insulin? I can control this by exercise and diet. I know what to do. My body will tell me if it is unbalanced.*" (Bangladeshi Man, aged 48 years)[5]

Reluctance to take insulin was also associated with specific aspects, most commonly with needle anxiety. For example, needle size[3, 9], act of injecting[6, 9], frequency of injections[5], fear of feeling pain [5,9], and fear of consequences of taking injections all the time[9]. In addition, patients mentioned fear of weight gain[5] and hypoglycaemia[5, 6], the most common side effects of insulin (Horvath et al., 2007, Holman et al., 2008). Hence, concerns of loss of freedom and dependence on others[5, 6] because of increased risk of hypoglycaemia and the act of injecting were voiced, as these quotes illustrate,

"*I will always have to have someone near me in case my blood sugar goes low.*" (Bangladeshi Woman, aged 61 years)[5]

"*If we take insulin then we have eat food immediately you know or our sugar goes down and you have to take insulin on time extremely regularly, with the tablets, if our timing is misplaced by either a hour lost or gained, it is not a source of worry for us...*

it's only that it's hard to manage when going out and doing things." Case Study 2 (Interview 17- South Asian female, 58yrs, T2D duration 10yrs, on OGDs 5yrs)

Insulin perceived as restricting and interfering with their lives[5], including their daily[6] and social[6] activities and travelling[5, 8]. Therefore these patients expressed they would rather take more medicines than injecting insulin[9], in order to avoid this stigma:

"*When they gave tablets it began to go low and I thought but then it started going up and the doctor said you will have to come onto injections, four years on. I said do not say the name injections. I will take as many tablets I as I need to. I don't have any problems with that...*"[9].

Past experiences with their medicines, particularly if perceived them unsuccessful in managing their diabetes, made them reluctant to accept insulin, as this woman explained:

"*The tablets don't work. Why should the insulin work any better?*" (Bangladeshi Woman, aged 57 years)[5]

Insulin was also perceived as a threat by patients[3, 6, 8], often used by HPs to encourage them to better control their diabetes:

"*I know several times the doctor told me your sugar is up, your sugar is up and he said it has to come down or else we put you on the insulin. I've been dreading that.*" (African Female, tablet group)[6]. Consequently, insulin was linked with failure to control diabetes with lifestyle and tablets [5, 6].

On the other hand, some patients although symptomatic prior to diagnosis of their diabetes and initiation of their medication, also made references to their diabetes as "*not being serious at all*", "*very insignificant in the big scheme of things*"[2A], and "*never affected me one way or the other*"[2A]. This appears to be as a consequence of

starting medication straight after diagnosis and, therefore, troublesome symptoms disappearing. Additionally, Lawton et al. (2005b)[2A] suggested the type and location of the service newly diagnosed T2D patients receive can change people's perceptions of their diabetes. In this case, the patient had received care at her own GP practice which she then associated as not as serious as those who receive care from the hospital[2A].

2.4.1.4 Expectations of Treatment

Some patients described key motivators which influenced their decision to accept and take their diabetes medicines. Some had expectations of instant success particularly with injectable treatment, while others were influenced by interactions with HPs who had informed them that these medicines could help both with weight loss and diabetes control, as the following quotes demonstrate:

"*They started me on tablets. They weren't making no difference* [evidence from HbA1c test result]. *They upped the tablets. They still didn't make no difference, so for a start they started me on a night injection, just have it at night, nothing through the day, carry on with the tablets. But it still weren't going down as it should have done, so they started me on insulin.*" (Interview 18: white female, on insulin therapy)[9]

"*When I was put on metformin it was almost sold as a good one that would help lose weight as well…*"[2C], and could help with relief of symptoms[2A]

2.4.1.5 Expectations of Care

The moment patients are prescribed a diabetes medication, there appears to be an increased need for further information about their diabetes and their new medicine, particularly prior to and during treatment initiation (Figures 2.2-2.3). Generally, individuals wish to consult an expert[1, 2A, 6], someone who, in their view, is trustworthy and makes them feel confident that their medications are appropriately prescribed[1, 11] and wished for continuity of care between primary and secondary care, or even between HPs [4]. Most information needs about insulin were associated with the advantages and disadvantages of taking insulin[4, 9, 14], the type of insulin and

doses required to control their diabetes and any changes required in the type and doses of insulin[3, 6, 7B], as well as guidance on dietary changes[6], and training to inject insulin correctly[6]. Following experience from taking their diabetes medicines, patients' needs for information are still high[2B, 2C,15, 16], despite not questioning any medication changes[2B] and expecting ongoing prescription of them[2A, 2B]. At the outset, they want to receive information about their medicines that it is easy to understand[11] using "*layman's*" language and avoiding "*technical terms*'' (White male, tablets, interview no. 20)[16]. Also, they want non-judgemental guidance[2B] on alleviating any negative experiences with their medicines and how to deal with missed doses.

Furthermore, patients want to be better informed about the need for their medicines; "*…I don't want to take drugs unless they are necessary…*" (White British male, aged 55, prescribed five medicines)[15], *"…I have no idea what that's for… 'cos I go to my doctor; they don't tell me what the tablets are for...."* (male 60–64 years with diabetes, cancer, asthma, tuberculosis)[16]. This is also important if they hold negative views about their medicines, for example

"… if you are on certain tablets and it doesn't work they don't take you off that tablet. They give you a next tablet to go on with the other rest that you take. I don't find that very helpful, because if the tablets are not working why should you go on taking a next tablet on top of there, and a next tablet." (African-Caribbean male, aged 72, prescribed seven medicines)[15].

2.4.1.6 Negative Perceptions of medicines

Negative perceptions associated with taking medicines were common in these patients. Although these may appear as general concerns rather than specific to their diabetes medicines, they are ongoing issues that require to be discussed with HPs. One of their major concerns is medicines' effects on their body and health. Patients described medications as being unnatural[1, 2B, 3, 12] because, *"you don't know what you're putting in your system"* (Female, Round 4)[2B] and hence, they were concerned

about the chemical nature of tablets[12]. The possibility of taking multiple medicines or doses long-term could be damaging to their health[1, 2B, 12] as this man describes,

"*Initially it was just two metformins a day, and then it was increased to four by the doctor. And then there's blood pressure tablets to take and then aspirins and so on. So it all adds up and, y'know, if you take seven, eight pills a day and you wonder [laugh] is it the right thing? This can't be good for me in the long run."* (Indian, male)[1]

Also, patients do have preferences in the amount of medicines per day that they can cope with taking[16]; suggesting that *"…I've more in the house than they have in a chemist shop"* (female 80–84 years with asthma, angina, diabetes, rheumatoid arthritis)[16], and *"…anyway the point is that I just don't want to take, I take enough medication for diabetes"* (male 70–74 years with osteoarthritis, diabetes, gastric reflux)[16]. Most patients on complex diabetes and non-diabetes medication regimes were worried that taking these medicines together could counteract their individual effects [1] or "*that's three lots attacking the kidney*" [2B], after patient information leaflets confirmed their suspicions. Therefore, they expressed the need to minimise the amount medicines or simplify the medication regime "*Like the metformin, I often wish it would double (strength), and it wouldn't be so many pills, y'know. Or instead of being 4 gliclizide, 4 metformin, I could just take one pill in the morning*" (F36.4)[2B], in order to help overcome their concerns and cope with the demands of managing their diabetes.

Patients taking insulin also feared developing possible complications[4], as well as worry about hypoglycaemia[4, 6, 8] whether they had already experienced it[6] or not[4]:

"*I think it's rather dangerous for a diabetic to be on his or her own you know, because I find that when I go into hypoglycaemic, sometimes it's a struggle to maybe get to the kitchen*." (Caribbean, Male, insulin group)[6].

Similar to patients who refused insulin, patients who started insulin were, too, worried about needle size and mastering the technical skill of injecting[3, 7A, 14].

Interestingly, patients' perceptions of insulin as a "threat" (see 2.4.1.3) had now transformed to a form of "punishment"[4], perhaps originated from the way in which insulin was introduced, believing it was unjust[3] and its association with negative stigma[4, 9]. Nevertheless, not all patients saw insulin in such a negative way. The study by Morris et al. (2005)[3] indicated that there was a gender divide, with women seeing insulin as a punishment whereas men saw it as a form of treatment which would help them[3]. However, Phillips (2007)[4] stated that most of her participants saw insulin as punishment. Both studies had small sample sizes (n=14), however, with equal numbers of men and women, so it is difficult to ascertain whether women are more likely to view insulin as a punishment than men.

Furthermore, an ongoing concern with insulin was the burden they experienced since they started taking it. Patients described anxiety about losing or affecting their driving licence[4] because of having to renew it every three years. They also described worry about their holiday insurance as they were required to complete extra forms[4], "*I can't do anything and I can't go abroad. I can't do anything 'cause I've got to take this insulin, and it devastated me*"[3]. Injecting in public was an issue; particularly for those who needed to inject at least once with meals:

"*It didn't bother me about using a needle but if people are watching you […] you don't know how they feel about seeing people inject themselves. So, normally, I try to do it in, like a private way.*" (Participant 42), "*I just don't think I would like to do anything like that (inject) in public, whether I did it in my stomach, on my arm or anywhere, no. No. They might think I'm a junkie!*" (Participant 31)[7B]

Having to take insulin for some patients was seen as an inability to live a normal life [3, 14] and that it is hard to manage their diabetes [4] and harder to lose weight [8]:

"*You become a slave to it. I know I still am a slave to it but not to that extent and if I can get off it altogether again I will. I will go down fighting – I will!*" (Mr 15, aged 65 years) [14]

2.4.1.7 Negative Experiences with medicines

Once patients started taking their OGDs they experienced difficulties mostly related to the side effects from their medicines[1, 2B,16], such as "*wooziness*", "*really bad stomach cramps*", "*bad diarrhoea*" or "*having hypos*"[2B] (Figure 2.2). On the other hand, initiation of insulin was described by patients as a traumatic experience "*It was … totally frightening. You don't look it and you don't like to say it, but you're really, really scared*."[3] (Figure 2.3).

Negative experiences and feelings of disappointment and failure were also the result of realising that their medicines had not helped them to feel better or worked for them[3,4,11], particularly when others had found great benefit from the same medicines, or when they expected to feel better instantly, as the following quotes demonstrate:

"...It's like my friend who came over and said 'I have got diabetes and I am taking these tablets and it is all normal for me' and then I said 'I take the same tablets—so why is it not working for me?' I just got worried on top.'' (South Asian male, interview no. 3)[11]

"[my] son …He says, "When you take this needle, the first one mam, you'll feel great." He said, 'you'll feel like dancing on the top of the world' …And I took my first needle and I sat there waiting for the euphoria and it didn't happen…" ([3] taking insulin for one month)

Managing diabetes with insulin was often described as "*frustrating*" and "*hard*"[4]:
"You do exactly the same thing, the same food everything the same, but then suddenly you see these high sugars again and you sit down and go through everything, but you can't find a reason" ([4] taking insulin for at least 2yrs).

2.4.1.8 Positive Experiences with medicines

Patients had positive experiences once they started taking their diabetes medicines, commonly claiming that they "*feel better*"[2B, 2C, 3] and healthier[4], they have "*much*

more energy now"[2B] and that these medicines "*are what really work*"[1]. Those who presented with symptoms prior to prescription, found relief from their symptoms[6] because they had either gone "*instantly*"[1] or had lessened; "*I'm only going to the toilet twice at night, so I feel that's come down a good bit"* (F16.4)[2B].

Once patients initiated insulin they were surprised to find they were using pens, which they saw as more discrete and easier to transport[7A]. Also, they claimed that injections were not as painful as they had anticipated[3, 4, 6, 7A] nor as difficult to do[3, 6], as the following two quotes describe:

"*Let people realise that having insulin is just as easy as having the tablet. Before, I did not think that*" (Caribbean Male, insulin group)[6]

"*Wow it was mega that, when I put it in me belly. I was dead chuffed 'cause I hardly felt anything*"[3]

2.4.1.9 Positive Perceptions of medicines

The positive experiences with medicines reinforced their positive perceptions, i.e. they are beneficial[2B, 15] and effective[1, 3, 7B] and help control diabetes and preserve health[3, 4, 6, 7B]. Some patients indicated that their medicines are more effective in managing their diabetes than lifestyle[2B], and insulin is better than tablets[4, 6], particularly when its effects were seen over time[3, 7B]. Patients also seem to prioritise certain medicines over others [1, 15] even if they are for the same condition, for example:

"*The gliclazide, comes with the er—the pioglitazone after that and then after that the ramipril to do with my blood pressure…*" (South Asian male, aged 53, prescribed four medicines),

"...metformin. This is one of the most important drugs to take for it." (Indian, male) (Pakistani, male)[1], and

"Well if the sugar and the blood pressure get high then you could have a heart attack. But with taking that (aspirin) it lowers the risk. But the metformin is the main one that's the main one that's helping." (African-Caribbean female, aged 82, prescribed three medicines)[15].

2.4.1.10 Self-Regulation

As seen in section 2.4.1.7, some patients found the self-regulation strategies brought negative feelings associated with the negative experiences of taking medicines. However, for others, the use of SMBG[2B, 11], or evidence from other external results from HbA1c tests[2B] (Figure 2.2, bottom box in figure 2.3) reinforced their positive experiences and perceptions of their medicines. These strategies, over time, proved that medicines had helped with blood glucose control[3, 7B, 11], as this man describes:

"…I've got this stick thing to measure it with and I have also got this machine and with that you know what it is, whether it is 7.5 or 8.5 or whatever.'' (South Asian male, tablets, interview no. 11)[11]

These strategies seemed to have more impact on those who were asymptomatic or were "*unconvinced*" that their medicines were effective until they attended a review of their diabetes in which the general practitioner "*tested it, and it's come down to seven point something and he's really pleased"*[2B] or tested themselves "*everyday for a week, take all the readings, then start taking the metformin and see if it makes a difference.*" Subsequently, the lower readings recorded provided the "*proof*" they needed that their "*tablets were working*"[2B].

Conversely, those patients who saw their diabetes medicines as useful for instant relief of symptoms, used these self-regulation strategies and predominantly took all their tablets when they considered their readings to be high[1]. Others expressed thoughts about coming off their tablets, as highlighted by this patient who was prescribed metformin,

"*I don't even consider myself having diabetes you know because the blood sugar has stayed within normal ranges since the first sort of month or two after being diagnosed...while I'm managing it myself then I don't need any real intervention at the moment from anybody else… now that the weight's gone my initial thought was 'well maybe I need to change what I'm on'. But I just asked when I was down there I said 'Is there any merit in me just coming off everything for a trial period?"* [male, 40yrs, round 3, off Metformin][2C].

2.4.1.11 Patterns of Medicine Taking Behaviour

Three different patterns of adherence were identified in this review; full adherence, unintentional non-adherence, and intentional non-adherence. These were then split into five different patterns depending on the level of emotions felt in relation to whether guilt was attached to the behaviour.

(i) Adherence and Unintentional non-adherence with guilty emotions (Figures 2.2-2.3)

Those patients who fully adhere to their diabetes medicines seem to strongly believe on the positive aspects of these medicines, specifically that they are beneficial and effective for their diabetes management, and seem to give greater importance to these medicines than other medicines for comorbid conditions[15, 16].

"*And like I said the heart tablets and the diabetes and the warfarin I never fail to take, like I said it's just sometimes it the cholesterol that I've forgotten."* (White British female, aged 67, prescribed four medicines)[15].

On the other hand, there were patients who despite strongly believing in the positive aspects of their diabetes medicines, they sometimes unintentionally non-adhered to their medicines[2A, 2B, 7B, 15]. In most cases, this was due to forgetfulness when routines were broken, particularly when they ate out and "*forgot to take them with me*" (M1.2), or if they are asymptomatic, as diabetes is not *"at the forefront of your mind"*[2B], or due to confusion when taking multiple medicines, as these quotes demonstrate,

"*What (name of nurse) said to me was to take it at bedtime. Which is fine except that I tend to go to bed very late and so we agreed that I would take the insulin at about 10 o'clock. Sometimes depending on what's happening and what I'm doing, sort of 10 o'clock's gone past and I haven't taken it and it might be 11 o'clock or half past 11 before I remember to take it.*"[7B]

"…believe me, if you take a lot of tablets, you've no idea when you've taken them, and what you've taken" (M37.4)[2B].

Guilty emotions were attached to this medicine taking behaviour, "*really conscious stricken if I forget or think I've missed it*" (M17.4)[2B]. Yet, despite the positive perceptions and their personal attempts to increase their adherence level, these patients voiced concerns about the negative perceptions of these medicines (See 2.4.1.6). This group of patients (adherent and unintentional non-adherents) attempted a number of strategies that promoted adherence (Figures 2.2-2.3). These included establishing routines in order to fit the medication into their life[2B, 7B], using medication boxes, carrying insulin pens in pockets/bags or keeping their basal insulin next to their bed or their prandial insulin in the kitchen, or identifying the logistics of where and when to inject[7B] or other visual reminders such as keeping drugs by the bedroom window and only closing the curtains after they had taken them[2B]. Family and friend support was also important as they would remind patients to take their pills[2B] or injections[4,7B], and partners would also encourage them[4, 7B]. Some patients found support in a group setting when they initiated insulin[4].

(ii) Unintentional non-adherence without guilty emotions (Figure 2.2)

Some patients unintentionally non-adhered to their medicines as a result of forgetfulness. It appears that this is also due to not having any diabetes related symptoms[2A]. However these patients did not appear to feel guilty as they rationalised their behaviour expressing that they are ''*a bit erratic*'' about taking their tablets, ''*I'm very bad for the one during the day, I forget that*'' (Mary, 47yrs, Round 2, Metformin)[2A]. The relationship between lack of guilt and lack of symptoms was therefore reinforcing their belief that diabetes is not serious.

(iii) Intentional non-adherence with guilty emotions (Figure 2.2)

There was one patient who intentionally non–adhered to his diabetes medicines by skipping doses in order to avoid side effects from this. This patient felt unable to ask his HPs whether he could skip doses of gliclazide "*to avoid hypos*" on "*a rare boozy night out*", fearing he might get his "*knuckles rapped*"[2B].

(iv) Intentional non-adherence without guilty emotions (Figure 2.2.-2.3)

This group of people engaged in intentionally non-adherent practices without feeling guilty, but did so for different reasons. In line with Campbell et al.'s (2003) review, guilt was not an issue for those who exemplified intentional non-adherence, as they were fully aware of what they were doing and the reasons for it. Some patients adjusted the amount of tablets by reducing their medicines' doses, or stopped taking them altogether because they strongly believed that their medicines would have a detrimental effect on their overall health and body[1, 16], as this patient explained:

"*No, but that's not to say I wasn't prescribed them, yeah, I didn't take them, I don't want nothing to do with tablets, i.e. my diabetes tablets, I've got boxes of them. When I get to about fifteen, twenty, I take them back to the chemist and say they over prescribed them and say I don't need them…*" (male 45–49years with cancer, diabetes, hypertension, asthma, depression)[16]

While, patients on insulin described that they either advanced or delayed their mealtime injections so that they could inject in the car on route to the restaurant, or upon arriving home[7B], as a result of avoiding the associated stigma with injecting insulin in public. Other patients skipped tablet doses in order to avoid experiencing side effects from their medicines, like when "*suddenly become dizzy"* (Pakistani, female)[1] or when "*they make you dry if you take too many*" (Pakistani, female)[1].

Patients who believed in the benefits and effectiveness of their medicines also adjusted the amount of tablets particularly if they strongly believed that these medicines work by instantly alleviating the symptoms of diabetes, as described by two Pakistani patients:

"…for the last three months I'm just taking them twice a day. It's just when I feel I'm tired I take another one. If I'm fine then I won't." (R26, Pakistani, male)[1]

"Oh I feel fine and I'll take one today, I won't take two." (Pakistani, female)

These patients also used SMBG as a strategy to take all tablets when they considered readings to be too high[1]; others manipulated their tablets according to their diet, as shown by this man:

"(I take)…*two [tablets] when I don't spread too much jam on my toast or even sometimes I don't even spread any. If I feel like a bit of a pleasure then I will put some on and then I will take the extra tablets."* (Pakistani, male)[1]

Health professionals also seem to influence patients' medicine taking behaviour. Participants who were advised by them to adjust their amount of tablets for religious purposes (such as during Ramadan), did so at other times usually without seeking medical advice[1].

2.4.1.12 Strategies to overcome negative aspects of insulin (Figure 2.3)

Patients appeared to be driven to return to some form of normality in order to avoid or overcome any of the negative aspects of insulin as discussed above (2.4.1.6-2.4.1.7). Strategies employed included talking to friends and family about how to treat hypoglycaemia[4], starting insulin in a group setting[4], or initiating group support in their work place[4]. They regularly referred to the original written material provided by HPs when they started insulin and actively sought further information on diabetes treatments[4], often encouraged by their partners and family[3, 4]. Some patients also became self-reliant in adjusting insulin doses, and this gave them a great boost of confidence[3]. In actively doing all of the above, many patients stated they became experts in diabetes over time[4, 14], even better than some HPs[4]. However, some patients consciously decided to change their social life in order to avoid injecting in public and would rather avoid eating out:

"*I wouldn't go out to lunch with them (friends) and in the end I had to tell them why. I said, 'I can't. I have got to have insulin. And I am not going to go into a toilet"* (participant 23)[7B].

Others mentioned they ate regularly to avoid feeling weak, which according to the authors was unlikely to be linked with low blood glucose[12]. Although most patients manipulated their diet and medication regimes to live a life as full as possible, some patients limited their social activities in order to adhere rigidly to medical advice; a finding in contrast to that of Campbell et al.'s (2003) review.

2.4.1.13 Lifestyle behaviour (Lifestyle Adherence and Non-Adherence)

Adherence to lifestyle measures was generally a first self-treatment attempt by patients following diabetes diagnosis or when they were prompted that they will need to take medicines for it[2B, 2C]:

"…we changed our diet overnight, for the whole of the family. The sugars went out and the fat went out and healthy food just came in immediately and that helps."(South Asian male, aged 53, prescribed four medications)[15]

Those patients who thought that their diabetes was not serious and those converted to insulin, also gave great importance to lifestyle measures[2C], making changes such as adhering to healthy eating plan[4], with some patients referring to being *"…cautious what I eat like*" (Caribbean Male, insulin group)[6], whereas others used a moderate approach[4, 6, 14] as highlighted by the following quotes:

"*Yeah but sometimes I taste a little thing what I know I don't supposed to really eat… You can eat everything but small amount of it.*" (Caribbean Female, insulin group)[6]

"*I'm trying to pass on my experiences. A little bit of what you fancy. Don't stop ice cream, don't stop biscuits, don't stop eating.*" (Mr 06, aged 71 years)[14]

However, over time patients struggled to keep up with the diet and the physical activity[2A, 2B, 4, 10] realising that their diabetes progresses *"…no matter how careful you are"* (Pakistani, female)[1]. Hence, they accepted that eventually they would be dependent on their medicines and changed their attitudes towards them, so that they believed them to be more effective in managing their diabetes than any lifestyle measures[2B, 2C, 15]. Moreover, those on insulin, often felt frustrated when they could not see the results of their efforts[4] and led to feelings of not wanting to bother[4] because it was impossible to achieve good diabetes control.

"You have to be more proactive on insulin' (Luke), and *'When you go onto insulin you take your diabetes more seriously. If I eat the wrong thing I start to feel sluggish"*[4]

Some even indicated that the lifestyle and medication are two alternative ways in which they could manage their diabetes, suggesting that once you take medicines they could eat what they want[2C, 6, 14], as medicine is the only way to control blood glucose levels[6]. Additionally, some patients taking insulin indulged on foods that they would have restricted whilst on tablets; "*With the insulin I eat ANYTHING*." (African Female, insulin group)[6].

Others were uncertain how to control their diabetes with diet as they could not identify if any changes to their lifestyle had an impact on their diabetes control [11], whereas when they take medicines they could see their effects through SMBG. Those who thought that their diabetes was not serious indicated "*being naughty*" and to *''doing wrong"* with their eating habits, probably ''*because I've got a bit complacent, I must admit''*[2A]. Therefore, it is no surprise that a four-year longitudinal study of retired T2D patients (aged 50-62) found that lifestyle behaviours, such as being on a special diet, following an exercise regime, or trying to lose weight, diminished over time (Nothwehr & Stump, 2000). The authors indicated that their participants showed lack of commitment to self-management practices but perseverance to lifestyle measures could be associated with individuals' change of views and attitudes towards their diabetes treatment including medications.

2.4.2 Line of Argument Synthesis: Patient's journey - the impact of diabetes medicines on re-evaluating oneself

This is the final stage of synthesis. After consideration of the two medicine maps separately and behaviour theories examined in section 2.3.4, they were, then, brought together to construct a line of argument (Noblit & Hare, 1988). Figure 2.4 visually represents this final synthesis. It illustrates patients' trajectories from receiving diagnosis and/or the prospect of prescribed medicines for their diabetes. Alongside the patients' journeys can be seen relevant HP labelling which has emerged through the review of the studies. Although patients' journeys were the main focus of this review, HP labelling was necessary as patients inevitably interact with HPs for managing their diabetes at various stages. Many of the studies were conducted by HPs or with health-related backgrounds. Health professionals, particularly GPs or consultants, are the first point of contact for confirming the diagnosis of diabetes and for prescribing medication. They also interact with patients through clinic appointments and various tests offering advice about how to best manage the condition.

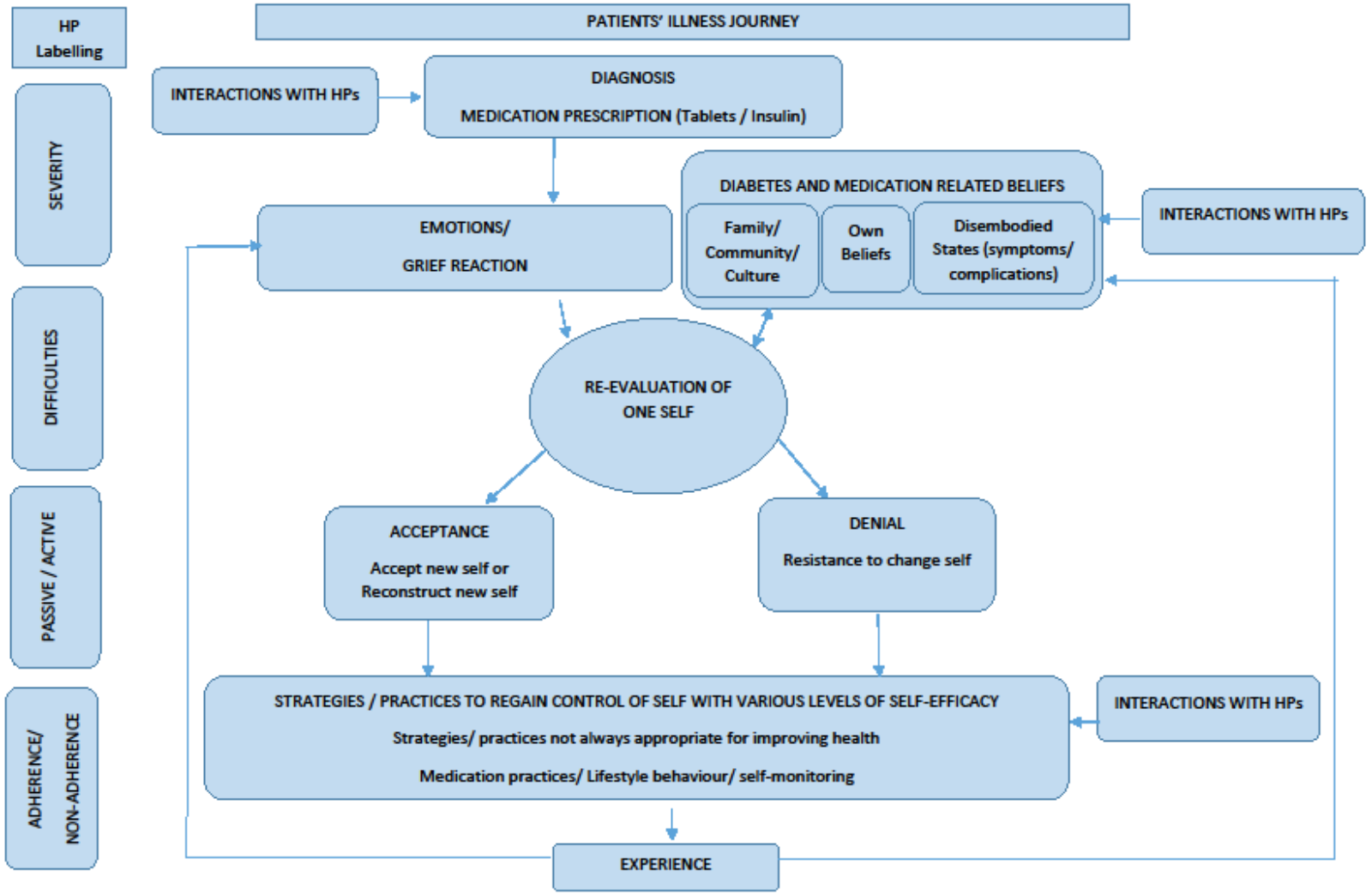

Figure 2.4: Line of Argument Synthesis

2.4.2.1 Severity

Both medicine maps revealed that patients associate the severity of their diabetes with the type of treatment (lifestyle versus medicine) and the type of medicine they are prescribed (tablet versus insulin). However, perceptions of severity of their diabetes appear to change over time. Interactions with HPs can influence patients' perceptions of severity of their disease, as indicated by these two patients:

"*My GP said my blood sugar was okay. He told me to keep my blood pressure down and my cholesterol good, and I would be fine.*" (Man, aged 55 years, advised to start insulin but refused) [(5)]

"*The doctor said anything under ten (mmol/l) was acceptable. I started testing my blood glucose levels and that was really when I began to realize that tablets weren't helping me. So I went to the doctor and said, 'I want to go on insulin.*" Patient 20 [(7B)]

The types of health care service they received also influenced their perceptions (Lawton et al., 2005b; Noakes, 2010)[(2A, 6)]. Patients generally recognised diabetes as a progressive disease and accepted that certain treatments may be required in the future for its management, as these quotes show:

"*I think I was told it was in the gradual stages... These are the type of tablets that you need to take. If you control your diet, you know, cut down on your sugars and fatty food that you'd be eating, it will take a long while, but eventually you will need to go on to insulin… So each time I went there was a bit more progress on there so they said 'Alright, okay this is what will happen. This will happen. This is the type of insulin you may have to take but not yet.' So it was all gradual. It wasn't all blunt and straightforward saying 'Right tablets for three years, insulin next year.' It wasn't like that. They said it will build up gradually. Eventually in the later years in your life you will be going on to insulin as all diabetics do.*" (Interview 09: South-Asian male, not on insulin therapy)[(9)]

"...from my experience of diabetes, it's just an inevitable part of it that you're going to end up being on insulin anyway...I was expecting it..." (Case study 4 interview 7 South Asian Male, 57yrs, DM duration 20yrs, on insulin for 5yrs)[9]

Health professionals and patients do share common views about diabetes (Cohen et al., 1994; Hunt et al., 2001), although these views are not totally congruent, partly because patients' views are influenced by many other factors (see 2.4.2.6).

2.4.2.2 Difficulties

Authors described the many difficulties that patients faced in managing their diabetes on a daily basis which included: confusion with taking multiple medications or understanding the purpose of their medications, injecting in public, integrating the regime (medication, diet and exercise) into their lives, acquiring relevant knowledge, and coping with social events[2B, 7B, 10, 11, 12, 13, 16]. These are common difficulties identified in other studies (Cohen et al., 1994; Haslbeck & Schaeffer, 2009). Studies in this review did not delve into HPs' views on managing their patients but the limited quotes suggested that patients and professional discussions were based on lifestyle and medication changes in order to control blood glucose or lose weight and reduce complications. While pathophysiological difficulties are a concern for health care providers (Cohen et al., 1994; Hunt et al., 2001), patients did not expect anything other than being prescribed an appropriate medication and consulting an expert for advice relating to avoiding medication side effects and practical ways for managing their medicines on a daily basis or special occasions.

2.4.2.3 Passive- Active Patient Role

Patients indicated that the decision for new prescription and changes to their medications were made by doctors[1, 2B, 3, 4, 6, 7B, 10, 11], often without questioning it or discussing it with them, and not fully understanding the reason for taking their medicines, unless supported by clinical evidence[2B, 7B]. Hence, they were seen by authors as having a passive role with regard to their diabetes self-management. Whereas, patients who indicated that they tried to negotiate their medication regime

or requested to be put on insulin were seen as being active participants[2B, 3, 9]. However, patients appeared to trust doctors and their expertise in making medication changes[1, 7B] as the following quotes suggest:

"[patient] *The doctors are trained to tell us what to do.*
[interviewer] *You could discuss the problems you are having in the rest of your life—like your housing, work or any of those things and tell the doctor how much they are effecting you.*
[patient] *Doctor is not there to do that, doctor is there to give us medicine, to make, to tell us what is wrong and then we take medicines*"(R5) [10]

''*I'm sort of following doctor's orders. As far as I know the stuff he's giving me is holding me nice and steady.*'' (White male, tablets, interview no. 20)[11]

2.4.2.4 Adherence or Non- Adherence

Authors often described participants' actions towards their medications and lifestyle behaviours as patterns of adherence or non-adherence[2B, 2C, 7B, 15]. The term adherence, as seen before, relates to the extent an individual takes their medicine or follows other health-related treatments which corresponds with agreed recommendations from a health care provider (WHO, 2003). Although this term is used in medical literature, it does not correspond with patients' perceptions of how well they are managing their diabetes medicines and lifestyle (see 2.4.2.9).

2.4.2.5 Grief Reaction

In this review, patients' journeys started either at the time of diagnosis and/or at medication prescription. What was identified throughout this review was the emotional reactions to changes in medication, which paralleled those seen at diagnosis. These reactions can be described as representations of grief (Brown, 1985) with emotions such as shock, guilt, denial, anger, bargaining, depression and finally acceptance/adjustment, as captured in these quotes:

"*In January of o seven they shocked me by saying, 'Well, we're going to have to put you onto a different injection' and I thought what, just the different injection? And they said 'No, no, as well, and by the way, up three times a day.' So I then realized, five times a day!*" (Participant 28)[7B]

"My health will remain good, by the Grace of God, so long as I keep praying." (Bangladeshi Man, aged 70 years)[5]

"So why have I got this diabetes when I've looked after me'self all these years? Why?" (Ruth [3])

"I was devastated [about being prescribed glipizide]. I wasn't happy at all. But it was explained to me that diabetes always progresses…" ([1], Pakistani female)

It is acknowledged that grieving takes time (Brown, 1985), and the revival of grief reactions during changes in medication have been referred to as chronic sorrow i.e. the reactions connected with repeated losses of independence, control, status, loss of identity as a healthy person generating a disparity between the current reality and the desired reality (Ahlstrom, 2007). This review identified that as patients progressed from diet to tablets to insulin, their emotional reactions were stronger and impacted upon the way they coped.

2.4.2.6 Diabetes and medication related beliefs

Authors often described that patients' understanding of diabetes and its treatment was influenced by the community and culture they live in and family experiences[3, 5, 6, 9, 11]. Patients' presentation or lack of symptoms and complications also appeared to have an impact on their perceptions of the condition and specifically about their own diabetes and its management[2A, 2C, 4, 9, 11, 12, 13, 14]. Authors discussed how patients perceived the lack of symptoms as their diabetes not being serious whereas the presence of complications was seen as a more serious form of the disease.

In addition, patients own beliefs about medications had a direct impact on the perceptions of their disease and vice versa as seen from the medicine maps and the final model. Those who had negative perceptions (greater concerns) over their diabetes medicines were more likely to report practices that suggested intentional non-adherence, whilst those who had more positive perceptions of their medicines (greater necessity) were more likely to report fully adhering to their medicines or the ways they had adopted to promote adherence. This balance of concerns over the negative effects of medicines and necessity for diabetes management is consistent with the necessity-concerns framework (Horne & Weinman, 1999). Furthermore, those who believed that their diabetes is serious were more likely to report greater necessity about their medication treatment and, therefore greater adherence.

2.4.2.7 Re-evaluation of one self

Together beliefs and emotions reinforced an evaluation of oneself leading to either accepting the "*altered self-image*"[3] or reconstructing a new self by adjusting their beliefs, or resistance to change, as the following quotes describe:

"*I just said to myself one day, 'you've got this diabetes, and you need the insulin to keep you well. You either don't take the insulin and you're not well, or you take the insulin and you're well. The choice is yours' …I [now] see insulin as something that will keep me healthy.*" (Ruth) [3]

"…So I am being a fool to meself where that is concerned, because I have been told I've got to take them [diabetes tablets], but I find that so long as I behave myself, then I'm fine." (male 45–49 years with cancer, diabetes, hypertension, asthma, depression) [16]

2.4.2.8 Acceptance-Denial

Generally, acceptance to change meant that medicines were accepted as part of the successful management of diabetes. However, resistance to change did not necessarily mean resistance to taking medicine as seen from the first medicine map

(Figure 2.2). Different levels of resistance and acceptance of their diabetes identity and self-management have been found in other research (Savoca et al., 2004; Ockleford et al., 2008). In this review, regardless of the patients' positions to either accept their new self or resist, they all employed a variety of strategies to regain self-control. This was apparent from the authors' use of descriptions such as, "*getting right or losing control*" [(4)], "*down to me, up to them*"[(2C)], "*losing normality*"[(3)].

2.4.2.9 Strategies to regain control

Medication taking behaviour, lifestyle behaviour and SMBG were all tactics patients engaged with to regain control. Such strategies were often associated with patients' levels of adherence or non-adherence to treatment, and to being passive or active in managing their diabetes. Although these terms (adherence/non-adherence, passive/active*)* are used in clinical research and practice (Figure 2.4), for patients these are rational decisions or actions which enable them to live as normally as possible and to minimise the impact of their diabetes and medicines in everyday life. This approach to life is often seen in patients with chronic conditions (Haslbeck & Schaeffer, 2009), although patients have different levels of self-efficacy and coping efficacy. Authors often described patients': "*commitment to taking medicines*" [(2B)], a "*sense of growing confidence*"[(3)], "*responsibility*"[(2B, 4)] and "*self-determinacy*"[(2C)]. Patients were "w*illing*", "*keen*", and making conscious and deliberate "*effort*"[(4, 7B)] and "*attempts*"[(2B)] to find out about diabetes and adapt their daily practices to fit their medication, with some "*requesting*" new medicine[(7B)] or "*negotiating*" their regime[(2B)]. Still others reported feeling "*powerless*"[(3)], and expressed "*concern*" or "*worry*"[(6)] because they had "*tried hard*"[(4)] but had been unable to make successful changes leaving them with feelings of "*not wanting to bother*"[(4)].

Although not all strategies as outlined in the medicines maps appeared appropriate for health improvement, those patients who seemed to effectively manage their diabetes medicines were those who identified specific strategies to help them adhere to their medicines. These strategies related to having established routines to overcome problems with taking multiple medicines, inconvenient schedules, and lack of reminders. From this data, it can be suggested that those patients with better

medication adherence have increased self-efficacy and coping-efficacy levels. Self-efficacy, as a factor predicting treatment adherence, was found in the meta-analysis by Gherman et al. (2011). The experience of successful and unsuccessful practices reinforces or undermines patients' beliefs about their diabetes treatment and leads yet again to a re-evaluation of self.

2.5 Summary

This systematic review was based on the meta-ethnographic approach as developed by Noblit and Hare (1988), which has become established in health research and enables to make evidence from qualitative research accessible to health professionals and policy makers (Campbell et al., 2011). This synthesis of 16 studies (19 papers) has shown how patients view and take their diabetes medicines, and how the experience of starting or changing to a new treatment results in a re-evaluation of themselves that they either accept or deny. The re-evaluation of self is an endless cyclic process depending on the daily positive and negative emotional and cognitive experiences of self-managing their diabetes alongside interactions with HPs. All patients engage with strategies to enable them to regain control of their life. Those who self-manage well are those who are confidently able to modify their daily routines to fit medication regimes overcoming challenging areas such as polypharmacy, inconvenient schedules and lack of reminders. Nevertheless, patterns of non-adherence (intentional and unintentional) were more common than patterns of adherence reflecting findings from other 'adherence' systematic reviews (Cramer, 2004; Krass et al., 2015).

Lack of sufficient information from health care providers around problematic areas of medicines such as negative beliefs and experience of side effects, can impact adherence and have detrimental effects on patients' health and quality of life. In addition, if patients' expectations of new diabetes medicines result in positive experiences, this can re-inforce the positive perceptions of their medicines and acceptance of them. It is apparent that acceptance of diabetes as a serious disease, acceptance of medicines as necessary for managing the condition, high levels of self-

efficacy and coping-efficacy, as well as positive experiences following new treatment are important for medication adherence. However, as people accept their medicines it seems that they have less faith in lifestyle changes as a way of managing their diabetes. Although weight loss is acknowledged by patients as part of making healthy lifestyle changes it seems it is not associated with self-managing their diabetes, despite the fact that many treatments are having an undesirable effect on body weight. Only a few people were aware of the effects of their medicines on their weight. Furthermore, as patients are not involved in the decision making about their medication treatment, it is unclear whether they are likely to choose a medication based on its ability to support weight loss or control (Purnell et al., 2014) and whether knowing the impact of the medicine on their body weight will affect adherence levels.

2.5.1 Application of theory in medicine taking behaviour for T2D

A number of theories were applied to individual studies in this review to explain medicine taking behaviour. The medicines map and the final line of argument synthesis prove that no single theory can be used to fully illuminate this kind of behaviour. Therefore, more than one theory is needed to explain medication taking practices for people with T2D. These include, in no particular order:

(i) Model of illness representations (Leventhal et al., 1980 cited in Bower et al., 2012) where emotional (guilt and grief reaction) and cognitive factors (illness and medication related beliefs, perceived self-efficacy and coping-efficacy) are involved in changing the self-view and self-practices.

(ii) Necessity-Concerns framework (Horne et al., 1998, 1999) relates to patients who showed they have ongoing concerns about their medicines and this coupled with their perceived need for their diabetes medicines influenced their medication adherence levels.

(iii) Although, the studies in this review did not specifically include HPs' views, from patients' accounts and authors' interpretations there was a sense that patients and HPs portray different explanatory models of illness (Kleinman et al., 1978) which led to the different medical labelling in the final model. So, what HPs see as non-adherence, patients see as rational

ways of taking control of their life. Discrepancy in patient and HP illness models can potentially impact adherence.

(iv) Starting a new medicine for T2D, and not just the onset of chronic illness, indicates a biographical disruption (Bury, 1982). Some of the studies described psychological insulin resistance whereas Jenkins et al. (2010) described psychological receptiveness. However, resistance and receptiveness are concepts very much related to the concepts of denial and acceptance to medicines based on patients' perceived seriousness of their diabetes. Overtime, patients who initiated insulin and were taking insulin for longer than two years were more accepting of this treatment. The final model shows the elements that can have an impact on evaluation of self and the ways in which patients reconstruct their biography.

2.5.2 Strengths and limitations of review

A number of strengths and limitations of this review are worth noting. This review was limited to English language studies and included only published papers, so relevant work in other languages, grey literature or book chapters is not represented. The studies and concepts analysed only focused on participants from the UK, therefore the findings and the final conceptual model may only be accurate for this country and may not be transferable to patients from other countries.

The medicine map, which focused on OGDs was mainly based on two studies and by the same group of authors with three papers derived from one study (see Table 2.6). Nevertheless, similar issues were found in other papers from the polypharmacy and the general diabetes medicines groups. Furthermore, only first and second order constructs were used which explicitly identified patients with experiences of diabetes medication, therefore constructs related to experiences of those patients on diet therapy only are not represented here.

The study by Bissell et al. (2005)[10], although included in the review, did not describe specific patterns of adherence or views about medicines. This was in spite of the

study's focus being on patients' views and experiences of T2D treatment with adequate information provided on the types of diabetes medicines patients were prescribed. One possible explanation for this, is that the paper was more narrowly focused than the others as it was centred on exploring the relationship between peoples' approaches to self-care and to their consultation encounters with HPs. Although issues of difficulties in managing self-care were reported, these were mainly on dietary regimens and how these were affected by other social (type of job-taxi driver) and psychological factors (depression). Nevertheless, the study fitted well within the areas of polypharmacy and multimorbidity and had a pivotal role in elucidating the different explanatory models of illness between patients and HPs.

The intention of the synthesis was to retain rich context of the data looking systematically at the influences of various contextual factors such as diabetes control, body weight, duration of diabetes, type of diabetes treatment, initiation and/or duration of treatment, and use of primary and/or secondary care services but this was difficult due to the failure of many authors to provide adequate descriptions of context or of the impact of context on findings. Furthermore, the process of synthesising is inherently interpretive, so other reviewers may produce different conceptual frameworks. However, many qualitative and quantitative reviews (Polinski et al., 2011; Gherman et al., 2011; Majeet-Ariss et al., 2013; Brudissini et al., 2015) and the meta-ethnographic review by Campbell et al. (2003) identified similar findings and models to this review suggesting that findings are triangulated and credible.

Most studies were descriptive or used a thematic analysis, therefore there were few papers which provided rich and insightful data to fully appreciate patients' experiences and practices with their diabetes medicines. There were only two longitudinal studies, but most studies were based on peoples' memories of past experiences and their views after medication changes had occurred and, therefore, prior to interviews or focus groups. Nonetheless, 19 papers provided sufficient data to reach a "line of argument" that resonates with other published reviews as noted before.

A strength of this synthesis is reflected by the systematic identification of papers including the use of different search strategies (broad and specific) and use of multiple databases. The critical appraisal by two of the research team and the inclusion of high quality papers with CASP scores equal or above seven certainly enhanced the rigour of the review. In addition, detailed discussions among the research team about the interpretation of the findings was conducted at each stage and this ensured the transparency and trustworthiness of the findings.

2.5.3 Research gaps

The synthesis shows that to understand medication adherence, more than one theory is needed. The final model and medicines maps demonstrate how the theories could be interlinked and applied to future research. Based on the findings of this synthesis further research is needed both to understand peoples' experiences of diabetes and its treatment in order to develop informed patient-centred approaches to improving treatment adherence among people with T2D. Research should focus on understanding how patients' views of their medicines change over time based on longitudinal studies. To go deeper into the "*subjective story"* we need to see and hear how it develops as it is lived (Charmaz, 2000), therefore we need to understand peoples' views prior to starting a new medicine and follow-them up to understand their experiences. Research should also examine the impact on adherence by investigating peoples' beliefs about other factors such as glycaemic control change, age, gender, diabetes duration, type of treatment including other injectable medicines, treatment duration, and degree of medication burden, as well as types of services and amount of information received. Most importantly, none of the studies in this review reported participants' BMI or body weight (see Table 2.7), therefore the relationship of medicine taking behaviour and body weight changes, as a result of their medication treatment, has not been explored in patients with T2D. Without knowing what causes changes in people's perceptions and behaviours there will be uncertainty as to which interventions can help support patients to improve their health and quality of life.

CHAPTER THREE: GENERAL METHODOLOGY AND RECRUITMENT STRATEGY

3.1 Introduction

This chapter provides information on the methodology of the current study and the recruitment strategy. Initially, an overview of what constitutes mixed methods research is given, followed by a justification for the methodology adopted in this study. Then, an outline of the aims is illustrated with questions and objective statements; with a justification of the study design, sample selection and sample size. Finally, a summary is provided of the recruitment strategy, and detailed information about ethical approval and considerations.

3.2 Mixed Methods Research

Tashakkori and Teddlie (2003, p.711) defined mixed methods research simply as the research design in which qualitative and quantitative approaches are used in types of questions, research methods, data collection and analysis procedures and inferences within a single study. It is important to note that there are different terms used in the literature to describe this approach, such as multimethod, mixed methodology, quantitative and qualitative methods. However in recent literature the term “mixed methods” is used, and will be used in this thesis.

Mixed methods research is an emerging dominant paradigm in health care research (Doyle et al., 2009). It has been described as the third paradigm, often called *Pragmatism* (Johnson & Onwuegbuzie, 2004). *Paradigm* is defined by Morgan (2007) as the set of beliefs and practices that guide a field, and most commonly associated with four distinct elements that are used to compare different paradigms. These elements include; Epistemology (how we know what we know), Ontology (nature of reality), Axiology (values) and Methodology (the process of research) (Morgan, 2007; Guba & Lincoln, 1994; Creswell, 2009). Traditionally, researchers proposed that constructivism and/or interpretivism (qualitative research) and positivism (quantitative research) are paradigms that have different world views, each with a distinct epistemological stance and conceptual framework (Sale et al., 2002; Morgan 2007). Many believe that these paradigms cannot be mixed or combined because of those distinct differences (Holloway & Wheeler, 2010). However, Allwood (2012)

argues that this distinction, which is often taken for granted, can be problematic and limited to the development of new research methods. According to Morgan (2007), the pragmatism approach offers a new framework that does not necessarily reject the two paradigms of positivism and constructivism. Instead, it shows how this new approach offers opportunities for advancing our knowledge and research practice. Despite the controversial debates about the issues surrounding mixed methods research, which started almost three decades ago, this has become a popular approach (Morgan, 2007) within the last decade (Wisdom et al, 2012), particularly in Health Care (Teddlie & Tashakkori, 2009). This is evident through published articles and funding (Weitzman & Levkoff, 2000; Cooper et al., 2003b; Walters et al., 2008; O'Cathain, et al., 2007; Clarke, 2009; Carr, 2009; Latter et al., 2010).

It is believed that the problems that are addressed by social and health scientists are complex. Therefore, the use of either quantitative or qualitative research individually is not adequate enough to address this complexity (Creswell, 2009). The combined use of methods provides a practical and outcome-oriented method of inquiry producing superior research compared to monomethod studies and an expanded understanding of research problems (Johnson & Onwuegbuzie, 2004; Creswell, 2009). This has huge potential in health care research where there are many different and complex factors that can influence health.

Many proposed motivations suit the combination of qualitative and quantitative research (Morgan, 1998; Johnson & Onwuegbuzie 2004; Bryman, 2006; Small, 2011). Often the descriptions of these motivations resemble one another, even though different terms have been reported in the literature. However, these motivations can be merged into three categories; Complementarity, Confirmation, and Expansion/Development. The function of *Complementarity* lies with the idea of maximising the strengths and minimising the weaknesses of both qualitative and quantitative research methods (Johnson & Onwuegbuzie, 2004). This, in turn, provides stronger inferences (Teddlie & Tasshakkori, 2009) producing a complete and comprehensive picture which contributes to the understanding of the study object (Tritter, 2007). Mixed methods research is used for *Confirmation* purposes in order

to verify and/or explain findings of one research method with another. For example, a small qualitative study is used to explain the findings [the statistical results of a survey] of a larger quantitative study by exploring participants' views in more depth (Creswell, 2009). It is also used to identify findings that either converge, diverge, or both (Creswell, 2009). Mixed methods research is used for *Expansion/Development* purposes resulting in our knowledge and understanding being expanded following one research method from another (Greene, 2008; Creswell, 2009). For example, themes/findings from a small qualitative research study are used to develop new hypothesis or an instrument (i.e. intervention or scale/ questionnaire) for follow-up quantitative research (Creswell, 2009).

In mixed methods research, there have been several typologies (research designs) described to identify mixed method strategies; however, a substantial amount of overlap exists. Regardless of which typology researchers adopt, it is understood that there are some significant characteristics which can influence the design of procedures for a mixed methods study (Creswell & Plano-Clark, 2007; Leech & Onwegbuzie, 2007; Creswell, 2009; Teddlie & Tashakkori, 2009; Small, 2011). These include; *Time Ordering* (whether the qualitative and quantitative data collection will be gathered sequentially or concurrently), *Nesting* (the extent to which multiple data types are collected from the same individuals, organisations or entities), *Weighting* (whether the weight of qualitative and quantitative research is equal or priority is given to one method over the other), *Mixing* (at which stage integration of the multiple data occurs- options are during data collection, data analysis, data interpretation or all three), and *Theorising* (whether theory will be made explicit or implicit in a study).

Doyle et al. (2009) state that choosing an appropriate design for a mixed methods study depends on a) which approach is best suited to answering the particular research question, b) the overall motivation for pursuing a mixed methods study and c) which typology is most appropriate to meet the aims and objectives of the research. However, Guest (2012) is concerned that researchers could be forced to use such typologies even when they do not fit adequately the study's design. Johnson

and Onwuegbuzie (2004) suggest that researchers can develop mixed method designs with multiple phases and features and they should not limit themselves to the designs that are suggested by leading authors. They recommend that researchers should mindfully create designs that effectively answer their research questions. In addition, Guest (2012) proposes to shift the focus to the *point of inference* between two data sets, which refers to any point in a study where two or more data sets are mixed or connected in some way. This provides an alternative way to describe the inherent complexity and fluidity of many mixed methods studies.

3.2.1. Justification for methodology

A mixed methodology is very common in health services research as it allows for exploration of issues from a range of angles (Borkan, 2004). As mentioned earlier, the use of either quantitative or qualitative research is inadequate to address the complex problems that social and health science encounter every day (Creswell, 2009). This is particularly true in complex conditions such as diabetes. Quantitative research in diabetes adherence has shown that many people with T2D rarely fully adhere to their medicines; both oral and injectable (Cramer, 2004, Krass et al., 2015). Although many factors have been identified which influence adherence to diabetes medicines (Borgsteede, 2011; Bailey & Kodack, 2011), some authors argued that this lack of adherence is due to fear of weight gain (Peyrot et al., 2009). However, this relationship has not been fully examined (see Table 2.7 under column weight/BMI). If this relationship is true, quantitative research alone would not be able to explain and verify the reasons why patients are not adhering to their diabetes medicines (including the types of medicines with different body weight effects), and how fear of weight gain and other factors affect adherence. Furthermore, we know little about individuals' experiences with diabetes medicines; past and present. In particular, we do not know enough about the transition prior to taking a new medicine and after experiencing its effects, and how patients' views of their medicines are shaped during this transition. Qualitative research, on the other hand, focuses on the complexities of how human beings make sense of their experiences, and therefore, how individuals with T2D perceive their medicines in ways that make sense to them, based on what is important to them. Therefore, a more complete understanding of

this phenomenon can be obtained by integrating qualitative and quantitative research in a single study.

Research that builds on the health needs expressed by a population group being studied, such as those with T2D, is relevant when the objective is to evaluate or develop health services (Tritter, 2007). Health outcomes can no longer be understood by medical and/or pharmaceutical interventions alone; patient participation on health care decisions means that health can be managed better or more successfully (Tritter, 2007). Measuring patients' health care outcomes as well as understanding their beliefs and expectations about their health and treatments, should enable the development of more effective health care services (Bowling, 2009; NICE, 2012). Clinical knowledge must be integrated with social science expertise and other disciplines in order to explore and understand contemporary health care (Tritter, 2007). Both qualitative and quantitative research, in mixed methods research, contribute to clinical practice (Holloway & Wheeler, 2010) and provide knowledge that could be used to determine health care policies (Doyle et al., 2009). Thus, a mixed methods approach will be used in this study.

3.3 Research Questions

This study addresses the following questions:

1. How do the expectations, beliefs and attitudes of people with T2D towards different diabetes treatments that either promote weight loss, are weight neutral or result in weight gain, change over time?
2. What is the impact of the change in beliefs and attitudes on patients' adherence to their medicine(s)?
3. What type(s) of intervention(s) promoting treatment options, focusing on effects on body weight, are acceptable to patients in order to increase their understanding of their diabetes treatment and improve adherence?

The subsequent objectives were formulated to consider the above research questions:

- Measure the change in patients' expectations, beliefs and attitudes towards glucose-lowering (and/or anti-obesity) drugs (including those with different body weight effects) prior to, during and after taking medicine(s) (where appropriate), within primary and secondary care using self-completed validated questionnaires. (Question 1)
- Explore in depth, using semi-structured interviews, the expectations, beliefs and attitudes towards these drugs (including those with different body weight effects) and associated lifestyle advice in a subsample of patients, and verify and compare the findings with the data from the above questionnaires. (Question 1)
- Investigate the relationship of these changes with patients' diabetes management (adherence) using self-completed validated questionnaires. (Question 2)
- Utilise integrated findings from the above questionnaires and interviews and the systematic review in chapter 2 to explore ideas for intervention(s) which promote understanding of diabetes treatment and adherence in patients with T2D. (Question 3)

3.4 Study design

This study incorporated a mixed methods approach to research adopting a complementary and confirmatory, multiple sequenced (sequential and concurrent), nested design using questionnaires, and qualitative interviews. The study can also be described as longitudinal in nature; that is the same type of information is collected on the same subjects at multiple points in time, due to the sequence of the data collection (Figure 3.1).

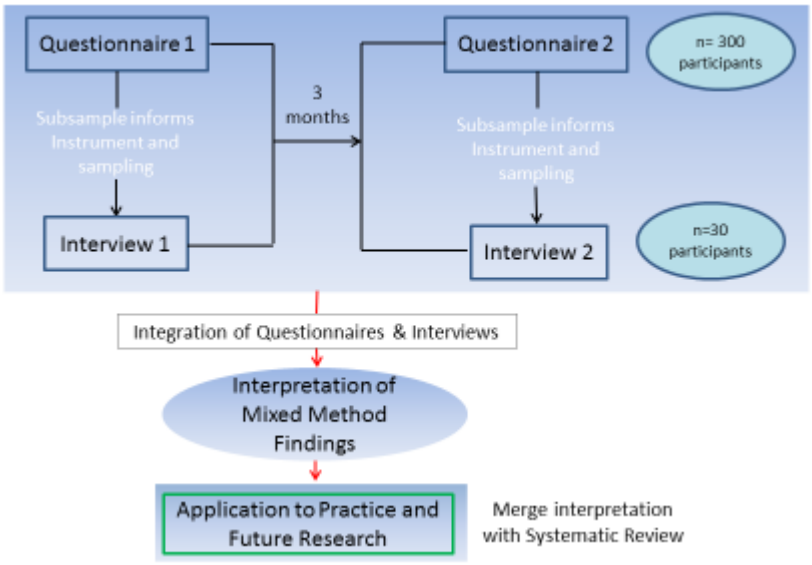

Figure 3.1: Visual Representation of Mixed Methods Study Design

The study used two self-completed validated questionnaires followed by qualitative face-to-face interviews in a subset of patients (See section 3.4.3). These investigated the experiences of T2D service users at different stages in their diabetes care after a medication change in their diabetes treatment; from diagnosis to long-standing diabetes and from monotherapy to complex medication management in primary and secondary care. A "change" in treatment was defined as the addition of, or change to, a new glucose-lowering or anti-obesity drug to the patient's current diabetes therapy. It was important to capture each patient's beliefs and attitudes prior to starting a new medication, as these may change as soon as they take it. For that reason, questionnaire 1 and interview 1 data, were conducted prior to a change in patients' diabetes treatment and questionnaire 2 and interview 2 data were collected three months after starting the new treatment. The three-month period was considered adequate to detect any changes in beliefs and attitudes as seen in other studies (Clifford et al., 2006; Aikens & Klinkman, 2012). The study integrated the findings from questionnaires and interviews with the findings from the systematic review. The steps undertaken were appropriate as a preliminary work for the development of an intervention and consistent with MRC Framework for evaluating complex interventions (MRC, 2008).

3.4.1 Justification of study design

The purpose of using this study design was to engage in the mixing of qualitative and quantitative approaches to view a specific phenomenon (i.e. medicine taking behaviour) using different perspectives to build up a clearer picture of the whole, therefore justifying the use of different methods (Morgan, 1998; Teddlie & Tashakkori, 2009). In addition, this study aimed to expand our knowledge using integrated data from the systematic review and the analysis and interpretation of data acquired from the same participants. The latter can be described as exploratory in nature (Creswell 2009). Also, the review in Chapter 2 demonstrated that there are a number of theories that could be applied in future research in order to understand medication adherence (section 2.5.1). This PhD study explored how these theories are interlinked to explain medication taking practices for people with T2D.

Although, the majority of the data collection (questionnaires and interviews) were concurrent, for a small subsample of participants a sequential approach was taken which allowed for the development of the interview guide and sampling strategy (Small, 2011; Schatz, 2012; Mayoh et al., 2012). This approach had the advantage of focusing on the next data collection in order to identify discrepancies, clarify issues sought in the first data set which were not adequately explained, and add value to the overall study (Mayoh et al., 2012). The concurrent design was appropriate in order to understand every stage of the transition for the participants who had a change in their diabetes treatment (Small, 2011); that is the transition from the unfamiliar new medicine to the experience of taking it and managing it.

Finally, this study used a nested approach, collecting quantitative and qualitative data from the same subsample of participants adding context to the responses from the questionnaires to the qualitative interviews (Small, 2011). This nested design is commonly used in studies where qualitative approaches (interviews or focus groups) are followed by surveys/questionnaires (Mayoh, 2012; Schatz, 2012). The qualitative and quantitative approaches in this study had equal weighting. In addition, it has been suggested that linking qualitative findings over time to longitudinal changes in quantitative data is a valuable contribution to our understanding of social

phenomena (Clarke, 2009) which has particular relevance to medicine taking in real life.

3.4.2 Study population (inclusion and exclusion criteria)

Type 2 diabetes prevalence in Liverpool for the period of 2010-2011 was 3.87%, however in the surrounding areas (St Helens & Halton, Knowsley, Wirral and Sefton) prevalence ranged from 4.25-4.99%, exceeding the England average of 4.07% (HSCIC, National Diabetes Audit, 2013). It was estimated that more than 2000 patients are diagnosed with diabetes every year locally (Liverpool Primary Care Trust [PCT], 2009; Rooney et al., 2010; Nayak, 2010). Therefore, GP practices and community pharmacies [CPs] were selected from the above locality areas to represent the socio-economic diversity of the populations they served as primary care providers. Also, this locality area was chosen as it mostly represented the catchment area for the only secondary care diabetes centre [SCDC], where GP practices were referring the more complex patients. All patients with T2D, eligible for glucose-lowering and/or anti-obesity drug prescriptions that were registered with these primary or secondary care services and required a medication change, as described above, were potentially eligible for the study. Table 3.1 provides a list of potential medication changes and their delivery system.

Table 3.1: List of diabetes and anti-obesity medications for eligibility criteria (not an exhaustive list)

Drug Name- Generic	Drug Name- Brand	Delivery System
Metformin/ Metformin MR	Glucophage/ Glucophage MR	Oral Tablet
Gliclazide/ Gliclazide MR	Diamicron;Zircon / Diamicron MR	Oral Tablet
Glimepiride	Amaryl	Oral Tablet
Repaglinide	Prandin	Oral Tablet
Acarbose	Glucobay	Oral Tablet
Pioglitazone	Actos	Oral Tablet
Pioglitazone & Metformin	Competact	Oral Tablet
Sitagliptin	Januvia	Oral Tablet
Sitagliptin & Metformin	Janumet	Oral Tablet
Saxagliptin	Onglyza	Oral Tablet
Vildagliptin	Galvus	Oral Tablet
Linagliptin	Trajenta	Oral Tablet
Dapagliflozin	Forxiga	Oral Tablet
Exenatide	Byetta	Injection
Exenatide Extended Release	Bydureon	Injection
Liraglutide	Victoza	Injection
All types of insulin (Human/ Analogue or Animal)	Long Acting insulin analogues (insulin detemir, insulin glargine) Rapid Acting insulin analogues (Novorapid/ Humalog [insulin lispro, insulin aspart, insulin glulisine]) Short Acting (Actrapid, Humulin S, Insuman Rapid) Intermediate Acting (Humulin I, Insulatard) Mixed (Hypurin Porcine 30/70, Novomix30)	Injection
Orlistat	Xenical	Oral Tablet

It was anticipated that 80% of the participants would be recruited from primary care and 20% from secondary care, to represent the current management of T2D in the NHS. The study excluded anyone under 18 years of age and adults with difficulty understanding English. In addition, patients were excluded if they suffered from terminal cancer or severe heart failure or if they were unable to provide informed consent due to mental incapacity or communication problems, and/or had difficult family circumstances (e.g. recent bereavement). Patients were excluded from the

interview stage if GP/consultant considered it to be clinically unsafe for patients to delay starting their new medication for up to one week prior to first interview, as outlined in section 3.5.2.

3.4.3 Justification of sample size

The primary outcome of this research was to measure the change in expectations, beliefs and attitudes of patients towards their glucose-lowering or anti-obesity drugs over time. As the focus was also on the body weight effects of the diabetes medicines, the secondary outcomes were to measure the change in expectations, beliefs and attitudes between users of the different classes of drugs that promote weight loss or result in weight gain, and the association of expectations with adherence with these medicines.

The sample size was based on the validated scales used in Naegeli and Hayes paper (2010) related to the expectations and experiences of insulin treatment (named EAITQ and EWITQ respectively). From this paper (2010), a clinically significant change score of ≥0.5[8] indicates patients' pre-treatment expectations exceeded their experience (treatment perceptions) of taking new medication compared to those whose expectations were met or not met by experience. The same paper (Naegeli & Hayes, 2010) also reported a standard deviation of 9.4 of the change score and a reliability coefficient of 0.69. Therefore, using this information, a sample size of 300 people was required using a 5% significance level at 80% power. Since response rates in survey questionnaires among patients vary considerably and generally generate a response of about 60% with a standard deviation of 21% (Asch et al., 1997), it was predicted that the first questionnaire would have an acceptable minimum response rate of 40%, however, the second questionnaire will yield an acceptable good response rate of 75% (Bowling, 2009). Therefore the study required a total of 1000 patients to be initially approached.

[8] The change score was calculate by subtracting the EAITQ score from the EWITQ score (see section 4.2.1.1).

With the assistance of the GP practices and the local CPs involved in the Primary Care Research Network [PCRN][9] (10 large GP practices with over 4000 T2D patients registered), and with the SCDC (over 3500 patients seen each year), it was anticipated that the sample size would be feasible over a 22-24 month period. Furthermore, a sub-sample of approximately 30 patients (10%) who completed the questionnaires would be required to participate in qualitative interviews (a total of two interviews per participant). This qualitative sample size was estimated to provide the most relevant and comprehensive information until saturation was reached (Lewis, 2003).

3.5 Recruitment strategy

The recruitment strategy details procedures of how potential participants were approached and who was responsible for informed consent processes as well as the timescales for each aspect of the study. A diagrammatic flowchart of the recruitment strategy can be seen in Figure 3.2.

[9] The PCRN based in the North West was part of the National Institute for Health Research and the UK Clinical Research Network during the period of the PhD study. Since, it has merged into the Clinical Research Network North West Coast. One of its role was to collate a register with GP practices, pharmacies and the public interested in being involved in research and provide ongoing support.

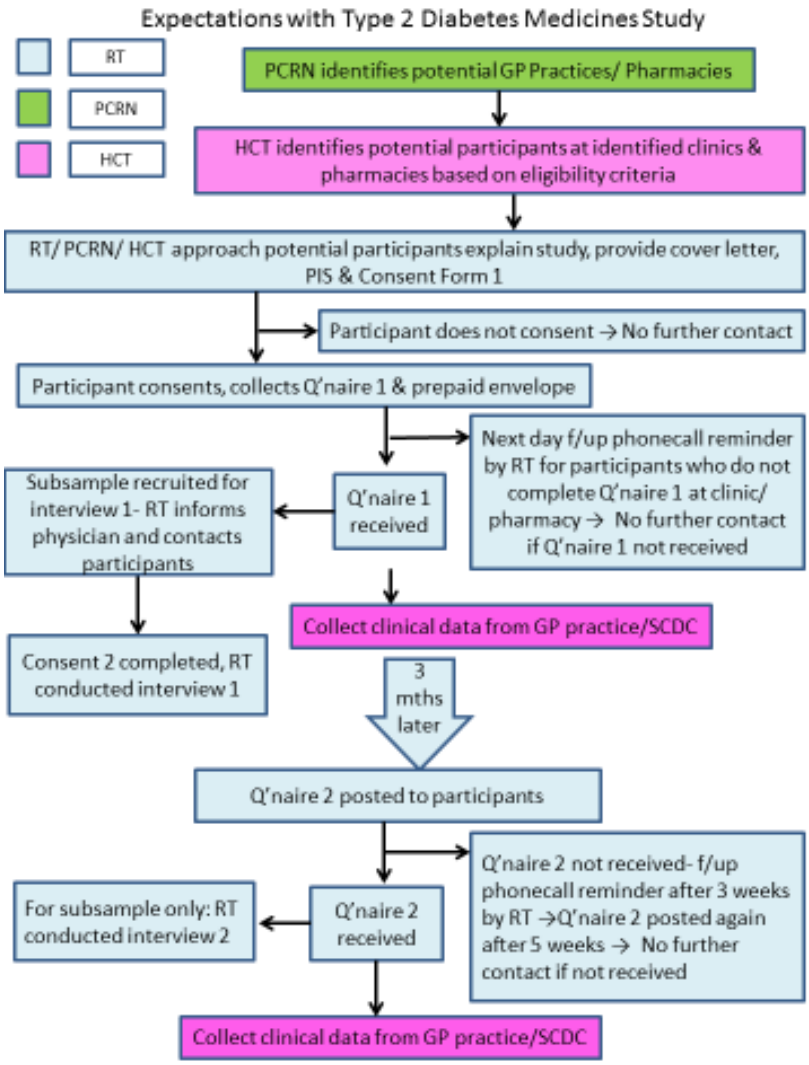

Figure 3.2: Research Study Flowchart

3.5.1 Recruitment for Questionnaire (Quantitative) Data

The self-completed validated questionnaires were administered at two different stages in patients' management identified before and 3 months after a "*change*" in treatment (see definition in section 3.4). This was following either a clinical review in identified clinics across primary and secondary care, or when potential participants collected new prescriptions for their diabetes management from identified CPs. A research flyer [Appendix 3.1] was distributed to encourage uptake amongst potential participants should they be eligible according to the inclusion criteria. The flyer was distributed at the following locations:

- GP practices, CPs and the SCDC already signed up to the research study

- Phlebotomy centres around the recruitment sites - this helped to raise awareness amongst potential participants when they went for their blood tests which were usually done prior to their annual diabetes review or 3-monthly follow-up appointments at their practice.
- With annual diabetes review appointment letters via GP practices and the SCDC, as well as prescription packs through the CPs, to raise patient awareness. It was hoped that this also served as a reminder to health care staff.

Potential participants were identified by the Health Care Team [HCT-GPs/Consultants, Nurses, CPs], in the first instance, based on the eligibility criteria at identified clinics in GP practices and SCDC. The research team [RT-Lead researcher or Research Nurses] then met the potential participants, explained the study and provided them with a covering letter [Appendix 3.2], the consent form [Appendix 3.3] and the participant information sheet [PIS] [Appendix 3.4]. The first questionnaire booklet [Appendix 3.5] and a prepaid envelope were administered via research team following consent to the study. Participants were also approached by pharmacists when they attended identified CPs to pick up their new prescription or by their HCT in GP practices that did not provide dedicated clinics for their T2D patients. In this case, pharmacists and/or practice staff approached patients, explained the study and provided them with the information, as described above.

The participants had a choice to either complete the consent form and questionnaire whilst in clinic or pharmacy in a private room, should they wish to take part in the study, or take the forms home and return them via a prepaid reply envelope. If participants did not respond at this stage, there was no further contact from the RT. If, however, participants did consent but they took the questionnaire with them, the RT contacted participants the following day by telephone to remind them to post it back to the research team. The participants were given 24 hours to consider taking part in the study, as recommended by national ethics guidance (IRAS QSG, 2009). This timeframe did not interfere with patient care in any way, and was used to minimise any delay in starting their new treatment. Where potential participants contacted

the RT directly as a result of the research flyer, the team explored their eligibility for the study based on the inclusion and exclusion criteria (section 3.4.2) and took verbal consent. The team then contacted participants' GPs to ascertain eligibility.

The second questionnaire [Appendix 3.5] was posted to participants after 3 months with two follow-up reminders at this stage. Three weeks after the first administration of the second questionnaire, the RT followed up with a phone call as a reminder to those who had not responded. After five weeks, a further copy was mailed to those who had still not responded. Reminders for questionnaire returns are common, and it is accepted that two reminders at two to three week intervals to non-responders can return up to 25%-33% of responses (Bowling, 2009).

3.5.2 Recruitment for Interview (Qualitative) Data

Participants who indicated in the consent form [Appendix 3.3] they wished to take part in the semi-structured, individual interviews, were invited to take part soon after completion of questionnaires before and 3 months after the medication change. Respondents' GPs/Consultants were informed to ensure that it was safe for patients to delay starting their new medication for up to one week prior to the first interview, in order to capture their expectations and attitudes before they take it. One week was allowed in order to arrange a suitable time and place to conduct the interview following completion of the first questionnaire and to minimise delays in starting the new treatment. Interviews were conducted primarily at the secondary care site within the first week following consent. However, under special circumstances, participants were offered an interview at a place of the patient's choice (in their own home or GP practice or other Primary Health Care venue). Prior to the first interview, participants were asked to sign a further consent form (Appendix 3.6). The interviews were digitally recorded and transcribed verbatim. Participants were also informed that interviews would last approximately 40 minutes to 1 hour.

3.6. Ethical considerations and Ethical Approval

The study was carried out in accordance with current NHS Research Governance requirements and approval was granted by the South-Central-Berkshire Research

Ethics Committee (12/SC/0076) under the proportionate review service on 9th February 2012, and the relevant NHS Trusts. A number of minor and substantial amendments were granted during the study and rationale for all changes can be found in Table 3.2.

Table 3.2: Rationale for Minor and Substantial Ethics Amendments

Amendment Number	Approval Date	Rationale
Substantial – number 1	23/4/2012	-Many GP practices throughout Merseyside do not provide regular T2D or chronic disease management clinics – care is mostly provided ad hoc in regular nurse/GP clinics. Therefore, we proposed GPs/PN staff to consent potential participants based on eligibility criteria and follow consent procedures as outlined in original application. All practice staff and pharmacists who consented patients received study specific training prior to recruitment. -Submitted newer version of questionnaires following formatting and addition of all copyright information.
Minor – number 2	2/7/2012	-Two letters drafted to inform the GPs of their patients' participation in the study and request to obtain clinical data and other relevant information as agreed by the patient on the consent form 1 (baseline and 3-month follow-up data).
Minor – number 3	30/8/2012	-Addition of new NHS Trust site to enhance recruitment
Substantial – number 4	14/1/2013	-Submission of Interview Guides (1 and 2) -Study Research Flyer development to enhance participation and recruitment into study -Project Timeline Plan changes due to delays in: R&D approvals, identification of suitable sites followed by training for consent procedures, and slow return of first questionnaire for preliminary analysis, which, consequently, delayed compilation of the interview guides.

The study was conducted with careful regard to the rights, interests and feelings of participants in accordance with ethical standards of voluntary participation, informed consent, confidentiality and security of collected data (DOH, 2001b). All participants were assigned an anonymity identification number and confidential data were stored in a password protected Excel spreadsheet on the University of Liverpool networked drive. Also, to ensure the confidentiality of interviewees, and to

anonymise their responses to questions in producing interview transcripts, all interviewees were given a pseudonym.

It was also possible that some participants would find the topic of diabetes and weight management sensitive during interviews. The researcher has the responsibility of providing personal safety and well-being to participants (Corbin & Morse, 2003; DOH, 2005a). Therefore, the lead researcher considered steps to be taken should an interviewee became upset, including stopping the interview and offering support, as appropriate. If the participant experienced distress, requiring further action, they were encouraged to seek avenues of support from their own GP and related health services. Although, none of the interviews were stopped due to upset, there were five interviewees who were given guidance at the end of the interview. This was to seek advice from their general practice or diabetes teams in terms of the new drugs that they were prescribed, or advice about managing their T2D or body weight. Also, to minimise the risk of harm to the researcher, the lone worker policy of the University of Liverpool and NHS organization was followed. The lone worker policy stipulates practical actions, processes and physical measures that can be put in place to help prevent incidents from occurring, such as violence, abuse or injuries (NHS Protect, 2017).

CHAPTER FOUR: DATA COLLECTION TOOLS AND DATA ANALYSIS METHODS

4.1 Introduction

This chapter lists all quantitative and qualitative instruments employed in this research study and provides details of their validity and reliability, as well as relevant pilot procedures. First, it begins with the quantitative data collection tools and the statistical analysis plan, continues with the qualitative interviews and the qualitative analysis plan, and concludes with the integrated analysis of the mixed methods data.

4.2 Quantitative Data Collection Tools

This study used two data collection tools for the questionnaire part of the study, including collection of demographic and clinical data. The sections below describe the development and formatting of these tools, as well as the rationale for their use in this research.

4.2.1. Questionnaires

An initial literature review through Medline, Pubmed, Web of Knowledge/Science and PsychINFO identified a range of scales used in health care research related to medication beliefs, satisfaction and adherence. Scales identified needed to be valid and reliable for the T2D population that this research was intended to study (Bowling, 2009). Broadly, the measure of validity assesses whether an instrument measures what it is supposed to measure, whereas reliability assesses the extent to which scale items measure the same construct consistently on different occasions, or by different observers, or similar tests. Instruments also needed to be responsive to changes and free from random error (Bowling, 2009; Streiner & Norman, 2008). This was important in this study in order to assess the change of people's expectations before and after a change in medication treatment.

After close examination of the validity and reliability criteria (Cohen, 1988; Husted et al., 2000; Salkind, 2008; Streiner & Norman, 2008), nine validated scales were used in both questionnaires (Table 4.1) and sections 4.2.2.1 to 4.2.1.7 describe them in more detail. These scales were appropriate for this study, as it is known that patients' judgements of satisfaction with their medication(s) can be mediated by their expectations and beliefs of their treatment (Shikiar & Rentz, 2004). These can form

as a result of a medication's impact on symptom relief, side effects, quality of life and functional status, but also as a result of other factors such as how easy or convenient patients find it to follow the regime, their self-confidence in managing taking their medication, how satisfied they are with the information they have received about their medication, their previous experiences with similar medications or medications in general and their disease and treatment history (Shikiar & Rentz, 2004).

Although some modifications were made to the scales used, minor ones related to wording which do not alter the meaning of the items/scale, for example replacing word "insulin" with "medicines" or specifying types of medicines as "diabetes/ weight loss" medicines, do not require revalidation (Streiner & Norman, 2008). However, modifications to scales such as increasing the scale items or the response options (i.e. number of Likert Scale points) may affect reliability/validity (Streiner & Norman, 2008). Hence, all reliability coefficients were recalculated and compared with the original values of Cronbach's alphas to ensure the consistency of the measurement scales in this study's population sample.

Table 4.1: Validated scales used in the questionnaires

Scale Name	Description of measurement	Number of Items	Modifications	Reference
Experience with Insulin Treatment (EITQ)/ Perceptions with Insulin Treatment (PITQ)	The expectations and perceptions of insulin treatment before and after treatment	10	Wording- changed "insulin" to "medicine" Delivery system questions to reflect both oral and injectable treatments	Naegeli & Hayes, 2010; Hayes & Naegeli, 2010
Beliefs about Medicines Questionnaire- Specific (BMQ)	The beliefs about *Necessity* and *Concerns* about specific disease medicines, i.e. diabetes	11 made to 12	Wording- "diabetes and/or weight loss medicines" One item added related to weight gain	Horne et al., 1999 Horne et al., 2004
Beliefs about Medicines Questionnaire- General (BMQ)	The beliefs about *Benefits*, *Harm* and *Overuse* of medicines in general	11	none	Horne et al., 1999 Horne et al., 2004
The Morisky Medication Adherence Scale (MMAS-8)	Intentional and unintentional non-adherence to medications	8 made to 10	Wording- "diabetes and/or weight loss medicines" Two items added related to skipping medicines and not taking medicines on holidays	Morisky et al., 2008
Satisfaction with Medication Information (SIMS)	Patient satisfaction with information received about prescribed medicines; related to *Potential Problems with Medicine* and its *Action and Usage*.	17 made to 18	One item added related to medicine's effect on body weight	Horne et al., 2001

Satisfaction About Diabetes Medicines (DiabMedSat)	Satisfaction with diabetes medicines related to *Efficacy*, *Burden* and *Symptoms*	23	Wording- "diabetes and/or weight loss medicines"	Brod et al., 2009a
Treatment Related Impact Measure of Weight (TRIM- Weight)	Impact of weight loss medication in areas of *Daily Life*, *Weight Management* and *Psychological Health*	22 made to 13*	Wording- "diabetes and/or weight loss medicines"	Brod et al., 2010
Self-Efficacy for Appropriate Medication Use (SEAMS)	Patient's self-efficacy with medication adherence, particularly *Under Difficult Circumstances* and *Under Conditions of Uncertainty*	13	From 3-point Likert scale to 5-point Likert scale Wording to two items from US English to UK English	Risser, 2007
Obesity and Weight Loss Quality of Life (OWLQOL)	Evaluation of patients weight, weight loss and treatment	17	None	Patrick et al., 2004

(*Only used three out of the five subscales, see details in 4.2.1.5)

4.2.1.1. Expectations About and Experiences with Insulin Treatment

There were two scales identified that measured a change in people's expectations and experiences before and after a new treatment. These were the Expectations *About* and Experiences *With* Insulin Therapy Questionnaires (EAITQ and EWITQ)[10] developed by Naegeli and Hayes (2010). Each scale includes 5 items that concerned insulin therapy in general, 5 items that concerned insulin delivery systems and 5 items on self-efficacy. This study only used the first 10 items from each scale which corresponded to the insulin therapy and delivery systems. The scales were adapted to fit the current study's aims by omitting the word "insulin" and replacing it with "medicine". In addition, question items were adapted to reflect all glucose-lowering and anti-obesity drugs investigated in this study, and delivery systems were defined to include all types of medicines i.e. oral tablets and injections. An advantage of the two scales was that they were originally developed and tested with T2D populations and included an item related to weight gain. Internal consistency, as described in Naegeli and Hayes's paper (2010), was also acceptable (Streiner & Norman, 2008) with Cronbach's alpha 0.80 for the EITQ and 0.72 for the PITQ. These scales are relatively short including 10 items in each on a 7-point Likert scale ranging from 1 (Strongly Disagree) to 7 (Strongly Agree). Out of the ten items in each scale, six were positively worded items and four were negatively worded items. The negatively worded items on the two questionnaires were reverse scored so that higher scores on both positively and negatively worded items corresponded to more positive expectations and experiences. The responses of the ten items were summed and divided by the number of items, giving a range of scores in each scale from 1 to 7, with a higher total score corresponding to more positive expectations or experiences (perceptions) respectively.

[10] The name of the two scales changed following a subsequent publication by Hayes and Naegeli (2010), where the EAITQ was renamed as "Expectation about Insulin Therapy Questionnaire" (EITQ) and the EWITQ was renamed as "Perceptions of Insulin Therapy Questionnaire" (PITQ). This thesis will be using the new acronyms throughout.

4.2.1.2. Beliefs and Attitudes about Medicines

Four scales were identified through the literature review, of which three were specifically for medicines (Horne et al., 1999; Farmer et al., 2006; Monahan et al., 2009) and the fourth scale, with its number of versions, was in general about illness perceptions with domains around treatment perceptions and efficacy (Weinman et al., 1996; Moss-Morris et al., 2002; Broadbent et al., 2006). In this study the scales based on peoples' specific and general beliefs about medicines questionnaire [BMQ] were used. These were developed by Horne, et al. (1999) originally for chronic conditions including diabetes.

The *BMQ-specific* assesses patients' beliefs about medications prescribed for a particular illness, in this case diabetes. It comprises of two scales assessing personal beliefs about the *necessity* of prescribed medication for controlling their illness, and *concerns* about the potential adverse consequences of taking it. The specific scale items were adapted for glucose lowering and anti-obesity drugs and an additional item was added that was related to worries about weight gain (item 12). The total items for the specific scale were 12, and respondents indicated their level of agreement with each statement about medicines on a 5-point Likert scale ranging from 1 (Strongly Disagree) to 5 (Strongly Agree). The sum of scores for each scale was divided by the number of items for each scale ranging from 1 to 5 for necessity (5 items) and 1-5 for concerns (7 items). A high score on the concern scale indicates high concerns about potential adverse effects of prescribed medicines, and a high score on the necessity scale indicates strong beliefs in necessity and efficacy of prescribed medicines (Horne, 2000). Cronbach's alpha measuring internal consistency in the original paper from Horne at al. (1999) was found to be 0.74 for the Necessity items and 0.80 for the Concerns items for patients who had diabetes. Another paper (Aitkens & Piette, 2009) also found similar internal consistency for Necessity (α=0.78) and Concern (α=0.68) items for T2D patients on glucose lowering medicines.

The *BMQ- general* assesses general beliefs about medicines and it comprises three scales assessing personal beliefs about the extent to which doctors place too much

trust in medicines (*Overuse*), beliefs about the intrinsic properties of medicines and the degree to which they are perceived as essentially harmful and, finally, beliefs about beneficial effects of medicines (*Benefit*) (Horne et al., 1999, 2004). The total items for the general scale were 11; three items for the Overuse scale, four items for the Harm scale, and four items for the benefit scale (Horne et al., 2004). Respondents indicated their level of agreement with each statement about medicines on a 5-point Likert scale ranging from 1 (Strongly Disagree) to 5 (Strongly Agree). The sum of scores for each scale was divided by the number of items for each scale ranging from 1 to 5 for all three subscales. A high score on the *Overuse* scale indicates strong beliefs that medicines are overused by doctors, a high score on the *Harm* scale indicates strong beliefs that medicines are "harmful" and "addictive", and a high score on the *Benefit* scale indicates strong beliefs about the benefits of taking medicines (Horne, 2000). Previous validation studies (Horne et al., 1999, 2004; Ramström et al., 2006) showed an acceptable internal consistency for all three scales ranging from 0.65-0.72 for the 3-item Overuse, 0.62-0.70 for the 4-item Harm, and 0.62-0.66 for the 4-item Benefit scales.

4.2.1.3. Medication Adherence

There were four scales identified that estimated medication adherence (Morisky et al., 1986, Horne et al., 1999; Morisky et al., 2008; Aikens & Piette, 2009; Stetson et al., 2011). The Reported Adherence to Medication [RAM] scale reported in Horne et al.'s paper (1999) was a non-validated measure devised for their study, which was reported again in another paper by Farmer et al. (2006); however the Cronbach's alpha ranged between 0.6-0.83. No other validity or reliability tests were reported in Horne et al.'s paper (1999). Stetson et al. (2011) developed a scale called the Personal Diabetes Questionnaire (PDQ) for both T1D and T2D individuals. This scale included a sub-scale for medication adherence, however no Cronbach's alpha was reported for this subscale.

A self-reported medicine adherence scale developed by Morisky et al. (2008) was used in this study. The Morisky Medication Adherence Scale [MMAS] originally had four items (MMAS-4) scored with *Yes* or *No* answers (Morisky et al., 1986). However,

recently, it was extended to eight items (MMAS-8) in order to measure intentional (e.g. due to side effects) and unintentional (e.g. forgetfulness) non-adherence to medications (Morisky et al., 2008).

The new MMAS-8 was significantly correlated with the original scale (MMAS-4) in a study on hypertensive patients ($r= 0.64$; $p<0.5$) (Morisky et al., 2008), and in a study with T2D Malaysian patients ($r=0.792$; $p<0.01$) (Al-Qazaz et al., 2010). In addition, the MMAS-8 has been shown to have greater reliability ($\alpha=0.83$) than the original MMAS-4 ($\alpha=0.61$) (Morisky et al., 1986; Morisky et al., 2008). The new 8-item scale has seven items with *Yes* or *No* response categories and the last item is based on a 5-point Likert scale. The last item asks how often participants have difficulty remembering to take all their medicines, ranging from *Never/Rarely* to *All the Time*. Scores on the MMAS-8 range from 0 to 8 with scores less than 6 reflecting low adherence, 6 to 7 reflecting medium adherence and 8 reflecting high adherence (Morisky et al., 2008). Furthermore, studies with T2D patients showed that those with a higher score on the MMAS had a lower associated HbA_{1c} measurement (Krapek et al., 2004; Gonzalez et al., 2013).

In this study, the MMAS-8 was adapted for glucose-lowering and anti-obesity drugs and two additional items were added that were related to whether patients skipped their diabetes or weight loss medicines when they went on holidays or if they gained weight (items 5 and 6). The total items for the medication adherence scale in this study were 10.

4.2.1.4 Satisfaction with Medication Information

One scale was identified that measured patient satisfaction with the information they received about their prescribed medicines. This was developed by Horne et al. (2001) and is called the Satisfaction with Information about Medicines Scale [SIMS]. This is a 17-item scale that includes a range of topics that are related to the action and usage of medicines and the potential problems with them. Respondents in this scale indicated the amount of information they received about each aspect of their

prescribed medicine. Those participants reporting that the information was *about right* or indicating *none needed* were classified as satisfied (scored 1). Those reporting that the information was *too little*, *too much* or indicating *none received* were classified as dissatisfied (scored 0). Scores range from 0-17 with high scores indicating a high degree of overall satisfaction with the amount of medicine information received. In addition, items in SIMS can be divided into two sub-scales; the Action and Usage subscale [AU] and the Potential Problems of Medication subscale [PPM].

Horne et al. (2001) reported an acceptable Cronbach's alpha overall for people with diabetes (α=0.81 insulin treated, α=0.88 on oral glucose-lowering agents). In addition, both of the subscales showed satisfactory internal consistency ranging from 0.77-0.79 for both diabetes groups with the exception of the PPM subscale in insulin treated diabetes patients where Cronbach's alpha was 0.61. The SIMS scale (Horne et al., 2001) appeared to be positively correlated ($r=0.31$, $p<0.05$) with patients' self-reported adherence (RAM scale, see 4.2.1.3) and negatively correlated ($r=-0.33$, $p<0.05$) with the BMQ-Concern specific scale (see 4.2.1.2) in a cardiac rehabilitation sample. In addition, two more studies which adapted the SIMS scale (reduced to 15 and 16 items) for people on glucose-lowering medicines reported Cronbach's alpha of 0.89 (Aikens & Piette, 2009) and 0.94 (van Geffen et al., 2011) respectively.

In this study, the SIMS was adapted by increasing the scale with an additional item making a total of 18 items. The new item was related to information received about whether the medicine will affect patient's weight (item 16).

4.2.1.5. Satisfaction about Diabetes/ Weight Loss Medicines

Satisfaction about Diabetes Medicines

Seven scales were identified that explored patients satisfaction with their diabetes medicines and/or treatment (Bradley et al., 1990; Atkinson et al., 2004; Brod et al., 2006; Donatti et al., 2008; Ruiz et al., 2008; Anderson et al., 2009; Brod et al., 2009b). Only two scales reported being sensitive to change (Bradley et al, 1990; Bradley, 1999; Brod et al., 2009a). Although the Diabetes Treatment Satisfaction

Questionnaire (DTSQ) measures satisfaction with diabetes medicines, including tablets and insulin injections, there are two separate versions of the scale for each delivery system (Bradley, 2006). However, the Diabetes Medication Satisfaction [DiabMedSat] scale developed by Brod et al. (2006) has been used for all delivery systems of diabetes medicines (i.e. oral, injectable) and also includes items related to weight gain, which the DTSQ does not include. The DiabMedSat scale contains 22 items that assesses treatment satisfaction in three related domains: *Efficacy, Treatment Burden and Symptoms* (side effects) as well as *Overall Treatment Satisfaction*. Each item is scored out of 100, and some items are on a 5-point and others on a 7-point Likert scale. Higher domain scores indicate greater treatment satisfaction for the concept measured by each domain.

The DiabMedSat has a Cronbach's alpha of 0.90 for the whole scale, and an acceptable internal consistency for each domain (Burden α=0.87, Efficacy α=0.87, Symptoms α=0.89) as well as correlation coefficients within acceptable range (r=0.48-0.85) suggesting moderate to strong associations between domains establishing construct validity (Brod et al., 2006). In addition, Brod et al. (2009a) reported that the effect size of DiabMedSat ranged from 0.535 and 1.645 indicating its ability to detect a moderate to large change for people with T2D who had been on biphasic insulin aspart 30 for 26 weeks. Also, Brod et al. (2009a) measured responsiveness of the DiabMedSat, using the Minimal Important Difference [MID] and the Standardised Response Means [SRM]. The study showed that MID ranged from 5.3-11.7 and indicated a medium to large SRM in all domains (range=0.43-1.16) between the group of patients who were slightly satisfied with their medication compared to the group of patients who were "neither dissatisfied nor satisfied".

Satisfaction about Weight Loss Medicines

Only one scale was identified that assesses the impact of anti-obesity drug medications in areas such as *Daily Life, Psychological Health, Weight Management, Treatment Burden* and *Experience of Side Effects* (Brod et al., 2010). The scale is called Treatment Related Impact Measure of Weight [TRIM-Weight] and consists of 22

items related to the areas mentioned above which also represent the 5 sub-domains. This measure was developed to be used either as a whole scale or to use the subdomains independently. This study has used the three following sub-domains; *Daily Life [TRIM-Wt-DL], Psychological Health [TRIM-Wt-PH], Weight Management [TRIM-Wt-WM]*. The other two subdomains were omitted as similar items can be found in the DiabMedSat subdomains of *Treatment Burden* and *Symptoms*. The *TRIM-Wt-DL*, the *TRIM-Wt-PH* and the *TRIM-Wt-WM* domains contain 6, 4 and 3 items respectively, all based on a 5-point Likert scale. Some of the items were reversed scored so that higher summed scores on each domain corresponded to a better health state with less negative impact related to the concept measured by each domain.

The TRIM-Weight has a Cronbach's alpha of 0.93 for the whole scale, and an acceptable to good internal consistency for the following domains: TRIM-Wt-WM (α=0.70), TRIM-Wt-PH (α=0.87), TRIM-Wt-DL (α=0.91). It also has correlation coefficients within acceptable range (r=0.48-0.85) suggesting moderate to strong associations between domains establishing construct validity (Brod et al., 2006).

In this study, both DiabMedSat and the three subscales of TRIM-Weight were adapted for glucose-lowering and anti-obesity drugs. It is well known that many diabetes medicines have different effects on body weight, i.e. promote weight loss or result in weight gain, and therefore can affect the psychological health and daily life of patients with diabetes (Inzucchi et al., 2012). In addition the only anti-obesity drug available currently on the NHS (Orlistat) has been shown to have side effects of similar severity to other diabetes medicines and positive effects on glycaemic control (Hollander et al., 1998; Miles et al., 2002, Kelley et al., 2002; Inzucchi et al., 2012).

4.2.1.6. Self–Efficacy for Appropriate Medication Use

One scale was identified that measured patients' self-efficacy with medication adherence suitable for chronic diseases developed by Risser et al. (2007), called the Self-Efficacy for Appropriate Medication Use Scale [SEAMS]. The scale contains 13

items that can be divided into two subscales; the self-efficacy on taking medicines Under Difficult Circumstances [UDC] and the self-efficacy on taking medicines under conditions of uncertainty [UCU]. The scale was assessed on a sample of patients with Coronary Heart Disease, of which 45% had diabetes. Cronbach's alpha was 0.89 for the overall scale and 0.86 and 0.79 for the UDC and UCU subscales respectively. In addition, SEAMS was positively correlated with Morisky Adherence Scale (MMAS-4); Spearmans rho=0.51 ($p<0.0001$). The original scale was based on a 3-point Likert scale ranging from 1 (not confident) to 3 (very confident), however the scale in this study was adapted to a 5-point Likert scale ranging from 1 (Not at all confident) to 5 (Extremely confident), as described in Carpenter et al.'s paper (2010). In addition, items 6 ("your" instead of "the") and 11 ("unwell" instead of "sick") were adapted slightly to ensure understanding of the questions by the sample population. The sum of scores for the modified SEAM scale was divided by the number of items of the scale and ranged from 1 to 5. A high score represents greater levels of adherence self-efficacy.

4.2.1.7. Obesity and Weight Loss Quality of Life Measure

Two obesity specific quality of life scales were considered, the Impact of Weight on Quality of Life-Lite [IWQOL-Lite] by Kolotkin et al. (2001, 2003) and the Obesity and Weight Loss Quality-of-Life [OWLQOL] by Patrick et al. (2004). However, the OWLQOL was used in this study. Although OWLQOL and IWQOL-Lite measurements show good construct validity and reliability (α=0.93-0.96, ICC=0.95 and α=0.84-0.96, ICC=0.94 respectively), the OWLQOL had less items (n=17) compared to IWQOL-Lite (n=31). This meant less of a burden to the participant with a mean completion time of 5 minutes, as they had to complete, in addition, all the other scales as reported above. Furthermore, both measurements have shown responsiveness to change, but OWLQOL has shown moderate to large responsiveness to shorter- and longer-term reductions in body weight (SRM=0.32-1.63) and has been assessed in pre- and post-treatment situations, which were similar to this study design. The OWLQOL measures a person's global evaluation of their weight, weight loss and weight loss treatment and hence, assesses a person's perceptions of body weight and trying to lose weight.

This is in contrast with the IWQOL-Lite that assesses function/ behaviour due to body weight and ability to complete simple tasks. Moreover, the OWLQOL is intended to be used alongside other patient reported outcomes including adherence to and satisfaction with treatment (Patrick et al., 2004).

The OWLQOL consists of 17 items all on a 7-pont Likert scale with responses ranging from *Not at all* (scored 0) to *A very great deal* (scored 6). All items are used to derive a single quality of life score by reversing scores for each item, then summing each item and transforming the raw score to a standardised scale of 0 to 100. A score of 0 indicates the greatest impact (i.e. poor quality of life) whereas a score of 100 indicates the lowest impact, therefore implying better quality of life. No change was made to this scale for this study.

4.2.2. Additional demographic and clinical data

Demographic data were also collected within the first questionnaire (Appendix 3.5, section A) to determine factors that predict discrete subgroups of the population. For example, subgroups included individuals with low, medium or high adherence levels or individuals prescribed a new diabetes medicine that has different effects on body weight. Demographic data included age (in years) calculated from date of birth at the time of entering the study, gender (male/female), ethnicity, marital status, education status, employment status, and socioeconomic status based on the Index of Multiple Deprivation [IMD] for 2010 by using the participant's home postcode in the Deprivation Map Explorer (http://apps.opendatacommunities.org/showcase/deprivation).[11] The dataset provides all Lower layer Super Output Areas (LSOAs) for England and Wales ranked by their 2010 IMD score. A rank of 1 is the most deprived (out of 32,482 areas). These scores are then also ranked in 5 categories from those who live in 20% most deprived

[11] The IMD is a composite score for a small neighbourhood, derived from aggregated responses to the ten-yearly national census and with some but not all components updated annually using local statistics. It consists of 38 indicators of deprivation grouped in 7 domains: household income, employment, health status and disability, crime, skills and training (including but not limited to formal education), barriers to housing and services, and living environment (including access to open spaces and leisure facilities). (Communities and Local Government, 2011)

areas to those who live in 20% least deprived areas (Communities and Local Government, 2011).

In addition, clinical data were also collected from medical records following participants' consent to the study [Appendix 4.1]. These data were collected to explore associations with subgroups as described above and identify total medication burden based on the number of medicines participants had to take every day. These clinical data were collected twice from the medical records; before and 3 months after a change in participants' diabetes treatment, to assess change overtime and compare with subgroups as described above.

4.2.3 Piloting of Questionnaire

The lead researcher (AP) engaged with a research steering group involving a service-user with T2D and relevant HPs (consultant, GP, diabetes specialist and research nurses, pharmacist and dietitian), who provided feedback on the questionnaire format and content, establishing face and content validity (Streiner & Norman, 2008). In addition, both questionnaires were piloted with two people with T2D on oral medication, in order to assess readability and avoid ambiguities (Streiner & Norman, 2008). Following feedback from both research steering group and individuals with T2D, a few American terms were changed to more common English terms (i.e. "feeling sick" to "feeling unwell"). Furthermore, it was decided to format the questionnaires using guidelines from DUK (www.diabetes.org) and National Research Ethics Service (www.nres.nhs.uk) in relation to background, font colour, font type and size, logos and language used. In addition, licence agreements for the scale measurements in sections 4.2.1.1-4.2.1.7 were drawn up, and changes as described above were approved from the relevant copyright author(s)/institution(s) prior to printing the questionnaires.

4.2.4 Data management and statistical analysis

Data from questionnaires and the clinical data forms at baseline and 3-month follow-up were inserted into a database on the Statistical Package for the Social Sciences

[SPSS] version 21. This statistical package was used to manage data coding and analysis. Prior to entering any data onto SPSS, all items for scales in sections 4.2.1.1.-4.2.1.7 that required reverse scoring where changed accordingly. All data entered on the database were manually checked for accuracy prior to any statistical analysis. Scale scores were transformed using the compute function on SPSS, creating additional variables in the form of a numeric expression (summed scores for whole scales or subscales as described in sections 4.2.1.1.-4.2.1.7). Descriptive statistics were used to explore the demographic characteristics of the sample. Frequencies (%) were calculated for gender, ethnicity, marital status, employment status, educational status and social status. In addition, frequencies (%) were calculated to determine the percentage of different categories of glucose lowering drugs; biguanides, sulfonylureas, meglitinides, thiazolidinediones, DPP-4 inhibitors, GLP-1 agonists, and insulins. Furthermore, frequencies were calculated for weight reducing, weight neutral and weight increasing drugs, as well as medication burden, and diabetes complications present.

Tests for normal distribution of the data were conducted using the Kolmogorov-Smirnov (for sample size over 100) or Shapiro-Wilk (for sample size less than 100) test when the data showed a reasonably normal distribution using histograms, and homogeneity of variance using the Levene's test (Coakes & Steed, 2006, Field, 2009). Mean and Standard Deviation [SD] values were used when the data showed normal distribution, otherwise median values and interquartile range [IQR] were used.

Analysis was carried out, firstly, using the whole group and then using the three subgroups based on the effect of a new medicine on body weight. The three weight-effect groups were classified as Weight Reducing [WR], Weight Neutral [WN] and Weight Increasing [WI]. The thesis will use these labels throughout for presenting the results. The primary outcome was to identify the change in expectations, beliefs, attitudes and adherence following the experience of taking glucose-lowering drugs (or anti-obesity drugs) that promote weight loss, are weight neutral or result in weight gain. Since the scale data were mostly skewed, then the non-parametric Wilcoxon signed-rank test (as opposed to the paired t-test) was used for comparing

dependent samples. This test was used for example for comparing attitudes and beliefs before and after change of medication. The non-parametric Kruskal-Wallis test was used to compare scales between the three independent weight- effect groups (WR, WN, WI) and adherence level groups (low, medium, and high), and the Mann Whitney U test for comparing skewed data between two independent groups, for example for comparing attitudes and beliefs between the WR and the WI group. Probability values (p-values) equal to or below 0.05, were considered significant. The Bonferroni correction method was used to minimise Type I error when there was multiple testing. In this case the criterion for statistical significance was modified by dividing the probability value of 0.05 by the number of comparisons to create a new cut–off value, for example, when there were 3 multiple comparisons between the weight-effect groups, the new probability cut-off value became 0.017.

In addition, the Standard Error of Measurement [SEM] (Wyrwich et al., 1999) was used to measure differences amongst individuals in the amount of change between baseline and three month follow-up, such as those whose expectations, attitudes and beliefs changed positively (improved), negatively (decreased) or remained stable. A change of one-SEM was used to determine whether participants had achieved a minimal significant change or MID (Wyrwich et al., 1999; Rejas et al., 2008). The SEM was calculated for each scale by multiplying the standard deviation of the baseline scale score (or the change score) by the square root of 1 minus its reliability coefficient (or reliability of the change score). All scales used the baseline standard deviation scores and the reliability coefficient, except for the EITQ/PITQ scale where the standard deviation of the change score was used and the reliability of the change score (Hayes et al., 2010). The reliability was measured by Cronbach's alpha coefficient (Appendix 5.4).

Using the one-SEM value for each scale as a reference and the difference score between baseline and follow-up scores, the participants were identified as [1] *improved* if the change score was greater than one-SEM (>1SEM), [2] *no change/stable*, if the change score was zero or within plus or minus one-SEM (±1SEM), and [3] *decreased* if the change score was equal or less than minus one-

SEM (≤-1SEM) (Wyrwich et al., 1999). For the EITQ and PITQ scales the difference scores were then used to categorise how expectations were met by experiences. If the difference score was zero, plus or minus one-SEM (±1SEM), expectations were met by experience. If the difference score was greater than zero plus one-SEM (>1SEM), expectations were exceeded by experience. If the difference score was less than zero minus one-SEM (<-1SEM), expectations were not met by experience (Hayes et al., 2010).

In order to assess the impact of participants' expectations, beliefs and attitudes as well as any change in these on medication adherence, univariate and multivariate regression analyses were performed with one or more independent variables. The type of regression analysis was based on whether the dependent variable of interest was binary, ordinal or nominal. Logistic regression is used when the dependent variable is binary, for example predicting medication adherence (MMAS-8) to be high (than low to medium). This regression analysis is concerned with the probability of a single outcome/event occurring given the level/s of one or more explanatory (independent) variables using the logit transformation (Log of the Odds) (Norušis, 2011). The models take the following form:

Log [p/(1-p)] = $\beta_0 + \beta x$ (for one explanatory variable)

Log [p/(1-p)] = $\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + ... + \beta_n x_n$ (for more than one explanatory variables)

Where p is the probability of the outcome occurring, β_0 (beta coefficient) is the constant, $x_1, \ldots, x_n$ are the explanatory variables and $\beta_1, \ldots, \beta_n$ the corresponding regression coefficients attached to that variable.

The log odds/logits can be converted into (relative) odds by applying the exponential to both sides of the equation and so, it is expressed as p/(1-p)= Exp ($\beta_0 + \beta x$), which in return can be used to find the probabilities with the following formula: p= Exp($\beta_0 + \beta x$)/ [1+ Exp($\beta_0 + \beta x$)] (Norušis, 2011). Hence the odds of being high adherent is defined as the ratio of the probability of having high adherence level over the probability of having low to medium adherence levels, so if the value is greater than 1 then it indicates that the predictor increases the odds of being high adherent, whilst

a value less than 1 indicates that the predictor decreases the odds of being high adherent (Field, 2009). SPSS gives the OR for the explanatory variables labelled as Exp(B), as well as displaying 95% confidence intervals.

Ordinal regression (or ordinal logistic regression) is used when the outcome/dependent variable has more than one category and is ordinal, such as the medication adherence (MMAS-8) which has three ordered categories (low, medium, high). The ordinal regression is concerned with the cumulative probabilities of an outcome/event occurring using the cumulative logit/ proportional odds model, i.e. the probability of an event occurring and all events that are ordered before it (Norušis, 2011). The model takes the following form:

Log $[p_j/(1-p_j)] = \alpha_j - \beta x$ *(for one explanatory variable)*

Log $[p_j/(1-p_j)] = \alpha_j - (\beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + ... + \beta_n x_n)$ *(for more than one explanatory variables)*

where *j* goes from 1 to the number of categories minus 1. Each logit has its own intercept α_j but the same coefficient β, that means the effect of the independent variables is the same across the different thresholds (outcome levels). This is the key assumption of the ordinal regression and is termed the assumption of proportional odds (or parallel lines in SPSS) (O'Connell, 2006).

In SPSS, the effects of the independent variables are subtracted rather than added to the intercepts. This is done so that positive coefficients suggest that higher values of the explanatory variable are associated with higher outcomes, while negative coefficients suggest that higher values of the explanatory variable are associated with lower outcomes (Norušis, 2011). For example, an analysis based on the dependent variable of medication adherence (MMAS-8) will create two models; one that predicts the likelihood of those who are medium to high adherent compared to those with low adherence levels and the second predicts the likelihood of high adherents compared to those with low to medium adherence levels. The test of parallelism is used to determine the validity of the assumption of the ordinal model compared to a model with separate coefficients for each threshold, so if the test is non-significant (i.e. $p>0.05$), then the ordinal model is significantly better, and the assumption of

proportionality is upheld suggesting that all parameters are the same across all thresholds (O'Connell, 2006).

The cumulative logits (i.e. threshold coefficients/parameter estimates) associated with being at or below a particular category *j* can be exponentiated to arrive at the estimated cumulative odds for that category. Then, predicted cumulative probabilities associated with being at or below category *j* can be calculated from the cumulative odds using the following formula: 1/ [1+ exp (cumulative logit)], however to find the predicted probability in a specific outcome the subtraction method is used (Norušis, 2011). Hence, the odds of becoming highly adherent is calculated by using the exponential value of the predictive cumulative logit. SPSS gives the estimate beta for the explanatory variables displaying 95% confidence intervals and calculates the predicted probabilities for each score/category.

Finally, when the outcome variable has more than two categories which are considered to be unordered, such as the variable related to the change in medication adherence levels (MMAS-8 improved, stable or decreased), then the regression analysis used is called multinomial regression. This analysis is the same as the logistic regression analysis with binary outcomes, in that it breaks the outcome variable into a series of comparisons between two categories. In this case, the analysis is made into two comparisons between "stable" and "improved" or "stable" and "decreased", whilst using one category ("stable") as the reference category for comparison (Field, 2009).

A univariate analysis was conducted initially to assess which variables were significant predictors of medication adherence (MMAS-8) and change in medication adherence levels including any demographic or clinical covariates and these were entered individually one at a time. Then, a multiple ordinal regression was used to identify a model that better predicts medication adherence at three months following an initiation of a new treatment (high adherence Vs medium and low adherence). The multivariate model was constructed based on the most significant variables in a forward stepwise method, starting with those with the highest

significant value (i.e. $p<0.001$). If the variables were significant with $p<0.05$, these were then retained in the model, however any variable with $p>0.05$ was later excluded. However, multiple logistic regression analysis was performed when the assumption of proportional odds was violated (i.e. $p<0.5$) to explore the variation in the odds or the explanatory variables at the different thresholds of the ordinal outcome. Furthermore, a multinomial regression was used, based on the forward stepwise method as explained above, to identify a model that detects significant predictors to medication adherence change, that is an increase or decrease in adherence levels over time by using those participants with stable adherence over time as the reference point (Field, 2009). The variable regarding the weight-effect of the new medicine (weight reducing, weight neutral, weight increasing) was forced into all final models as a covariate, to ascertain whether the weight-effect of the medicine can predict and/or influence medication adherence levels.

To determine the ability whether a multivariate model improves the ability to predict the outcome, the chi-square statistic was used to indicate whether the multivariate model was performing better ($p<0.05$) than the baseline intercept-only model which has no independent variables. The goodness of fit tests, Hosmer & Lemeshow and the Pearson's chi square (and deviance) test for logistic and ordinal regressions respectively, were used to indicate that the multivariate model is a good fit to the data when $p>0.05$ (Field, 2009; Norušis, 2011). In addition, the Nagelkerke's R^2 value, a pseudo R^2 statistic, was used to explain how much variation in the outcome is explained by the model (Field, 2009; Norušis, 2011). Multicollinearity was assessed with a correlation matrix. Pearson's r values of less than 0.8 between any two explanatory variables suggested that there was no perfect relationship and no concern for multicollinearity (Filed, 2009). However, if values of 0.8 and above were found, SPSS provided further collinearity diagnostics such as the Variance Inflation Factor (VIF) and the tolerance statistic. A VIF value of less than 10 and tolerance of close to 1 for each explanatory variable suggest no multicollinearity (Field, 2009).

4.3. Qualitative Data Collection Tools

4.3.1 Interviews

Unlike quantitative approaches, qualitative inquiry does not always generalise findings but provides rich accounts of peoples' experiences and the meanings they attach in relation to their everyday lives and different settings (Brown, Crawford & Hicks, 2003). In doing so, the researcher needs to present the research process which resulted in a set of conclusions, so that the research study can be regarded as reliable, trustworthy, valid and transferable (Lewis & Richie, 2003). Crucial aspects to consider throughout the research process include: a "symbolically" representative sample with known features for non-response (where applicable), a consistent approach to interviewing which effectively allows participants to portray their experiences; a comprehensive and systematic data analysis procedure which is triangulated by other methods and allows for all perspectives to be explored, and finally, identification and interpretation of the data that reflects the meanings assigned by the participants and is supported by evidence and displayed in such a way that remains "true" to the original data (Lewis & Richie, 2003). Finally, a qualitative research study can be regarded as transferable if the findings can be applied to a wider population, to other contexts, or to the development or enhancement of theory (Lewis & Richie, 2003).

The aim of the interview, as a data collection tool, was to explore ideas, perceptions, experiences, feelings and thoughts of the participants in their own unique words (Taylor, 2005; Wilkinson & Birmingham, 2003). It also aimed to enrich understanding of the quantitative findings and participants' experiences through their treatment changes. Although the questionnaires included a number of domains assessing patients' satisfaction with medication, in order to understand their impact on adherence, satisfaction measurements alone are not sufficient to understand patient adherence (Shikiar & Rentz, 2004). The topics under examination were potentially sensitive and, therefore, it was beneficial for them to be explored in depth (Wilkinson & Birmingham, 2003). Semi-structured face–to-face (individual) interviews are focused interviews with a relatively small number of open-ended questions that

allow the researcher to identify respondent's own ideas, views and attitudes. In this way the questions become more relevant to the participants and they gain an element of control over the interview (Corbin & Morse, 2003). Employing semi-structured interviews allowed for flexibility to generate insights that otherwise could not have been accessed if the method was more structured (Taylor, 2005). The semi-structure nature of the interview permitted consistency to the conduct of the interview with the intention of enriching study credibility (Lewis & Ritchie, 2003).

Interviews were conducted by the lead researcher, who has a background as a dietitian and experience in counselling patients, in particular dealing with overweight and obese clients with T2D, and experience in conducting research interviews. As a health professional who has worked in the past in similar research (Psarou & Brown, 2010) it was important to note during the conduct of the interviews the potential effects on the participants, as well as the potential resource and benefits of prior experience and background brought into the research process (Holloway, 2005). Furthermore, conducting repeated interviews helped to increase the rapport between interviewer and participant (Schatz, 2012).

4.3.1.1 Purpose of Interviews

The purpose of the interviews was to explore participants' expectations and perceptions of diabetes/weight loss medication in relation to their:

1. past experiences of taking medicines in general, diabetes/weight loss medicines and effects on their blood glucose and body weight (1st interview)
2. lived experiences in taking their new medication and effects on blood glucose and body weight (2nd interview)
3. past and current experiences of diabetes services re: medication prescription and guidance received (including lifestyle changes i.e. diet, physical activity and behaviour) (1st and 2nd interview)
4. past and current experiences of barriers and facilitators for managing (accepting) new diabetes/weight loss medicines [based on previous experiences, beliefs about medicines and interaction with HPs] (1st and 2nd interview)

This study used two data collection tools for the interviews, labelled "Interview Guides 1 and 2" (Appendix 4.2). The sections below describe the development and formatting of the interview guides and the data management and analysis of the interview data.

4.3.1.2 Development of interview guides

The interview guides were developed following a preliminary analysis of the quantitative findings from the first participants completing the questionnaires (questionnaire 1 n=45, questionnaire 2 n=30) triangulated with literature and after consultation with the research steering group. The preliminary analysis of the questionnaires identified areas to be explored further, which resulted in the interview guides being designed around the following relevant themes:

- Benefits and disadvantages of taking medicines – including any lifestyle changes as a result of taking medicines
- Experiences of medication use for diabetes (or weight loss) and impact on daily life prior to new medicine and as a result of new medicine
- Expectations of new medicine prescribed and perceptions of outcomes for now and in the future related to diabetes and body weight.
- Factors that impact on managing and adhering to medicines and to new medicine
- Practical aspects that help with adherence to medicines and to new medicine
- Perceptions of support provided and interactions with HPs prior to prescription of and whilst taking the new medicine
- Potential help and support

The interview guides were piloted verbally with two HPs (one specialist diabetes nurse and one practice nurse with an interest in diabetes), and four patients with T2D who were not participating in the interviews (one commencing on liraglutide, one on insulin and two on oral tablets). The pilot work was done to ensure understanding of the questions and remove any ambiguity. Following this a few minor changes were made which were mainly due to the order of some of the questions within each interview guide.

4.3.1.3 Sampling techniques and sample size

The sampling technique employed was purposive, in order to achieve adequate representation of participants and avoid selecting a biased sample (Schatz, 2012). This sampling approach has an element of process that relates to, and ensures, theoretical saturation (Oppong, 2013).The choice of this purposive sample of T2D patients was to achieve representation in relation to the phenomenon being researched and the setting, i.e. participants prescribed new glucose-lowering or anti-obesity drugs, which were either oral or injectable, in primary or secondary care (Lewis, 2003). Furthermore, participants were recruited from each stage of disease, i.e. from diagnosis to complex management by years since diagnosis, drug experience and gender. The sampling frame (Figure 4.1) was developed from a second preliminary analysis from the questionnaires (n=98), and participant characteristics (Table 4.2). It was estimated that approximately 30 participants would be sufficient to explore in depth the phenomenon under study, and that the sample could be more or less depending on whether saturation was reached i.e. the point at which no new findings were emerging from interviews (Holloway & Wheeler, 2010).

Sample Matrix based on Medicines Class -Primary Care								
Medicines	Orlistat	GLP-1 (Liraglutide, Exenatide, Exenatide ER)	DPP-4 (Sitagliptin, Linagliptin, Saxagliptin)	SGLT-2 (Dapagliflozin)	Biguanides (Metformin/ Metformin MR)	Sulphonylureas (Gliclazide, Gliclazide SR)	TZD	Insulin Regime
Participants Number	1	5	2	1	2	2	1	3
Sample Matrix based on Medicines Class -Secondary Care								
Medicines	Orlistat	GLP-1 (Liraglutide, Exenatide, Exenatide ER)	DPP-4 (Sitagliptin, Linagliptin, Saxagliptin)	SGLT-2 (Dapagliflozin)	Biguanides (Metformin/ Metformin MR)	Sulphonylureas (Gliclazide, Gliclazide SR)	TZD	Insulin Regime
Participants Number	0	5	2	1	0	1	0	4
Total	1	10	4	2	2	3	1	7

Sample Matrix based on Medicines Form															
	High Adherence VS Medium-Low Adherence (55:45)		Age Group 18-40/ 41-60/60+ (11:38:51)			Overweight VS Obese VS Morbidly Obese (23:51:26)			Setting Primary Care VS Secondary Care (80:20)		Gender Male VS Female (60:40)		Multiple Meds (>5 per day) VS non-complicated (<5 per day) (93.7:6.3)		Diabetes Duration Newly Δ VS >5 years (25:75)	
Medicines Oral (45%)	8	5	1	5	7	3	7	3	10PC	3SC	8M	5F	12	1	3	10
Medicines Injections - Insulin/non-insulin (55%)	10	7	2	6	9	4	9	4	13PC	4SC	10M	7F	16	1	5	12
Total	18	12	3	11	16	7	16	7	23PC	7SC	18M	12F	28	2	8	22

Numbers within parenthesis denote ratios

Figure 4.1: Sampling Framework

Table 4.2: Participant characteristics for the development of sampling framework

Participant characteristics	
Gender (n=98)	58.2% Male 41.8% Female
Marital Status (n=96)	14.6% single, 65.6% married, 7.3% separated, 12.5% widowed
Education status (n=96)	7.3% University or higher 9.4% A level equivalent 19.8% GCSE or equivalent 3.1% Diploma 13.5% Vocational 46.9% No formal qualifications
Employment Status (n=94)	25.5% Full-time 6.4% Part-time 12.8% unemployed 45.7% retired

	9.6% other	
Class of medicines (n=98)	10.2% Biguanides 7.1% Sulphonylureas 31.6% GLP-1 19.4% DPP-4 29.6% Insulin 1% Meglitinides 1% Anti-obesity drugs	37.7% WI Drugs 29.6% WN Drugs 32.6% WR Drugs
Age (n=98)	59.0yrs ± 11.5yrs	
Years of T2D diagnosis (n=88)	8.9yrs ±8.1yrs	
BMI kg/m^2 (n=44)	35.8 ±8.0	
HbA1c mmol/mol (n=43)	79 ±19	

Data are % or mean±SD

4.3.1.5 Data management and analysis

All interviews were transcribed by a professional and independent transcription company which signed a confidentiality agreement prior to any transcription. All transcriptions were quality checked by the lead researcher and most items labelled "unclear" by the transcriber were identified. These were items related to participants' regional accents or local expressions. Clarification was obtained by replaying the digital recordings and referring to interview notes which were collated as part of an audit trail. Furthermore, transcripts were anonymised prior to analysis, by removing names that could identify the participants themselves or health care professionals involved in their care.

Data coding and analysis was managed using QSR NVivo version 10. Transcripts were coded into themes using the framework approach developed in Britain for policy research (Richie et al., 2003). This 'framework' approach consists of five steps; familiarisation with the data set, identification of descriptive codes from independent repeated readings of transcripts, then identification of emerging themes on the basis of initial indexing, hierarchical grouping of codes, and discussion of individual transcripts. The framework approach is a systematic method of qualitative data analysis based on a matrix, and therefore, enables the researcher to explore the data in depth whilst maintaining a rigorous and transparent audit trail

(Richie et al., 2003). In this study, the familiarisation process continued until the diversity of circumstances and characteristics of the data set had been understood, followed by an initial identification of recurring themes or ideas. Each individual participants' transcripts were reviewed to determine what aspects changed for these individuals following the new medicine prescription, what aspects remained stable during the study period, and the process of change over time. These were recorded as summaries for each case in Nvivo.

Nvivo facilitated the creation of an index of the emerging open themes, which later were grouped into smaller numbers of broader "main" themes creating an initial hierarchy of a thematic framework (Appendix 4.3). Transcript passages were added to relevant themes in a systematic way, and, where newer themes emerged, previous transcripts were revisited to ensure consistent labelling and indexing. Any changes to names of themes or process of indexing was recorded in Nvivo with dates via the "Memo" function. Throughout the process of indexing and coding, emergent ideas, spontaneous thoughts or conceptual themes were also noted in a separate memo to facilitate analysis particularly if there were signs of interconnections between themes or participants characteristics, such as adherence level and everyday medication practices. In Nvivo, framework matrices were produced for each individual main theme which included all sub-themes in columns and all participants in rows. Data were summarised and synthesised within the matrix by linking these with the raw data. Furthermore, participants' expressions and phrases were retained within the summary, so context and content was not lost. The framework matrices enabled the researcher to study and synthesise data across all participants, noting the range of perceptions, experiences and behaviours as part of a theme (Richie et al., 2003) paying particular attention to "outliers" or "deviant cases" (Holloway, 2005). This allowed the researcher to display the diversity of the phenomenon explored.

The effects of patient characteristics, such as gender, age, degree of overweight or obesity, type of medication experienced, expectations, beliefs and attitudes and adherence levels, were explored in the analysis by entering these data as attributes

from the questionnaire results. This is a common approach to an initial integration of mixed method data (Bazeley, 2010). The framework matrices were also used to compare and contrast findings between subgroups (i.e. weight-effect groups) whilst maintaining context for individual cases. The process of such analysis helped for the identification of associative patterns within the data and plausible explanations of why such patterns occur. Interpretation of the findings was verified using independent transcript analysis by the lead researcher and through discussions with the supervisors, and the research steering group who examined emerging themes to guide development of the initial thematic framework.

4.3.1.6 Presentation of Findings

Although participants' interpretations can be diverse and multifaceted, it is also accepted that these are influenced by the researcher's understanding of the phenomenon whilst striving to be as objective and neutral in their presentation (Ritchie & Lewis, 2003). Where findings were generalised these were supported with use of quotes from the original data, yet only a limited amount of quotes per theme or sub-theme were presented to avoid overuse of quotes and distraction from the clarity of the main commentary (White et al., 2003). Quotes often represented more than one theme/sub-theme, therefore a quote was used only once to avoid repetitious reading and, its length was edited by the use of ellipses (…). Words added, to aid comprehension, were inserted in brackets (White et al., 2003). Furthermore, the frequency or dominance of findings were displayed with the use of the following words; "few", "most", "all", "rare", "commonly" or "recurrent", instead of specific numbers or proportions (White et al., 2003).

4.3.2 Mixed Method Data Management and Analysis

Quantitative and qualitative data analysis was combined into a matrix created in NVivo. This common mixed method analysis (Caracelli & Greene, 1993, Bazeley, 2012) serves to compare the two data types through data transformation, i.e. questionnaire data transformed into narrative descriptions of the variables that they represent. This type of analysis helps to observe any overlapping or inconsistent

aspects when the two data types are transferred into the matrix. The data from this combined analysis were then consolidated to uncover fresh insights or new perspectives (Caracelli & Greene, 1993). Finally, a group case analysis was undertaken (i.e. comparing the three weight-effect groups and/or adherence level groups) to gain an in-depth understanding of the reasons for any inconsistencies between the qualitative and quantitative data (Caracelli & Greene, 1993). This mixed method analysis served to legitimise (otherwise validate) the findings that stem from both qualitative and quantitative data of the PhD study to portray combination of both data into a coherent whole (Onwuegbuzie et al., 2011) to explain the phenomenon of medicine taking behaviour in people with T2D.

CHAPTER FIVE: QUESTIONNAIRE RESULTS

5.1 Introduction

This chapter presents the results of the analysis of the questionnaires (pre and post new diabetes treatment) and clinical data collected in this study. It starts with the presentation of the response rates to the survey, reliability of the scales used and proportion of missing data. The demographic characteristics of participants and their clinical data follow. In addition, each section then presents the results for each scale within the two questionnaires, as well as information on the responses to questions and overall individual change for each scale. These sections answer the first key research question:

1. How do the expectations, beliefs and attitudes of people with T2D towards different diabetes treatments that either promote weight loss, are weight neutral or result in weight gain, change over time?

Then, the multivariate analysis is presented which focuses on the second key research question:

2. What is the impact of this change on patients' adherence to their medicine(s)?

Finally, a summary of the key findings is provided at the end of the chapter.

5.2 Recruitment, Survey Response and Data Screening

The study recruited participants from both primary and secondary care. There was one secondary care site, a hospital diabetes centre, and in primary care there were forty-two sites. The primary care sites consisted of twenty-five GP sites and seventeen community pharmacies; these were spread across the Merseyside and included the following PCTs; Knowsley, Sefton, Liverpool, Halton and St Helens, and Wirral. The figure 5.1 shows the number of potential participants approached and eventually recruited by NHS Trust.

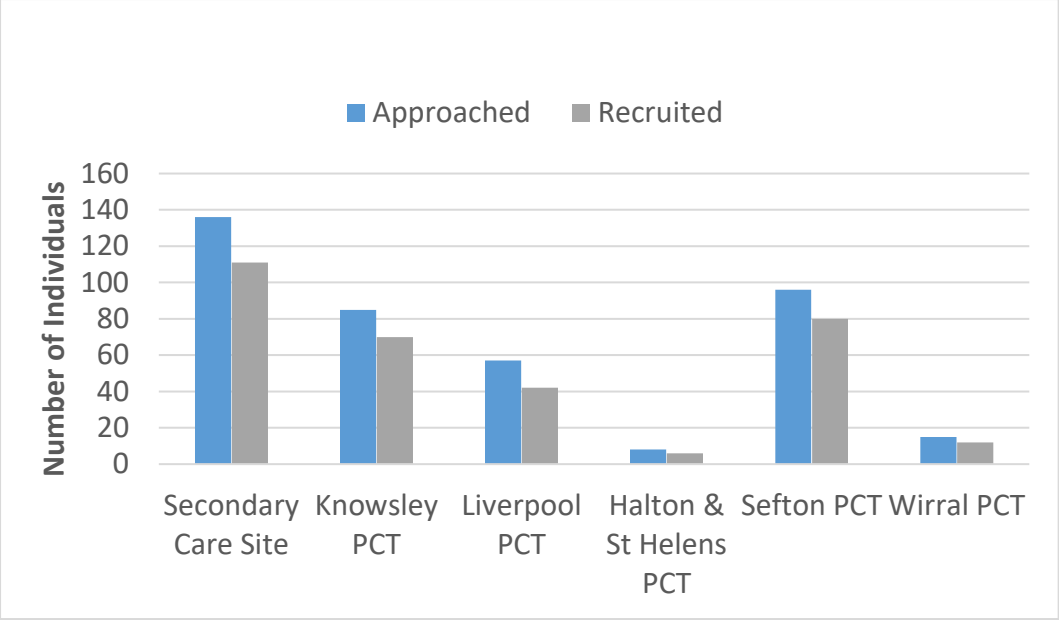

Figure 5.1: Number of potential participants approached and recruited in in primary and secondary care NHS Trusts

The disposition of patients approached to take part in the study is shown in Figure 5.2. The study achieved a response rate of 77% for the first questionnaire, which is much higher than the expected 40% rate commonly seen in surveys. Of those who returned the first questionnaire, 86% returned the second questionnaire following the two reminders.

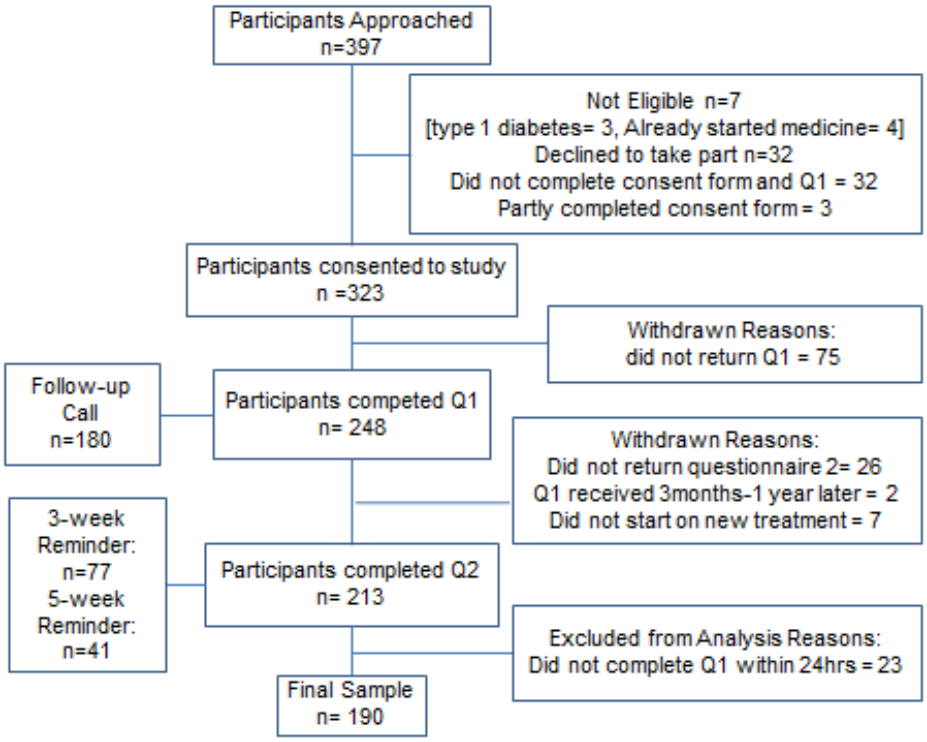

Figure 5.2: Recruitment Flowchart

Missing data for most scales was negligible and random, ranging between 0 and 5% for the first questionnaire. However, 6.6% of data for the DiabMedSat and the MMAS-8 scales were not applicable data, as those participants were prescribed diabetes medication for the first time. Missing data ranged between 0 and 2% for the second questionnaire. In addition, negligible data were missing from the demographics of the participants (0.8-1.2%), however overall baseline clinical data ranged from 1.6% to 25.4% (Appendices 5.2 and 5.3). Furthermore, missing follow-up clinical data ranged from 18.3%- 69.5% most notably for the blood lipids (Table 5.2). However, it is common practice to repeat such measures on a 6-monthly or yearly basis, than at three months. Clinical data such as BMI and HbA1c were not always available at the 3-month cut off point (~25%), so these were recorded whenever they were available from the medical notes at the GP/Hospital and usually ranged between 2 and 4 months from the baseline measure.

5.3 Internal Reliability

The reliability of the scales used in the questionnaires was tested for internal reliability using Cronbach's α shown in Appendix 5.1. The internal reliability ranged from 0.59 to 0.98, and scales performed similar or better in this study than other related studies with the exception of EITQ, TRIM-Wt and MMAS-8. The difference in the reliability of the scales could be due to the sample population, as the study by Naegeli and Hayes (2010) was based on a sample recruited via a clinical trial for an inhaled insulin, the study by Brod et al. (2010) was based on an online sample prescribed anti-obesity drugs and the study by Morisky et al. (2008) was based on a hypertensive sample. However, it is acknowledged that values of Cronbach's alpha are dependent on the length of the scale, the sample size and the type of response within the items (binary Vs Likert scale) (Streiner and Norman, 2008). For example, the TRIM-WT subscales have a small number of items with the TRIM-Wt-WM only consists of three items and the MMAS-8 scale consists mostly items with a binary response, therefore, such characteristics could reduce the value of alpha (Streiner and Norman, 2008). Furthermore, Cronbach's alpha values found for both of the questionnaires were equally similar indicating that the majority remained above 0.70. To retain consistency between baseline and follow-up, no changes were made to the scales. However, the 10-item medication adherence version (4.2.1.3) although it had improved its reliability with the additional two items, this was only a slight improvement (α=0.64). Hence, the thesis used the original MMAS-8 scale (α=0.60) for subsequent analysis in order to be comparable to previous research.

5.4 Participants

5.4.1. Whole Group

Information on the characteristics of the whole group (n=248), as well as those participants completing only questionnaire one and those completing both questionnaires is provided in Appendices 5.2 and 5.3. Those in retirement were more likely to return the second questionnaire than those in full-time employment ($p<0.01$). In addition, significantly lower creatinine and higher eGFR values were found ($p<0.05$) in those who returned only questionnaire one compared to those

who returned both questionnaires. It is common practice with patients whose kidney function is not well controlled to move onto insulin therapy and there was a non-significant trend for those patients to have a lower eGFR. There was no other statistical difference between the two groups.

On inspection of the first questionnaire, 89% of participants completed questionnaire one prior to taking the first dose of their new medicine (n=190)[12], whereas 11% completed it after the first dose (n=23). A sensitivity analysis shown that there were no differences in most demographic or clinical data between those two groups, except that those who were widowed were significantly more likely to complete the first questionnaire after they had taken their first dose of their new medicine (p=0.021). Furthermore, those who completed the questionnaire after they had taken the first dose of their medicine, were found to have significantly stronger beliefs that prescribed medicines are overused by doctors (Median=3.33 Vs Median=2.67, p=0.034), and that medicines are "harmful" and "addictive" (Median=2.75 Vs Median=2.50, p=0.001), and were significantly less satisfied with their diabetes medicines in relation to how burdensome they are (Median=75 Vs Median=81.81, p=0.030). Tables 5.1 and 5.2 present the demographic and clinical characteristics of those participants who completed questionnaire 1 prior to taking the first dose and include the final sample in this study (n=190). On review of the second questionnaire, 76.3% (n=145) of participants indicated that they still continued to take the new medicine, whereas 7.4% (n=14) indicated that they had discontinued this treatment, and 16.3% (n=31) were missing data.

Table 5.1: Sample Characteristics (n=190) - Demographic

	Baseline n(%)
Centre Site: GP Practice SCDC CP	 107(56) 66(35) 17(9)
Age(yrs)	60.5 (51.0, 69.0) [Range 24-86]
Gender	

[12] Participants who completed the first questionnaire within 24 hours of taking the first dose of their new medicine were included in the final sample (see section 3.4).

Men	103(54)
Women	87(46)
Ethnicity	
Caucasian	188(99)
Asian	1(0.5)
Mixed	1(0.5)
Marital Status	
Alone/Single	21(11)
Married/with partner	141(74)
Divorced/Separated	16(9)
Widowed	12(6)
Level of Education	
University/Higher Degree	19(10)
Diploma	9(5)
Vocational	28(15)
A level	19(10)
GCSE	36(19)
No Formal Qualifications	78(41)
Missing Data	1(0.5)
Employment Status	
Full time	40(21)
Part-time	15(8)
Unemployed	21(11)
Retired	90(47)
Other [most on benefits]	24(13)
IMD	
20% most deprived	114(60)
21% to 40%	27(14)
41% to 60%	24(13)
61% to 80%	15(8)
20% least deprived	10(5)

Data are % or Median and IQR reported as (Q1, Q3)

Table 5.2: Sample Characteristics (n=190)-Clinical

	Baseline n(%)	**Follow-up** n(%)
Years Diagnosed with T2D	7.0 (3.0,13.0) [Range 0-59yrs]	
Missing Data	3(1.6)	
No of Diabetes Complications-		
None	85(44.7)	74(38.9)
One	58(30.5)	41(21.6)
Two	28(14.7)	19(10)
Three	13(6.8)	16(8.4)
Four	2(1.1)	1(0.5)
Five	2(1.1)	2(1.1)
Missing Data	2(1.1)	37(18.9)
Total Medicine Burden (number per day)	7 (5,10) [Range 1-21]	7(5,11) [Range 2-21]
Missing Data	8(4.2)	39(20.5)
Diabetes Regime-		
None	18(9.5)	
Tablets only	111(58.4)	53(27.9)
Tablets & insulin	30(15.8)	38(20.0)
Insulin only	10(5.3)	6(3.2)
Insulin & GLP-1	1(0.5)	5(2.6)
Tablets, insulin & GLP-1	1(0.5)	14(7.4)
Tablets and GLP-1	17(8.9)	37(19.5)
GLP-1 Only	0(0)	3(1.6)

Missing Data	2(1.1)	34(17.9)
Total Diabetes Medicine Burden (number per day)	2 (1,2) Range (0-4)	2 (2,3) Range (1-5)
BMI (kg/m2) Missing Data	35.0 (31.0, 40.6) [Range 22.10-61.10] 5 (2.6)	35.5 (31.5, 40.7) [Range 22.7-59.6] 48 (25.3)
HbA1c(mmol/mol) Missing Data	77 (66, 92) [Range 42-134] 7 (3.7)	67 (56, 80) [Range 35-123] 45 (23.7)
Systolic Blood Pressure(mmHg) Missing Data	134±15 8 (4.2)	130±16 87 (45.8)
Diastolic Blood Pressure(mmHg) Missing Data	75±11 8 (4.2)	75±11 87 (45.8)
Cholesterol(mmol/L) Missing Data	4.1 (3.5, 5.0) 36 (18.9)	3.7 (3.5, 4.6) 117 (61.6)
LDL(mmol/L) Missing Data	2 (1.5, 2.8) 56 (29.5)	1.8 (1.4, 2.4) 132 (69.5)
HDL (mmol/L) Missing Data	1.1 (0.9, 1.2) 39 (20.5)	1.1 (0.9, 1.3) 120 (63.2)
Triglycerides(mmol/L) Missing Data	2.12 (1.5, 2.9) 46 (24.2)	1.85 (1.4, 3.15) 126 (66.3)
eGFR(ml/min) Missing Data	78 (56, 90) 15 (7.9)	73 (56, 88) 73 (38.4)
Creatinine(µmol/L) Missing Data	79 (67, 102) 16 (8.4)	81 (69, 109) 69 (36.3)

Data are % or Median and IQR reported as (Q1, Q3), or mean±SD

5.4.2 Groups according to effect of new medicine on body weight

A wide range of medicines were prescribed in this study that cover all glucose–lowering drugs available for T2D. These medicines were classified according to effects on body weight as WR, WN or WI (Table 5.3). The most common new treatment prescribed was liraglutide, a GLP-1 agonist (Table 5.3). The highest proportion of prescribed drugs in the weight reducing group were GLP-1 analogues (85%); in the weight neutral group were DPP-4 inhibitors (62%) and in the weight increasing group were insulin injections (72%). These three drug classes had also the highest proportion of prescribed drugs within the whole group (31%, 19%, and 24% respectively). When comparing the three weight-effect groups in relation to participants who completed just the first questionnaire and those who completed both questionnaires, a similar number of participants in each group completed both questionnaires (Figure 5.3).

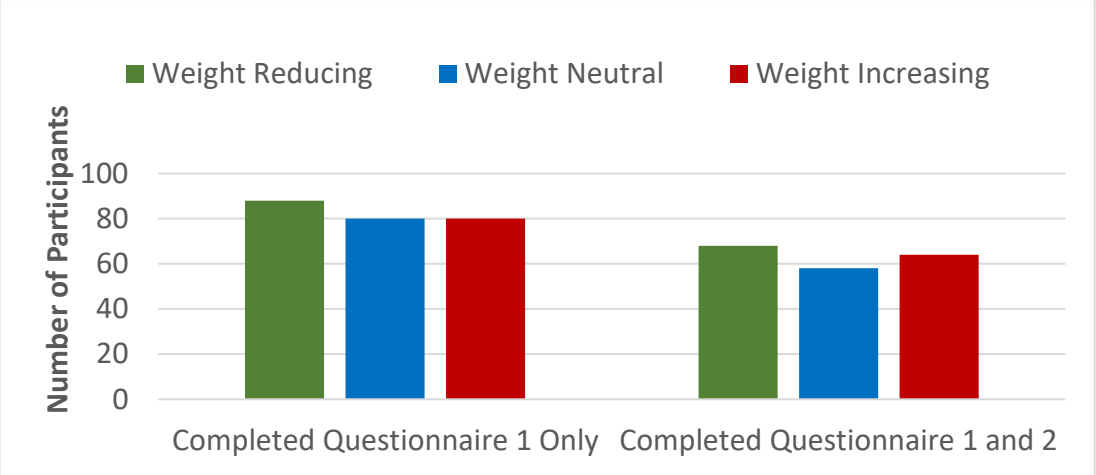

Figure 5.3: Number of participants completing questionnaires in each weight-effect group.
The first set of bar charts shows the number of participants who completed the first questionnaire and the second set of bar charts shows the number of participants who completed both questionnaires.

Table 5.3: Proportions of types of new medicine prescribed

Weight Group n(%)	**Drug Class n(%)**		**Drug Name n(%)**	
Weight Reducing 68 (36)	GLP-1 agonist	58(31)	Exenatide	14(7)
			Exenatide ER	9(5)
			Liraglutide	35(18)
	SGLT-2 Inhibitor	8(4)	Dapagliflozin	8(4)
	Anti-Obesity	2(1)	Orlistat	2(1)
Weight Neutral 58 (31)	Biguanides	22(12)	Metformin	13(7)
			Metformin MR	9(5)
	DPP-4 Inhibitor	36(19)	Linagliptin	12(6)
			Sitagliptin	19(10)
			Saxagliptin	5(3)
Weight Increasing 64 (34)	Sulphonylureas	16(8)	Gliclazide	15(8)
			Gliclazide SR	1(0.5)
	Insulin	46(24)	Novomix Mixtard 30	12(6)
			Insulin Detemir	13(7)
			Insulin Glargine	9(5)
			Novorapid	2(1)
			Basal Bolus	4(2)
			Humulin I	3(2)
			Humulin M3	2(1)
			Hypurin Porcine	1(0.5)
	Thiazolodinediones	2(1)	Pioglitazone	2(1)
	Meglitinides	0(0)	Nateglinide	0(0)

Table 5.4 shows participants' characteristics for each weight-effect group at baseline and at 3-month follow-up with comparisons made within time period. At baseline, participants were more likely to be prescribed a diabetes medicine with weight neutral effect in primary care and be recruited from a community pharmacy than from secondary care ($p<0.0001$). Participants were less likely to be recruited from a community pharmacy if they were prescribed a diabetes medicine with WR effect ($p<0.001$).

Those prescribed WR medicines had a significantly higher BMI at baseline than the other two weight-effect groups ($p\leq0.001$) and this remained significantly higher at three-month follow-up compared to those treated with WN ($p<0.05$) and WI medicines ($p\leq0.001$). Furthermore, at baseline, they were significantly younger than

the WN group ($p<0.05$), and were more likely to be women. Those prescribed WI medicines had significantly higher HbA1c at baseline compared to the other two groups ($p\leq0.001$) and this remained significantly higher at three month follow-up ($p<0.01$). They also had higher creatinine levels at three month follow-up compared to the WR group ($p<0.05$). Those prescribed WN medicines were taking a significantly lower number of medicines overall per day both at baseline and three-month follow-up compared to the WI group ($p\leq0.01$). In addition, the same group was taking significantly less number of diabetes medicines both at baseline ($p\leq0.001$) and at three-month follow-up ($p\leq0.01$) compared to the other two groups.

Overall, the whole group significantly lost weight (median=0.9kg, $p<0.001$) and reduced their HbA1c (median=8mmol/mol, $p<0.001$) at 3-month follow-up. However, those prescribed WR medicines lost significantly more weight ($p<0.01$) and those prescribed WN medicines had significant lower HbA1c ($p<0.01$) at three-month follow-up.

Table 5.4: Study participant characteristics at baseline and follow-up for each weight-effect group

	BASELINE			3-MONTH FOLLOW-UP		
Participant Characteristics n(%)	**Weight Reducing**	**Weight Neutral**	**Weight Increasing**	**Weight Reducing**	**Weight Neutral**	**Weight Increasing**
Total N	68	58	64	68	58	64
Centre Site- SCDC GP Practice CP	 28(41.2) 38(55.9) **2 (2.9)**	 **10(20.1)** 36(62.1) **12(20.7)**	 28(43.8) 33(51.6) 3(4.7)			
Gender-Men	**27 (39.7%)**	35 (60.3%)	41 (64.1%)			
Age (years)	**56.5 ±9.2**$^{+}$	**62 ± 10.6**$^{+}$	60.6 ± 12			
Diabetes Duration (yrs) Missing	7.5(4.0,12.0) 0(0)	6.0(2.0,13.0) 1 (1.7)	9.0(4.0,14.0) 2(3.1)			
Weight Change(kg) Missing Data				**-2.5 (-5.0, -0.7)**$^{***++}$ 8(11.8)	**-0.6 (-2.8, 1.2)**$^{++\$\$}$ 25(43.1)	**1.0(-0.4, 2.3)**$^{***\$\$}$ 18 (28.1)
BMI(kg/m2) Missing	**37.8 (35.3,42.0)**$^{*** +++}$ 1 (1.5)	**32.4 (28.1, 38.8)** $^{+++}$ 3(5.2)	**32.5 (30.8, 37.9)** *** 1(1.6)	**37.5 (34.0, 42.0)** $^{+ ***}$ 8(11.8)	**33.6 (30.1, 40.0)+** 23(39.7)	**33.1 (30.3, 38.3)** *** 17(26.6)
HbA1c(mmol/mol) Missing	**73 (65, 86)***** 2 (2.9)	**72 (60, 85.5)**$^{+++}$ 1(1.7)	**88 (76, 97.5)**$^{***+++}$ 4(6.3)	**64 (51, 75)**** 19(27.9)	**60 (53, 79)++** 13(22.4)	**76 (62, 91)****++ 13(20.3)
HbA1c Change (mmol/mol) Missing				-8 (-16, -2) 21 (30.9)	-8 (-17, -2.5) 13 (22.4)	-13 (-22, -1.5) 15 (23.4)
BP systolic	136.12±14.6	130.49±13.93	136.10±18.24	131(120, 140)	125(116, 136)	136(120, 153)

Missing	3(4.4)	1(1.7)	(6.3)	33(48.5)	27(46.6)	27(42.2)
BP diastolic	76.26±11.5	72.51±10.9	77.35±9.6	76(70, 81)	70(63, 80)	77(70, 84)
Missing	3(4.4)	1(1.7)	4(6.3)	33(48.5)	27(46.6)	27(42.2)
Total Cholesterol	4.1 (3.5, 5.0)	3.9 (3.5, 5.1)	4.2 (3.6, 5.0)	3.7 (3.5, 4.4)	3.7 (3.5, 4.4)	4.2(3.4, 5.6)
Missing	19(27.9)	11(19)	6(9.4)	49(72.1)	35(60.3)	33(51.6)
LDL	1.9 (1.5, 2.6)	2.0 (1.4, 2.9)	2.1 (1.6, 2.6)	1.75 (1.4, 2.2)	1.78(1.3, 2.1)	2.2(1.1, 3.4)
Missing	25(36.8)	15(25.9)	16(25)	50(73.5)	41(70.7)	41(64.1)
HDL	1.1 (0.9, 1.4)	1.1 (1.0, 1.3)	1.0 (0.9, 1.2)	1.1(0.9, 1.2)	1.1(0.9, 1.2)	1.1(0.9, 1.4)
Missing	20 (29.4)	11(19)	8(12.5)	49 (72.1)	36 (62.1)	35(54.7)
Triglycerides	2.3 (1.6, 2.7)	1.8 (1.3, 2.8)	2.2 (1.5, 3.4)	1.95 (1.6, 2.6)	1.6 (1.2, 3.2)	2.0 (1.5, 3.2)
Missing	22(32.4)	13(22.4)	11(17.2)	50(73.5)	39(67.2)	37(57.8)
Creatinine	73 (65, 90)	79 (68, 124)	81 (69, 108)	**75(65, 93)+**	83(69, 133)	**84(76, 109)+**
Missing	7(10.3)	4(6.9)	5(7.8)	28(41.2)	20(34.5)	21(32.8)
eGFR	81 (68, 90)	76 (50, 90)	74 (54, 90)	73(65, 89)	80(44, 89)	66(57, 84)
Missing	6(8.8)	4(6.9)	5(7.8)	29 (42.6)	21(36.2)	23(35.9)
Total Medication Burden	7 (4, 11)	**6 (4, 9)****	**9 (6, 11)****	7 (5,11)	**6 (4,9)****	**9 (6,11)****
Missing	4 (5.9)	2(3.4)	2(3.1)	13(19.1)	10(17.2)	16(25)
Total Diabetes Medication Burden	**2(1, 3)+++**	**1 (1,2) +++*****	**2 (1, 3)*****	**2 (2, 3)++**	**2 (1,3)++****	**3 (2, 3)****
Missing	0(0)	1(1.7)	1(1.6)	10 (14.7)	9(15.5)	16(25**)**
Diabetes Complications	1 (0, 1)	1 (0, 1)	1 (0, 2)	1 (0, 2)	0 (0, 1)	1 (0, 2)
Missing	1(1.5)	1(1.7)	0(0)	12(17.6)	10(17.2)	15(23.4)

Data are Median (IQR) Or n(%) Or Mean(±SD). Difference between pairs within time period: +p<0.05, **p≤0.01, ++p≤ 0.01, $$p≤0.01, +++p≤0.001***p≤0.001, Bonferroni Correction p<0.017

Table 5.5: Baseline and Follow-up scores for all scales for the whole group and each weight-effect group

	Baseline					**Follow-up**				
Medication Adherence Level	Whole Group	Weight Reducing	Weight Neutral	Weight Increasing	P value	Whole Group	Weight reducing	Weight Neutral	Weight Increasing	P value
Total N	188	67	57	64		188	67	57	64	
EITQ (baseline)/ PITQ (Follow-up)	5.5 (5.1, 6.0)	5.6 (5.1, 6.0)	5.6 (5.1, 6.1)	5.5 (4.9, 5.9)	0.301	5.6(5.1,6.0)	5.6 (5.2, 6.0)	5.6 (5.3, 6.0)	5.6(5.0,6.0)	0.594
SIMS	13 (9, 16)	13 (8, 16)	13 (10, 16)	13 (9, 18)	0.730	15 (9, 17)	16 (12, 18)	15 (8, 17)	14 (9, 18)	0.243
SIMS-AU	8 (6, 9)	7 (6, 9)*****	8 (6, 9)	9 (7, 9)*****	**0.008**	8 (6, 9)	8 (7, 9)	7 (6, 9)	9 (7, 9)	**0.048**
SIMS-PPM	5(2,8)	5 (3, 8)	5 (3, 8)	5 (2, 9)	0.885	7 (3, 9)	7 (5, 9)	6 (2,9)	6 (3, 9)	0.208
BMQ-Concerns	2.9 (2.4, 3.3)	2.9 (2.4, 3.1)	2.9 (2.4, 3.4)	3.0 (2.4, 4.4)	0.944	2.7(2.3,3.3)	2.7 (2.3, 3.1)	2.7 (2.3, 3.3)	2.9(2.2,3.5)	0.189
BMQ-Necessity	4(3.4, 4.2)	3.8(3.4, 4.2)*****	3.8(3.4, 4.2)	4.0(3.6, 4.8)*****	**0.015**	3.8(3.4,4.4)	3.8 (3.2, 4.2)	3.8(3.2, 4.0)	4.0(3.6,4.6)	0.061
BMQ Necessity – Concern Differential	0.94 (0.46, 1.51)	0.93 (0.46, 1.45)	0.73 (0.28, 1.44)	1.11 (0.60, 1.69)	0.124	0.91 (0.41, 1.67)	0.89 (0.43, 1.71)	0.89 (0.35, 1.44)	1.14 (0.44, 1.66)	0.602
BMQ-Overuse	2. 7 (2.3, 3.3)	2.7 (2.3. 3.3)	2.7 (2.3, 3.3)	2.7 (2.3, 3.3)	0.936	3.0(2.3,3.3)	3.0 (2.7, 3.3)	3.0 (2.3, 3.7)	3.0(2.3,3.5)	0.736
BMQ-Harm	2.5 (2.0. 2.8)	2.5 (2.0, 2.8)	2.5 (2.0, 2.8)	2.3 (2.0. 2.8)	0.483	2.5(2.0,2.8)	2.5 (2.0, 2.8)	2.5 (2.3, 2.8)	2.5(2.0,2.8)	0.620
BMQ-Benefits	4.0 (3.8, 4.3)	4.0 (3.5, 4.3)	4.0 (3.8, 4.1)	4.0 (4.0, 4.5)	0.056	4.0(3.8,4.3)	4.0 (3.8, 4.0)	4.0 (3.8, 4.5)	4.0(4.0,4.5)	0.075
SEAMS	3.7 (3.0, 4.0)	3.4 (2.9, 3.9)	3.7 (3.1, 4.2)	3.9 (3.1, 4.4)	0.117	3.8(3.1,4.1)	3.7 (3.2, 4.4)	3.8 (3.1, 4.0)	3.8(2.9,4.2)	0.774
SEAMS-UCU	3.5 (2.7, 4.0)	3.3 (2.3, 4.0)	3.4 (2.7, 4.0)	3.8 (2.8, 4.2)	0.108	3.7(3.0,4.0)	3.9 (3.0, 4.1)	3.7 (3.0, 4.0)	3.8(2.8,4.0)	0.544
SEAMS-UDC	3.8 (3.1, 4.1)	3.6 (3.0, 4.0)*****	4.0 (3.6, 4.4)*****	4.0 (3.0, 4.4)	**0.039**	4.0(3.3,4.1)	3.9 (3.4, 4.8)	4.0 (3.4, 4.0)	3.8(2.8,4.0)	0.93
OWLQOL	65.7 (33.1, 84.5)	42.6 (23.8, 68.1)***^**	71.6 (56.6, 91.2)*****	78.3 (39.7, 89.9)**^**	**<0.001**	72.0 (43.6, 86.5)	53.4(27.2, 76.5)**+^**	77.4 (83.2, 90.7)**+**	78.4, 52.2, 90.7)**^**	**0.001**
Total N	170	64	45	61		170	64	45	61	170
MMAS-8	6.8 (5.5, 7.8)	6.8 (4.8, 7.7)	7.0 (5.7, 7.7)	6.8 (5.7, 8.0)	0.513	7.0(5.7,8.0)	6.5 (4.7, 8.0)	7.0 (6.0, 8.0)	6.8(5.1,8.0)	0.120

Total N	166	65	43	58		166	65	43	58	
DiabMedSat	65.2 (55.6, 75.4)	66.7 (56.6, 75.1)	71.8 (52.9, 80.8)	63.1 (55.0, 70.6)	0.061	72.5 (61.3, 80.4)	73.6 (65.0, 80.3)	73.5 (58.8, 82.9)	68.5 (57.9, 77.0)	0.174
DiabMedSat-Efficacy	53.3 (36.7, 63.3)	55.0 (37.5, 63.3)	60.0 (48.3, 69.6)*****	45.0 (28.5, 56.7)*****	**0.003**	61.7 (48.376.7)	62.5 (48.7, 76.7)	60.0 (49.6, 76.7)	61.7 (41.7, 78.3)	0.938
DiabMedSat Burden	81.8 (68.9, 91.3)	86.4 (68.6, 91.7)	82.6 (68.4, 93.4)	77.6 (71.2, 87.1)	0.20	84.9 (75.0, 93.3)	87.1 (78.2, 94.5)*****	87.1 (75.4, 95.5)	79.5 (68.9, 89.4)*****	**0.027**
DiabMedSat Symptoms	68 (52, 80)	64 (52, 78)	68 (49, 84)	68 (52, 76)	0.642	72 (56, 78)	72 (60, 80)	72 (56, 80)	64 (55, 76)	0.135
TRIM-Wt-DL	66.7 (54.2, 79.2)	66.7 (50.0, 79.2)	70.8 (54.2, 79.2)	66.7 (58.3, 75)	0.552	75.0 (58.3, 79.2)	72.9 (62.5, 79.2)	75.0 (62.5, 83.3)	70.8 (50.0, 100)	0.106
TRIM-Wt-WM	33.3 (16.7, 50.0)	25.0 (16.7, 33.3)*****	33.3 (25.0, 50.0)	41.7 (25.0, 58.3)*****	**0.002**	41. 7 (25.0, 66.7)	50.0 (25.0, 66.7)	41.7 (29.2, 66.7)	41.7 (25.0, 66.7)	0.908
TRIM-Wt-PH	75.0 (50.0, 93.7)	71.9 (39.1, 92.2)	75.0 (56.2, 100)	75.0 (50.0, 100)	0.168	75.0(50.0, 93.7)	75.0 (50.0, 93.7)	75.0 (56.2, 100)	75.0 (56.2, 93.7)	0.468

Values are Median (Q1, Q3), Significant difference between weight-effect groups, Bonferroni correction *p<0.017, +p<0.017, ^p<0.017

5.5 Changes in expectations, beliefs and attitudes overtime

This section describes in detail how participants' expectations, beliefs, attitudes, and adherence levels changed over time, as well as any differences between weight-effect groups. The Table 5.5 (previous page) presents participants' scale scores at both baseline and follow-up for the whole group and for each weight-effect group.

5.5.1 Expectations and perceptions of new medicine (EITQ, PITQ)

5.5.1.1 Whole Group- Baseline versus Follow-up

There was no significant difference between participants' perceptions (median=5.6) and expectations (median=5.5) about their new diabetes treatment, (p=0.463). (Figure 5.4; Table 5.5).

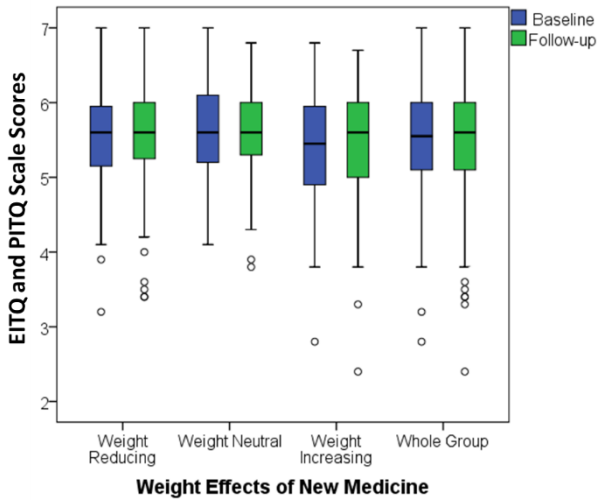

Figure 5.4: Expectations (EITQ) and Perceptions (PITQ) about new medicine at baseline and follow-up

Although the majority of participants were classified as having their expectations met or exceeded by experience[13], there was still a third of the group (33%) who felt that their expectations of their new medicine were unmet (Figure 5.5, Appendix 5.5).

[13] Changes were calculated based on SEM (Section 4.2.4 and Appendix 5.4)

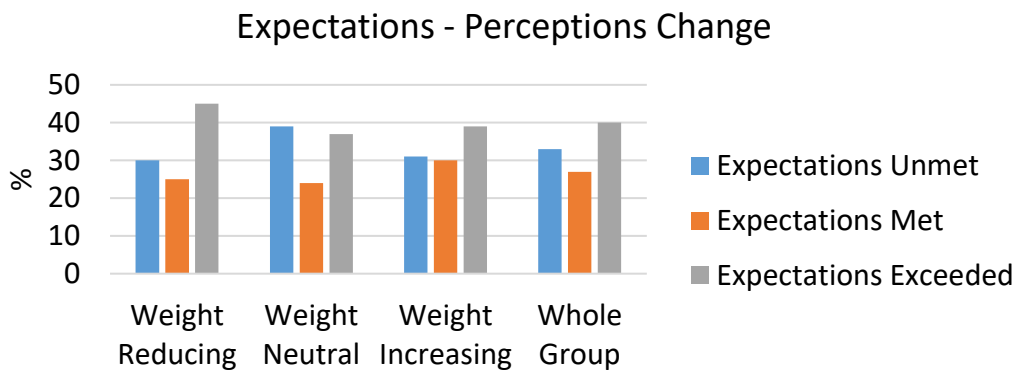

Figure 5.5: Percentage of participants whose expectations of new medicine were unmet, met or exceeded by experience

5.5.1.2 Weight-Effect Groups – Baseline versus Follow-up

For each weight–effect group (Figure 5.4, Table 5.5), there were no significant differences between participants' perceptions and expectations about their new diabetes treatment (WR Group: baseline median 5.6 Vs follow-up median 5.6 p=0.221, WN Group: baseline median 5.6 Vs follow-up median 5.6 p=0.582, WI Group: baseline median 5.5 Vs follow-up median 5.6 p=0.658).

Weight Reducing Group

A closer look at single items from the EITQ/PITQ revealed that a significantly higher proportion of this group agreed with the statements that their new medicine will make it easier to control their blood sugars (**p=0.001**), and make them feel better (**p<0.001**) compared to follow-up (Figures 5.6 and 5.7), suggesting that they had higher expectations prior to taking their new medicine than perceptions at three month follow-up.

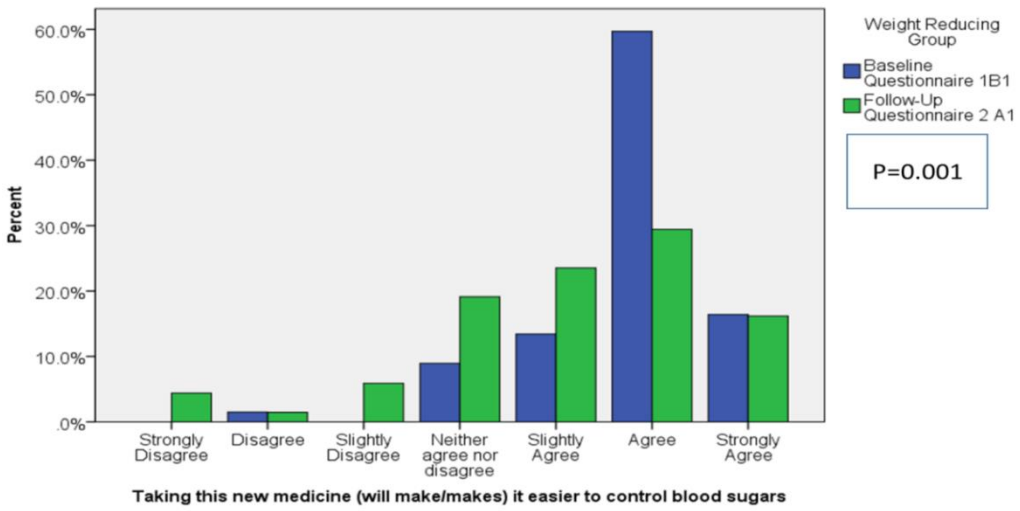

Figure 5.6: Percent agreement to EITQ/PITQ item "taking this new medicine (will/makes) it easier to control my blood sugars" at baseline and follow-up for WR group.

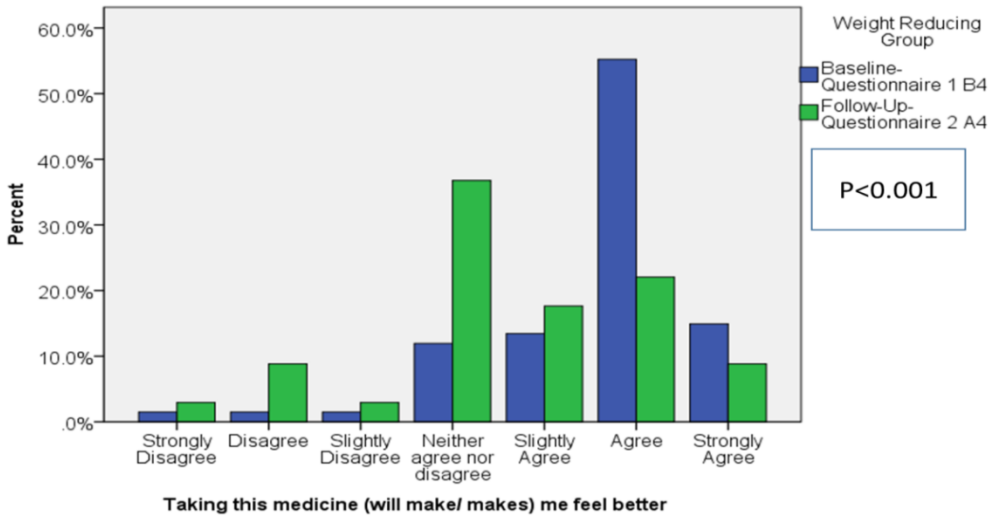

Figure 5.7: Percent agreement to EITQ/PITQ item "taking this new medicine (will/makes) me feel better" at baseline and follow-up for WR group.

In addition, a significantly higher proportion of participants in this group, disagreed with the statement that the delivery system was physically painful (or difficult to swallow) (p=0.049) (not shown), and agreed that it was easy to use away from home (or as prescribed) (p=0.004) (Appendix Figure 5.1) and that it was convenient (p=0.007) (Appendix Figure 5.2). This shows that this group were more positive about their new medicine at follow-up than at baseline.

Weight Neutral Group

Those treated with weight neutral medicines also had higher expectations about their new medicine in relation to how easy it was going to be to control their blood sugars (**p=0.001**) (Figure 5.8), and make them feel better (**p<0.001**) (Figure 5.9). They also had more positive perceptions about their new medicine as they thought it did not cause them to have severe episodes of low blood sugar (p=0.026) (not shown).

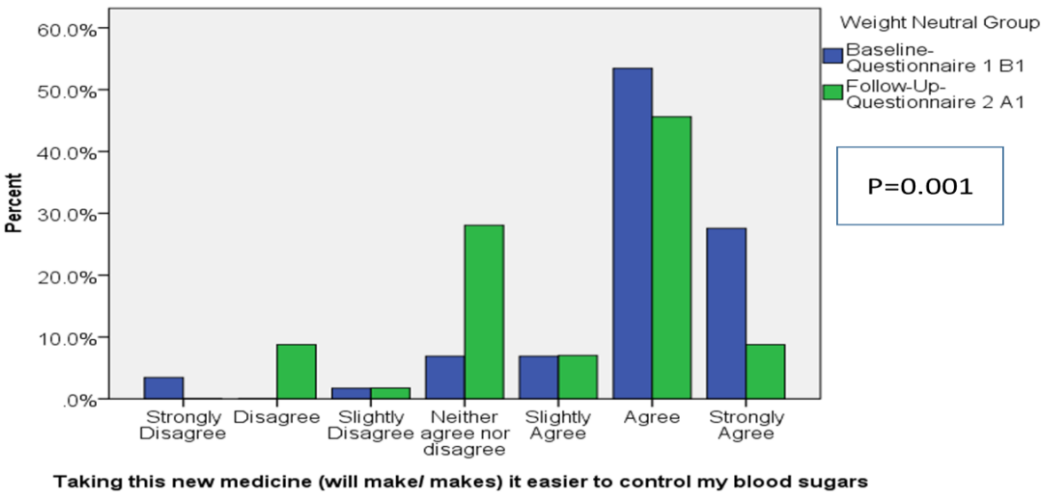

Figure 5.8: Percent agreement to EITQ/PITQ item "taking this new medicine (will/makes) it easier to control my blood sugars" at baseline and follow-up for WN group.

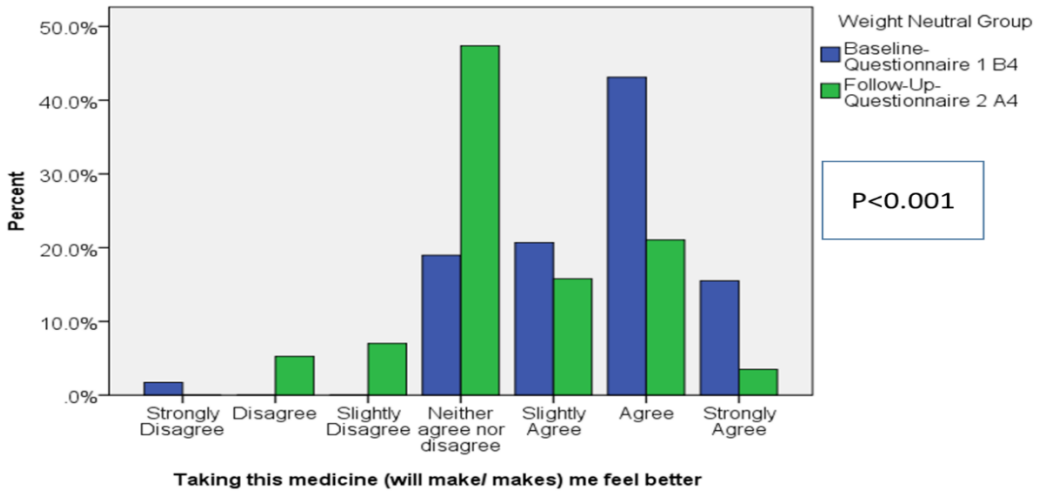

Figure 5.9: Percent agreement to EITQ/PITQ item "taking this new medicine (will/makes) me feel better" at baseline and follow-up for WN group.

Weight Increasing Group

Those treated with weight increasing medicines also had higher expectations about their new medicine in relation to how easy it was going to be to control their blood sugars (p=0.042), and make them feel better (**p=0.001**) (Figure 5.10). They also had more positive perceptions about it, as they thought it did not cause them to have severe episodes of low blood sugar (**p<0.001**) (Figure 5.11). In addition, they had more positive perceptions about the delivery system, particularly that it was easy to get the dose or amount with the delivery system (p=0.046) (not shown).

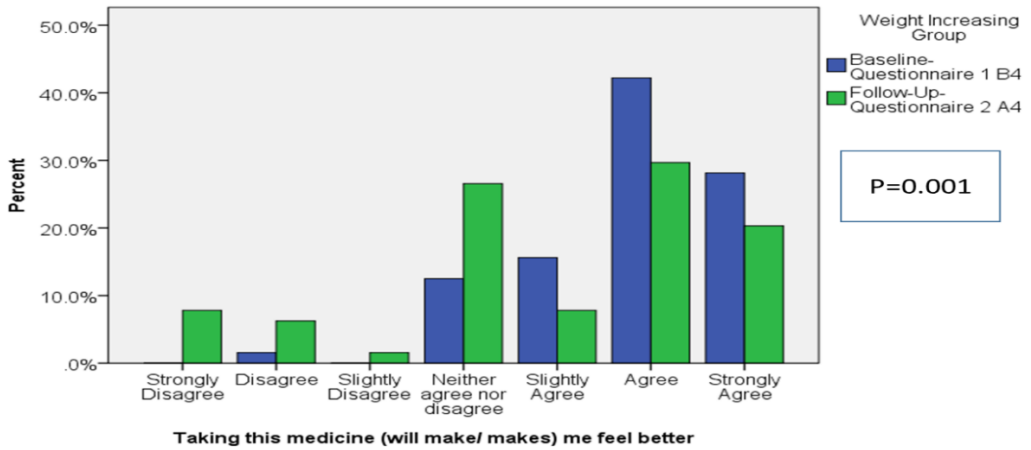

Figure 5.10: Percent agreement to EITQ/PITQ item "taking this new medicine (will/makes) me feel better" at baseline and follow-up for WI group.

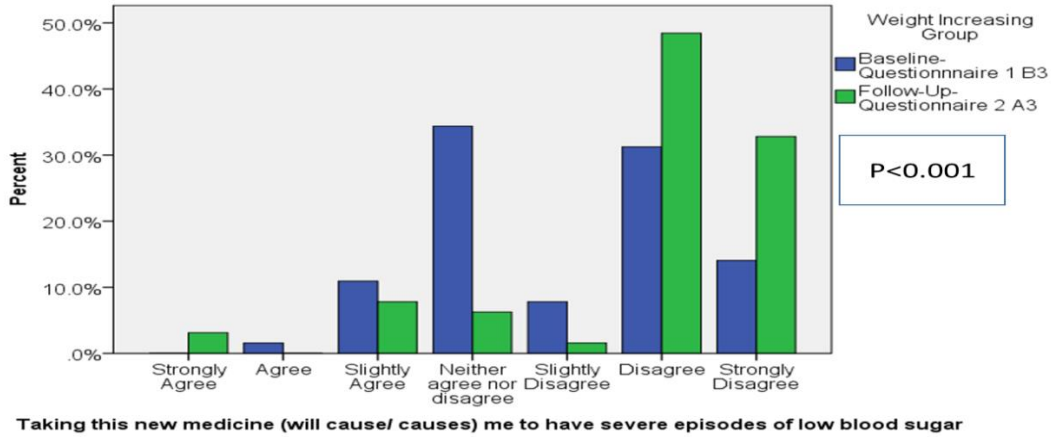

Figure 5.11: Percent agreement to EITQ/PITQ item "taking this new medicine (will cause/causes) me to have severe episodes of low blood sugar" at baseline and follow-up for WI group.

5.5.1.3 Weight-Effect Groups – Comparison between groups

There were no statistical differences between baseline expectation scores (EITQ p=0.301) or follow-up perception scores (PITQ p=0.594), when all three weight-effect groups were compared (Table 5.5). Overall, those treated with weight reducing medicines had the highest proportion of participants in whom their expectations were exceeded by experience (45%, n=30), and those treated with weight neutral medicines had the highest proportion of participants in whom their expectations were unmet (39%, n=22), (Figure 5.5). There was no statistical difference between the groups in relation to changes in scores (p=0.560) (Appendix 5.5).

5.5.2 Satisfaction with information about medicines (SIMS)

5.5.2.1 Whole Group- Baseline Versus Follow-up

Participants were significantly more satisfied with the overall information they received about their new medicine at three month follow-up (median=15), than at baseline (median=13) (**p=0.004**) (Figure 5.12; Table 5.5).

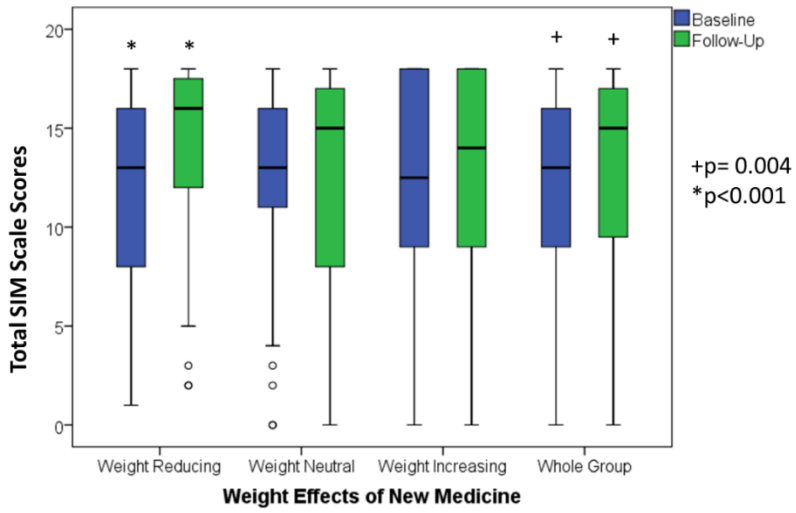

Figure 5.12: Overall satisfaction with amount of information about new medicine (SIMS) at baseline and follow-up. +Indicates significant difference between baseline and follow-up for the whole group, * Indicates significant difference between baseline and follow-up in the WR group

There was no difference in scores about the satisfaction of information received relating to the action and usage of their new medicine before (median=8) and after treatment (median=8), p=0.353 (Figure 5.13; Table 5.5). However, participants were significantly more satisfied with the information they received about the potential problems with the new medicine at three months follow-up (median=7), than at baseline (median=5), **p=0.001** (Figure 5.14, Table 5.5).

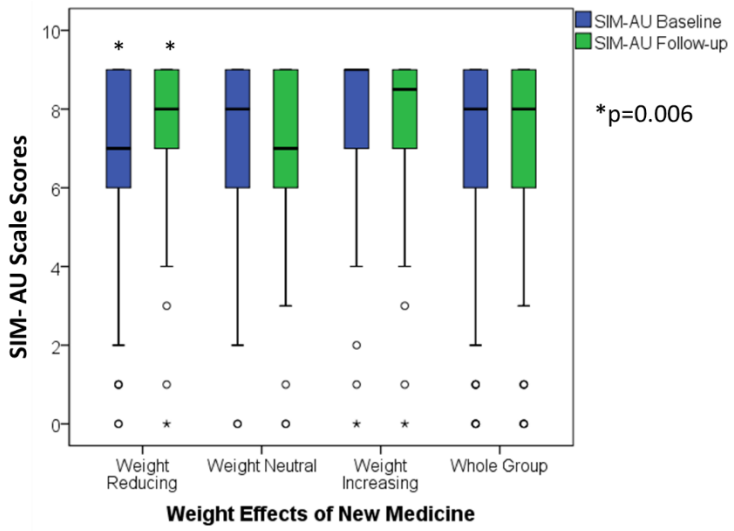

Figure 5.13: Satisfaction with amount of information related to action and usage of new medicine (SIMS-AU) at baseline and follow-up. * Indicates significant difference between baseline and follow-up in the WR group

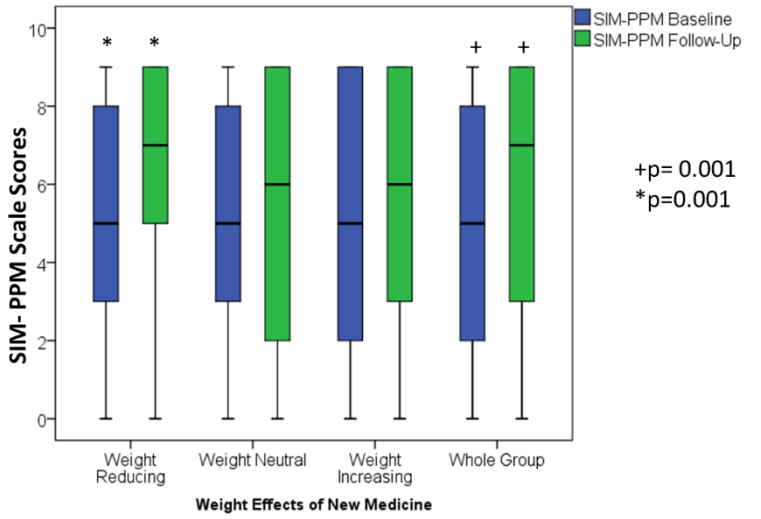

Figure 5.14: Satisfaction with amount of information related to potential problems with new medicine (SIMS-PPM) at baseline and follow-up. +Indicates significant difference

between baseline and follow-up for the whole group,* Indicates significant difference between baseline and follow-up in the WR group

Although satisfaction levels with the overall information received about the new medicines (SIMS) either increased or remained stable over time, for a quarter of the whole group (22%, n=41) the satisfaction levels decreased at three month follow-up (Figure 5.15, Appendix 5.6).

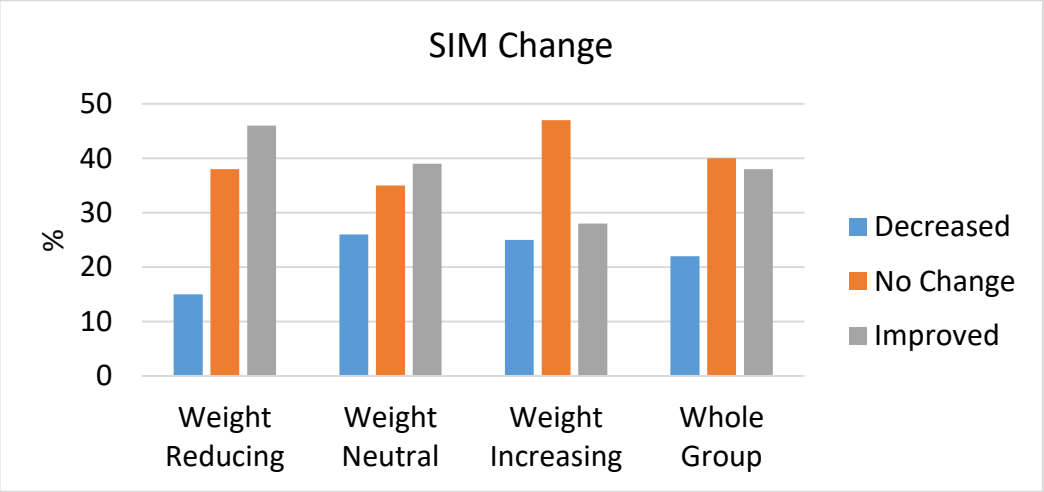

Figure 5.15: Percentage of participants who showed improvement, no change or reduction in satisfaction with information received about new medicine (SIMS)

Similar satisfaction changes can be seen in the whole group in relation to information about the action and usage of their new medicine (Figure 5.16) including information about potential problems (Figure 5.17). More participants were less satisfied about the information relating to action and usage of their new medicine (28%, n=52), compared to those who were less satisfied with the information about potential problems with their new medicine (18%, n=31).

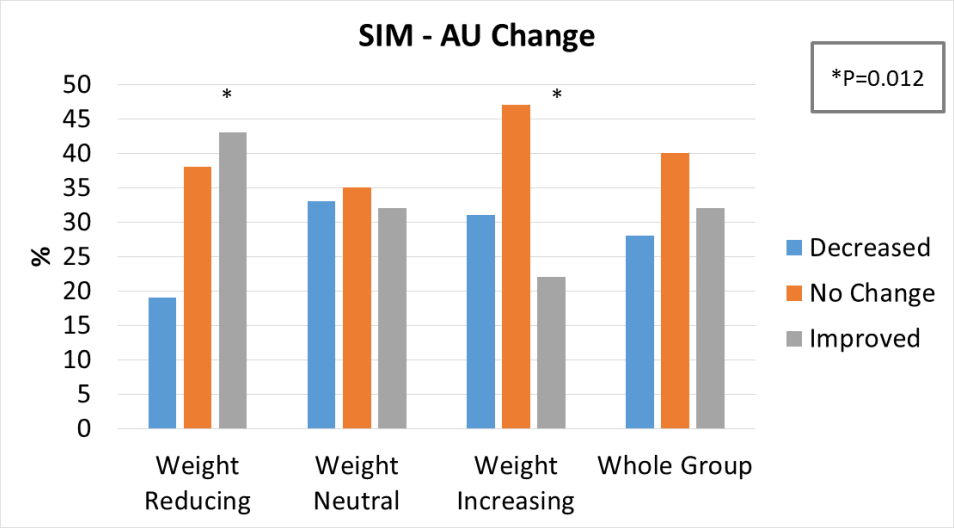

Figure 5.16: Percentage of participants who showed improvement, no change or reduction in satisfaction with information received about new medicine related to action and usage (SIM-AU)

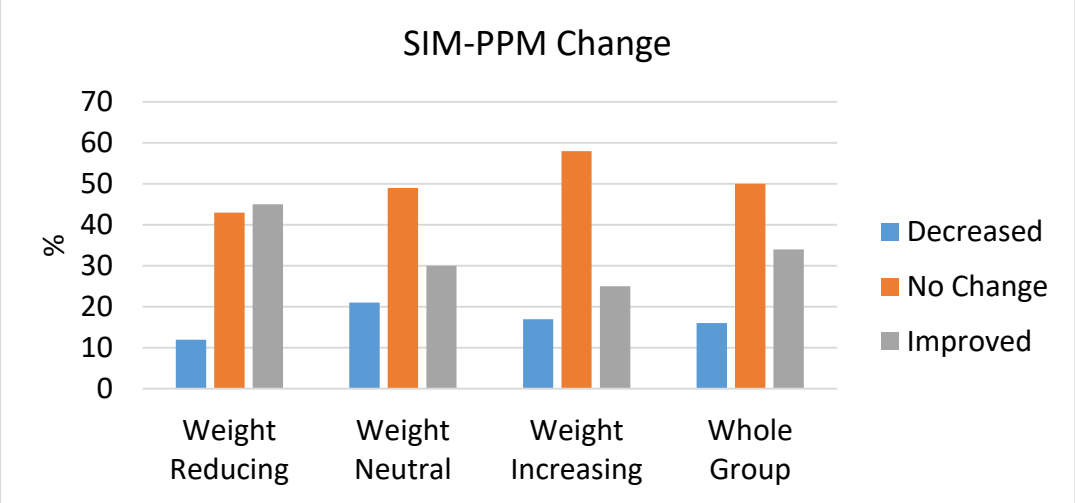

Figure 5.17: Percentage of participants who showed improvement, no change or reduction in satisfaction with information received about new medicine related to potential problems with medicine (SIM-PPM)

5.5.2.2 Weight-Effect Groups – Baseline Versus Follow-up

Weight Reducing Group

The WR group were significantly more satisfied with the information they had received about their new medicine at three months follow-up (median=16) compared to baseline (median=13), **p<0.001**. Similar effects were found for the same

group in relation to information about the action and usage of their new medicine (median=7 Vs median=8, **p=0.006**) and the potential problems with their new medicine (median=5 Vs median=7, **p=0.001**) (Figures 5.12-5.14).

There was also significant difference in single items within the SIM scale for the WR group. Significantly more participants were satisfied with the following information after initiation of the new treatment; how long it will take to work (p=0.025) (not shown), how you can tell if it is working (p=0.018) (not shown), how to get further supplies (p=0.002) (Appendix Figure 5.3), whether you can drink alcohol (**p<0.001**), whether medicine will make you feel drowsy (p=0.002) (Appendix Figure 5.4), whether medicine will affect your sex life (p=0.002), and what you should do if you forget a dose (**p<0.001**) (Figure 5.18).

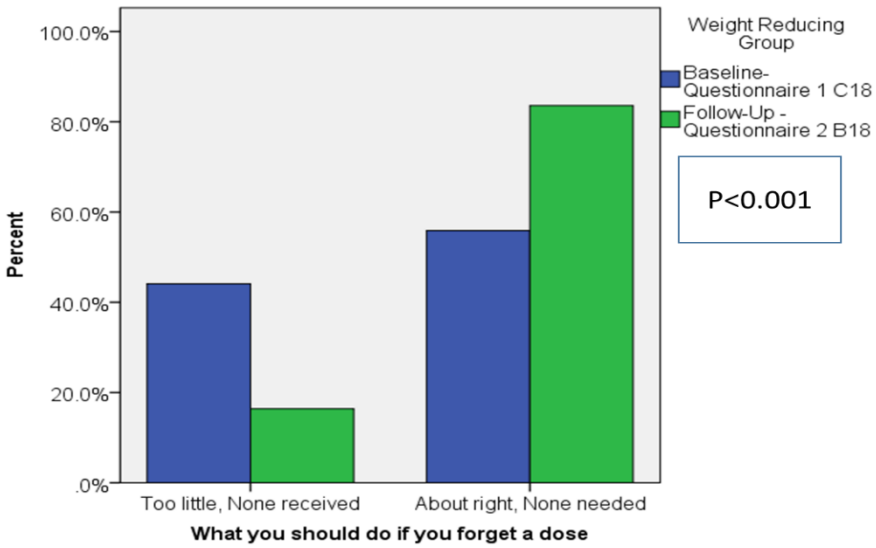

Figure 5.18: Percent agreement to SIMS item "Have received enough information about what you should do if you forget a dose" at baseline and follow-up for WR group.

Weight Neutral Group

Although there was no overall significant difference before and after their new treatment for this scale (SIMS p=0.449, SIMS-AU p=0.542, SIMS-PPM p=0.338, Table 5.5), the WN group was generally dissatisfied with the information they received about their new treatment. They were significantly less satisfied with information relating to how it works (p=0.048) (not shown) and what you should do if you

experience unwanted side effects (p=0.02) (not shown). On the other hand, they were significantly more satisfied with the following items after their new treatment started; whether the medicine will affect their sex life (p=0.018) (not shown), and what they should do if they forget a dose (p=0.046) (not shown).

Weight Increasing Group

The WI group had mixed levels of satisfaction with the information they received about their new treatment despite no overall significant changes between baseline and follow-up (SIMS p=0.233, SIMS-AU p=0.586, SIMS-PPM p=0.194). This group was significantly more satisfied at three months follow-up relating to information about what they should do if they experience unwanted side effects (p=0.02) (not shown) and whether they can drink alcohol (p=0.005) (Appendix Figure 5.5).

5.5.2.3 Weight-Effect Groups – Comparison between groups

When the three weight-effect groups were compared, there was a statistically significant difference in the scores obtained on the SIMS-AU, both at baseline (p=0.008) and at follow-up (p=0.048) (Table 5.5). However, after Bonferroni correction ($p<0.017$), only the scores obtained at baseline were statistically significant. That is, the WR group were less satisfied with the information they received about the action and usage of their new medicine (median=7) compared to the WI group (median=9) p=0.002 (Figure 5.19). There were no other significant differences between the other groups (Table 5.5).

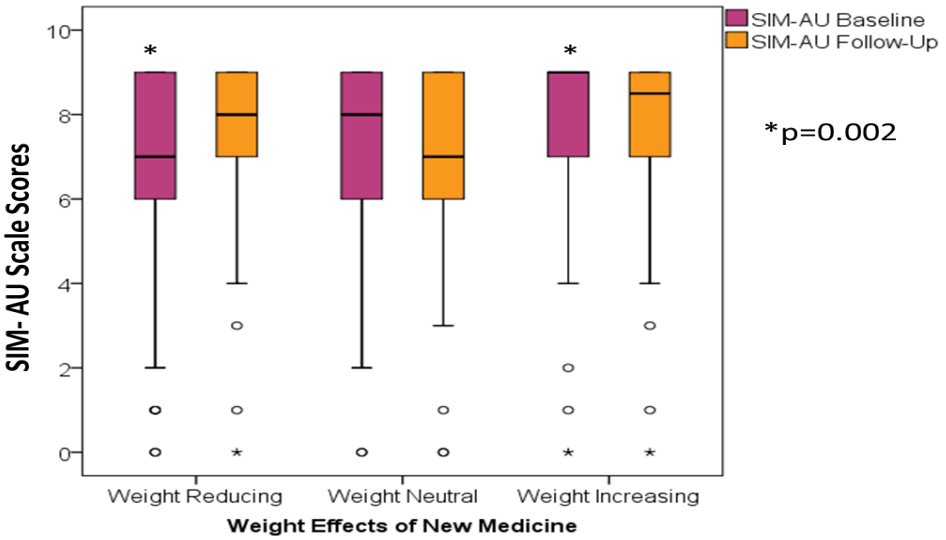

Figure 5.19: Differences in satisfaction with amount of information related to action and usage of new medicine (SIMS-AU) at baseline and follow-up. *Indicates significant difference between WR and WI groups for baseline scores

Generally, the WR group had the highest proportion of participants in whom satisfaction levels about the information they received about their new medicine improved (46%, n=31), followed by the WN group (39%, n=22). However, satisfaction levels decreased over time in about a quarter of participants in the WN and WI groups (26% n=15; 25% n=16 respectively) (Figure 5.15, Appendix 5.6).

A significantly higher proportion of participants in the WR group (43%, n=29) had improved satisfaction levels in relation to the action and usage of the new medicine at three month follow-up compared to the weight increasing group (22%, n=14) (p=0.012) (Figure 5.16 Appendix 5.6). Almost half of the same group (45%, n=30) had increased satisfaction levels regarding the information related to potential problems with the new medicine (Figure 5.17, Appendix 5.6). Nevertheless, the WN and WI groups appeared to be less satisfied at three months follow–up with the information related to action and usage of their new medicine (33% n=19; 31% n=20 respectively) compared to potential problems with it (Figure 5.16).

5.5.3 Beliefs about Medicines (BMQ)- General and Specific

5.5.3.1 Whole Group- Baseline Versus Follow-up

There was no difference in participants' beliefs relating to the necessity of their diabetes medicines before (median=4.0) and after (median=3.8) the new treatment, p=0.075 (Figure 5.20; Table 5.5).

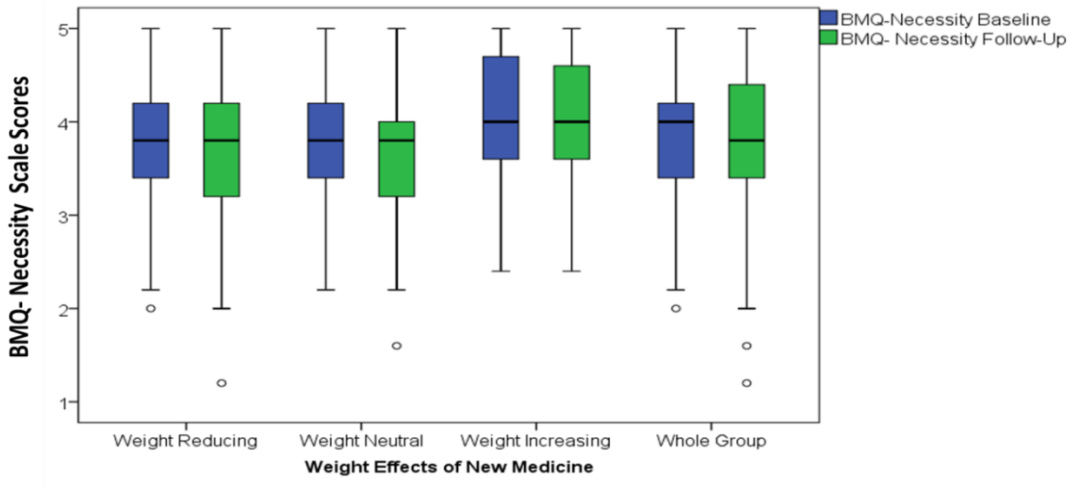

Figure 5.20: Beliefs about necessity of new medicine (BMQ-Necessity) at baseline and follow-up.

Participants were significantly less concerned about the potential adverse effects of their prescribed diabetes medicines at 3-month follow-up (median=2.71) than at baseline (median=2.86), **p=0.005** (Figure 5.21, Table 5.5).

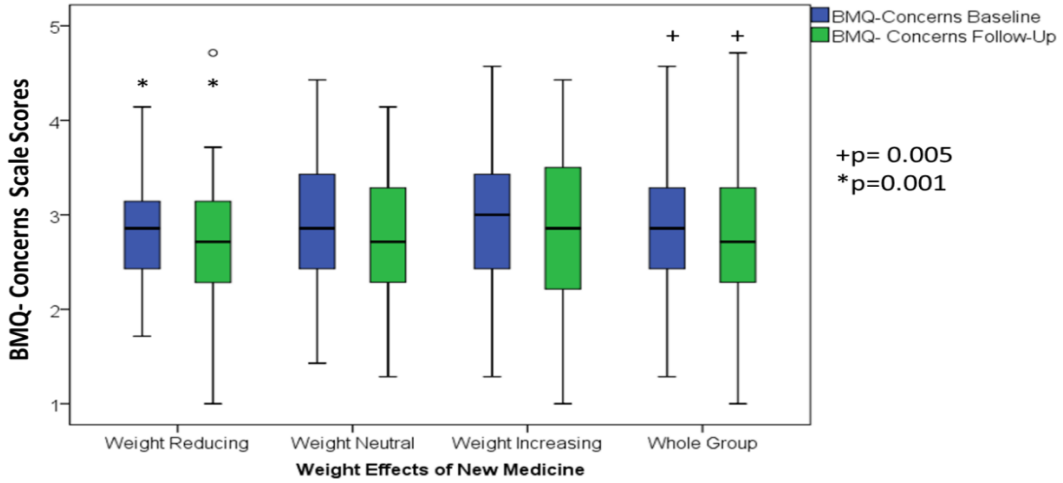

Figure 5.21: Beliefs about Concerns of new medicine (BMQ-Concerns) at baseline and follow-up. +Indicates significant difference between baseline and follow-up for the whole group,* Indicates significant difference between baseline and follow-up in the WR group

Figure 5.22 shows that the majority of the participants fell into the ambivalent group (high necessity and high concerns) at both baseline and follow-up, whereas only a fifth of the group (20% and 22% respectively) accepted their new medicines (high necessity, low concerns). There was no difference in the necessity-concern differential before (median=0.94) and after (median=0.91) the new treatment (p=0.370).

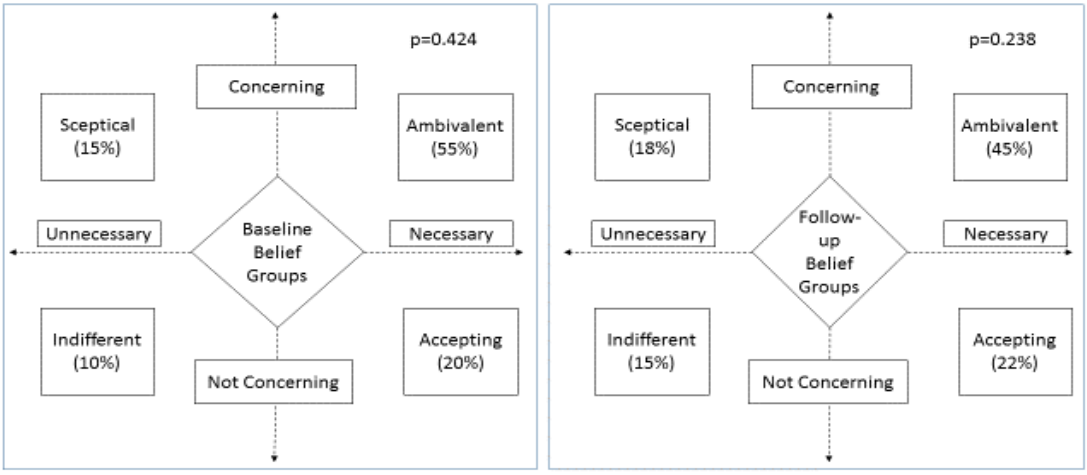

Figure 5.22: Diabetes Medicines Belief Groups at baseline and follow-up. Four different groups created based on median split for BMQ-Necessity and BMQ-Concerns. No significant difference found between belief groups and weight-effect groups both at baseline and follow-up.

There was no difference in beliefs that prescribed medicines are harmful and addictive before (median=2.5) or after (median=2.5) the new treatment, p=0.293 (Figure 5.23, Table 5.5), nor was there a difference in participants' beliefs about the benefits of medicines in general before (median=4.0) or after (median=4.0) the new treatment, p=0.631, (Figure 5.24, Table 5.5).

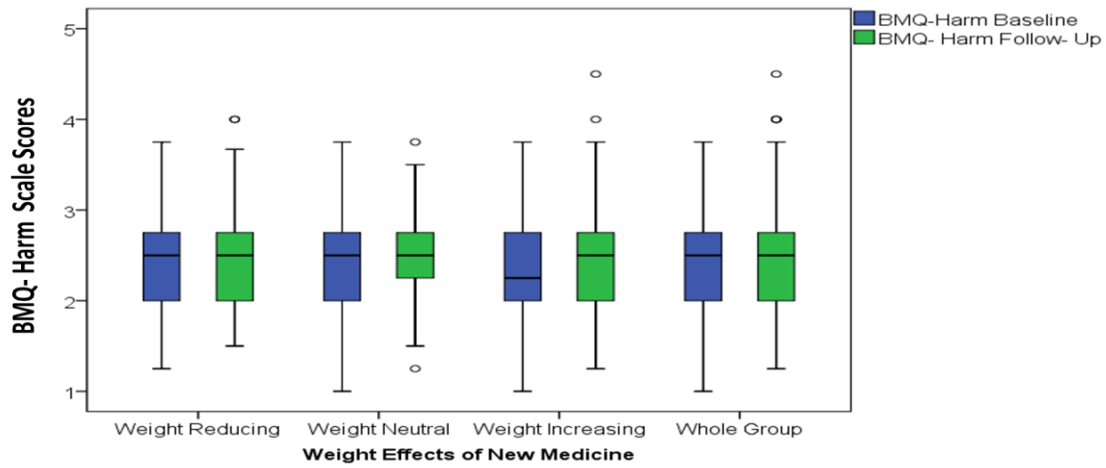

Figure 5.23: Beliefs about Harm of medicines in general (BMQ-Harm) at baseline and follow-up.

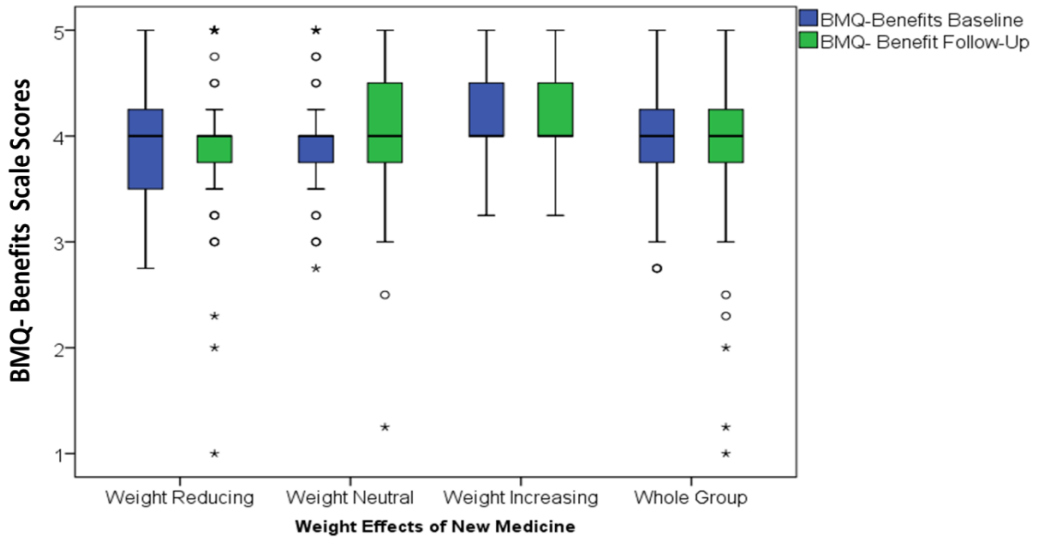

Figure 5.24: Beliefs about Benefits of medicines in general (BMQ-Benefits) at baseline and follow-up.

Participants significantly believed that medicines are overused by doctors; these beliefs were stronger at 3-month follow–up (median=3) than at baseline (median=2.7), p=0.006, (Figure 5.25, Table 5.5).

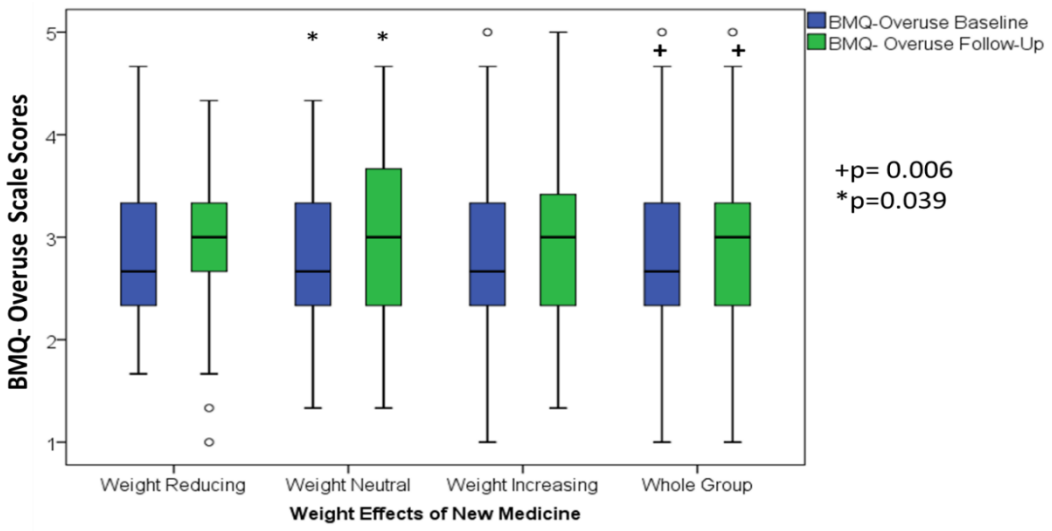

Figure 5.25: Beliefs about Overuse of medicines in general (BMQ-overuse) at baseline and follow-up. +Indicates significant difference between baseline and follow-up for the whole group,* Indicates significant difference between baseline and follow-up in the WN group

The majority of participants' beliefs about their medicines in relation to necessity (41%, n=77), concerns (44%, n=83), harm (65%, n=123), benefits (62%, n=116) and overuse (60%, n=112) did not change following initiation of new treatment. However, about half of the participants' beliefs did change over time; either becoming stronger or decreasing (Figures 5.26-5.30, Appendix 5.7). In particular, 35% (n=66) believed the necessity of their new medicine was less at three months follow-up, whereas 24% (n=46) had stronger beliefs (Figure 5.26, Appendix 5.7).

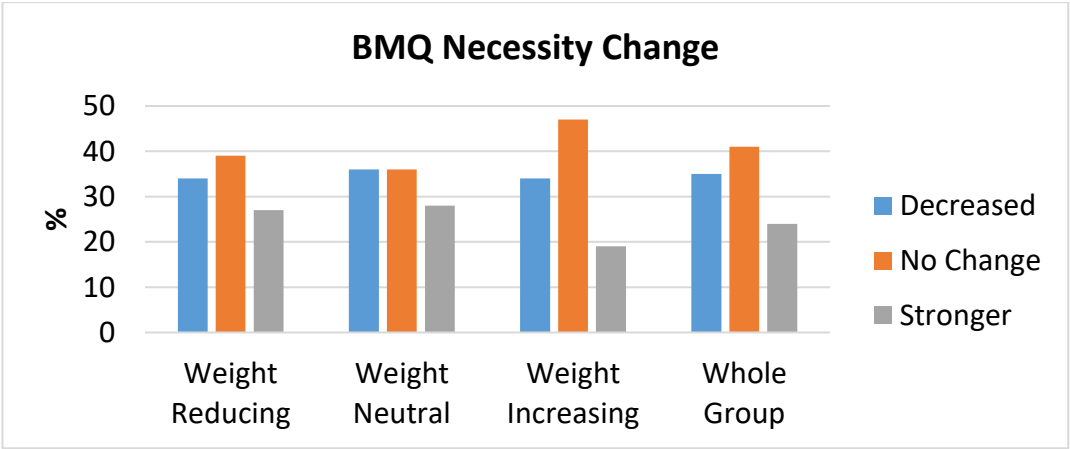

Figure 5.26: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about the necessity of new medicine (BMQ-Necessity)

A third of the participants (35%, n=66) had less concerns about the potential adverse effects of their new medicine, whereas 21% (n=40) had stronger beliefs on this aspect. (Figure 5.27, Appendix 5.7).

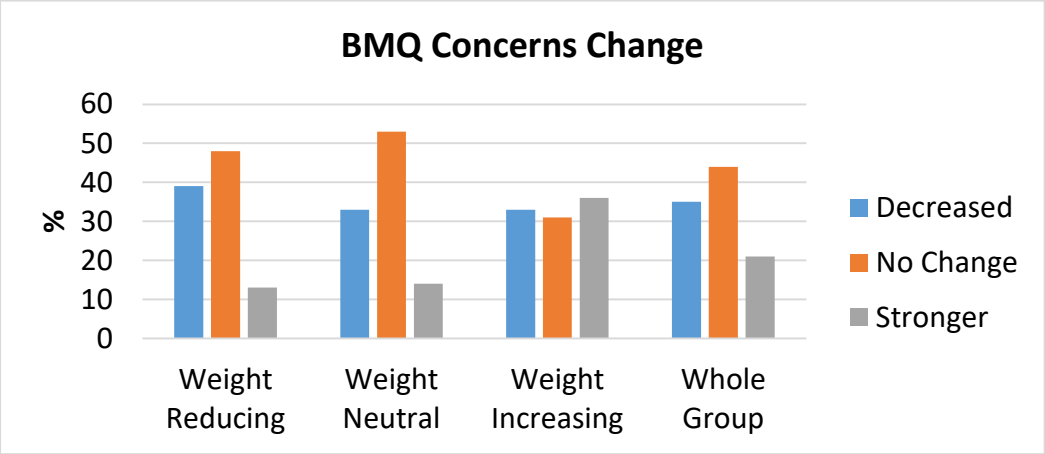

Figure 5.27: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about concerns over the new medicine (BMQ-Concerns)

Overall a quarter of the group (25%, n=47) had stronger beliefs about the overuse of medicines by doctors, whereas a smaller proportion (15%, n=29) felt less strongly about this aspect (Figure 5.28, Appendix 5.7).

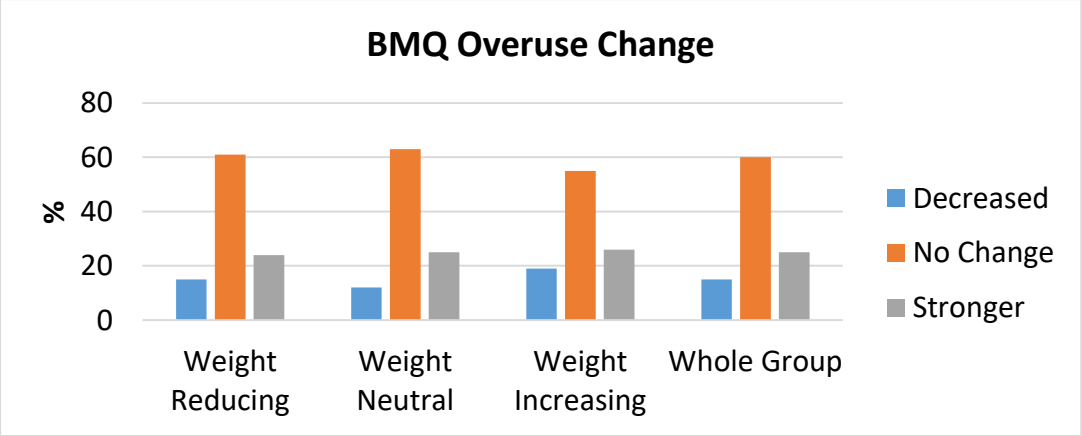

Figure 5.28: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about overuse of prescribed medicines (BMQ-Overuse)

Also, 18% (n=33) had stronger beliefs about the benefits of medicines whereas in 20% (n=38) this decreased. (Figure 5.29, Appendix 5.7).

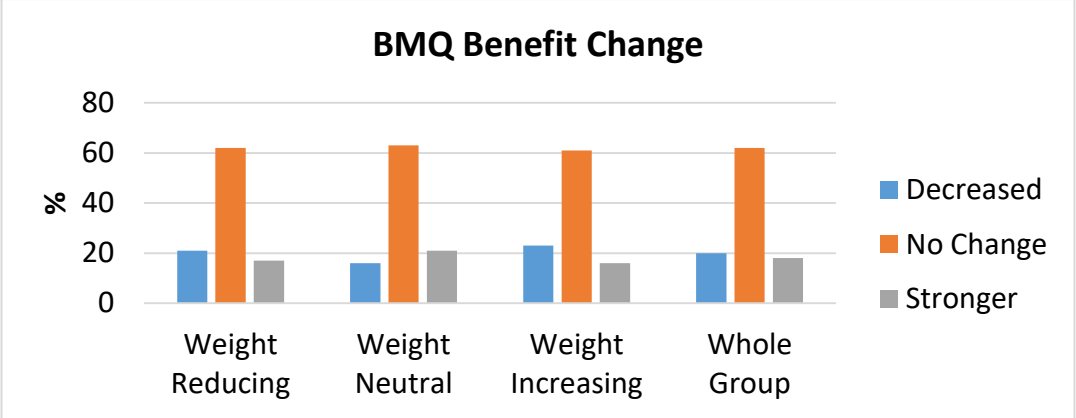

Figure 5.29: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about benefits of prescribed medicines (BMQ-Benefits)

In addition, 18% (n=34) had stronger beliefs about the harm of medicines in general and this decreased in 17% (n=31). (Figure 5.30, Appendix 5.7).

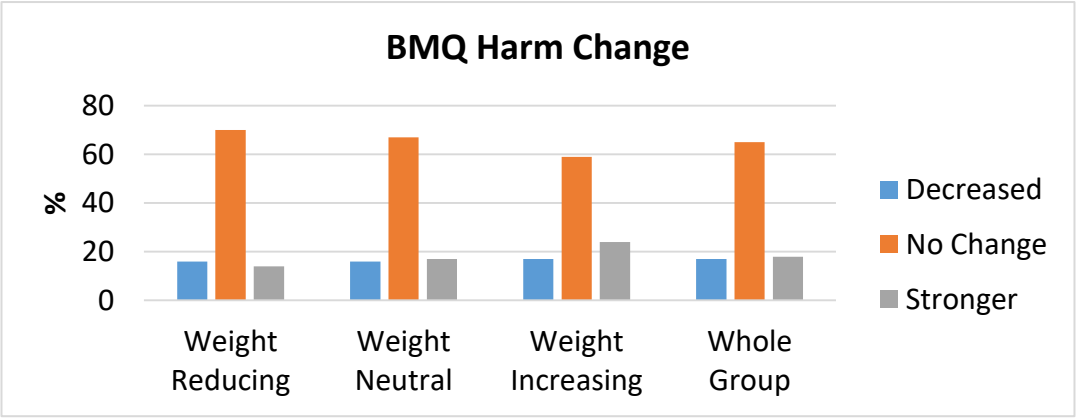

Figure 5.30: Percentage of participants who showed stronger beliefs, no change or reduction in beliefs about harm of prescribed medicines (BMQ-Harm)

5.5.3.2 Weight-Effect Groups – Baseline versus Follow-up

Weight Reducing Group

Participants in the WR group had significantly less concerns about their new medicine at follow-up (median=2.71) than at baseline (median=2.86), **p=0.001** (Figure 5.21). On closer inspection of the BMQ-specific scale; significantly more people in this group disagreed at follow-up with the statement that their medicine disrupts their life (p=0.016) (not shown) and that taking this medicine will cause them to gain weight (**p=0.001**). Nevertheless, approximately a third (28%) were still uncertain at

follow-up whether their new medicine would cause weight gain (Figure 5.31). There were no other significant differences in this group regarding their beliefs about their diabetes medicines (BMQ-Necessity p=0.3936, BMQ-Harm p=0.803, BMQ-Benefits p=0.464, BMQ-Overuse p=0.213).

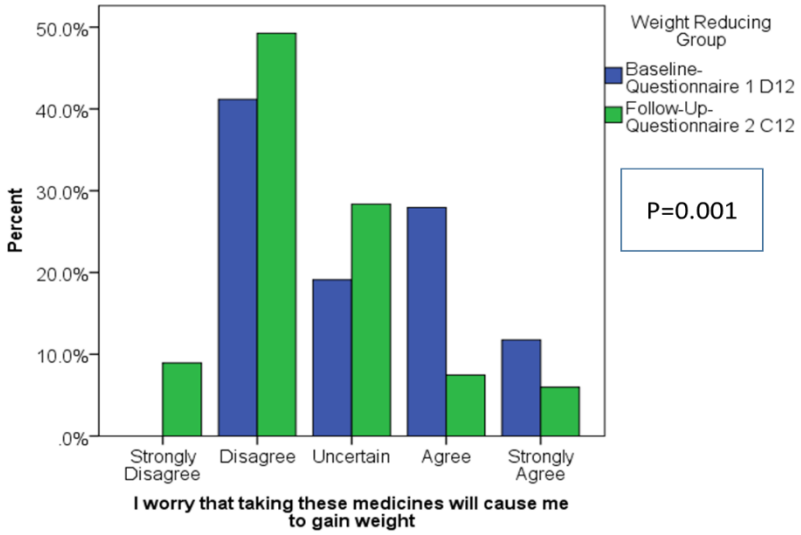

Figure 5.31: Percent agreement to BMQ item "I worry that taking these medicines will cause me to gain weight" at baseline and follow-up for WR group.

Weight Neutral Group

Participants in the WN group had stronger beliefs that medicines are overused by doctors at follow–up (median=3.0) than at baseline (median=2.7), **p=0.039** (Figure 5.25). This was specifically influenced by the item "doctors place too much trust on medicines"; with a slight increase (5.6%) in proportion of participants who agreed with this statement at follow-up. Overall, 39% of participants in this group were uncertain about this statement at 3 months whereas 23% agreed. There were no other significant differences in beliefs about their diabetes medicines in this group (BMQ-Necessity p=0.447, BMQ-Concerns p=0.069, BMQ-Harm p=0.25, BMQ-Benefits p=0.604).

Weight Increasing Group

Although the WI group did not show a significant difference in their beliefs about medicines scales (BMQ-Necessity p=0.118, BMQ-Concerns p=0.909, BMQ-Harm

p=0.348, BMQ-Benefits p=0.632, BMQ-Overuse p=0.121; Figures 5.20-5.25), two single items showed significant response from baseline to follow-up. Although the majority of participants agreed with the statement that their health in the future will depend on these medicines, there was less agreement in that statement at follow-up (86 % baseline Vs 84% follow-up, p=0.024). Furthermore, at follow-up, a higher proportion of patients were uncertain (39% vs 28%) or agreed (39% vs 33%) that if doctors had more time with patients they would prescribe fewer medicines (p=0.014).

5.5.3.3 Weight-Effect Groups – Comparison between groups

When the three weight-effect groups were compared, there were no differences in their scores related to beliefs about concerns, harm, overuse and benefits of their medicines. Whereas, there was a statistical difference in scores relating to the necessity of their new diabetes medicines (p=0.015, Table 5.5). The WI group had stronger beliefs about the necessity of their new medicine (median=4.0) compared to the WR group (median=3.8) at baseline, **p=0.002** (Figure 5.32).

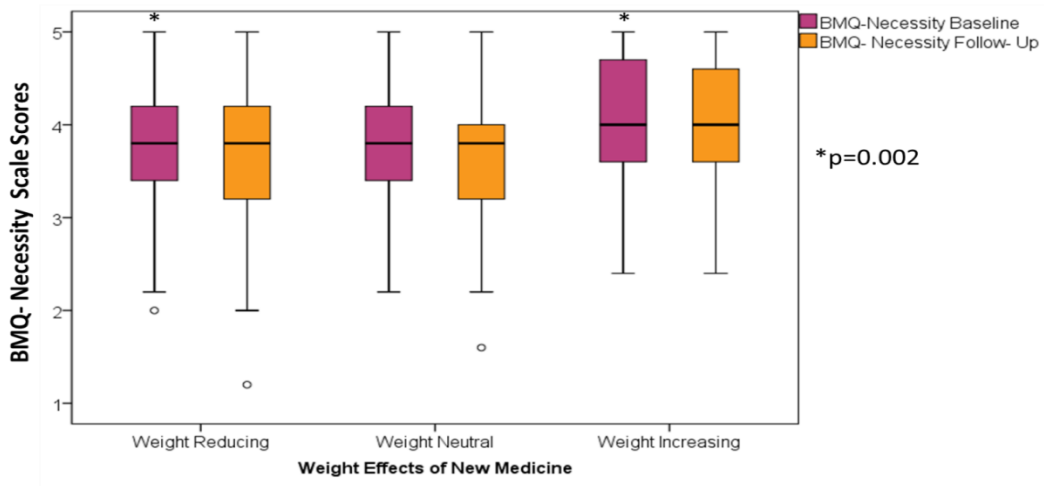

Figure 5.32: Differences in beliefs about Necessity of new medicine (BMQ-Necessity) at baseline and follow-up. * Indicates significant difference between WR and WI groups for baseline scores

Changes in beliefs about harm, overuse and benefits of medicines changed for a small proportion of patients for all weight-effect groups (Figures 5.26-5.30). However, there was more variation in change scores related to the necessity and concerns of

their new diabetes medicine. A quarter of each of the WR and WN groups had stronger beliefs about the necessity of their new medicine, whereas for all groups approximately a third reduced their beliefs about the necessity of their new medicine at follow-up (Figure 5.26). Similarly around a third of all weight-effect groups had less concerns about their new diabetes medicines at follow-up. Although there was no significant difference between the weight-effect groups, more participants in the WI group (36%, n=23) had stronger beliefs about the concerns of their new diabetes medicines compared to the WR group (13%, n=9) and the WN group (14%, n=8) (Appendix 5.7).

5.5.4 Satisfaction with Diabetes Medicines -DiabMedSat

5.5.4.1 Whole Group- Baseline Vs Follow-up

On the whole, participants were significantly more satisfied with their diabetes medicines (median=72.5) at 3-month follow-up than at baseline (median=65.2), **p<0.001**, (Figure 5.33, Table 5.5).

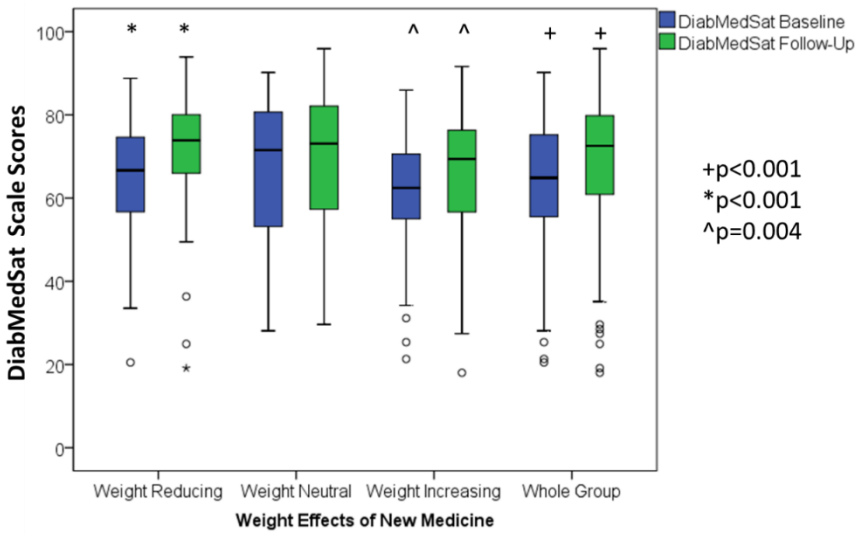

Figure 5.33: Total Satisfaction about diabetes medicines (DiabMedSat) at baseline and follow-up. +Indicates significant difference between baseline and follow-up for the whole group,* Indicates significant difference between baseline and follow-up in the WR group, ^ indicates significant difference between baseline and follow-up in the WI group

They found their diabetes medicines less burdensome at 3-month follow-up (median=84.9) than at baseline (median=81.8), **p=0.014**, (Figure 5.34, Table 5.5), and were more satisfied with their efficacy at the 3-month follow-up (median=61.7) than at baseline (median=53.3), **p<0.001**, (Figure 5.35, Table 5.5).

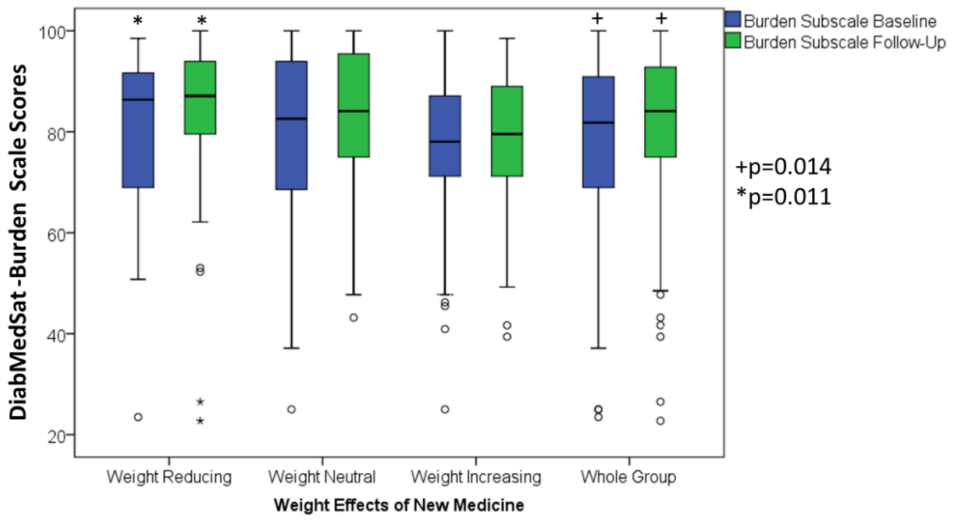

Figure 5.34: Total Satisfaction, burden scale, about diabetes medicines (DiabMedSat-Burden) at baseline and follow-up. +Indicates significant difference between baseline and follow-up for the whole group,* Indicates significant difference between baseline and follow-up in the WR group

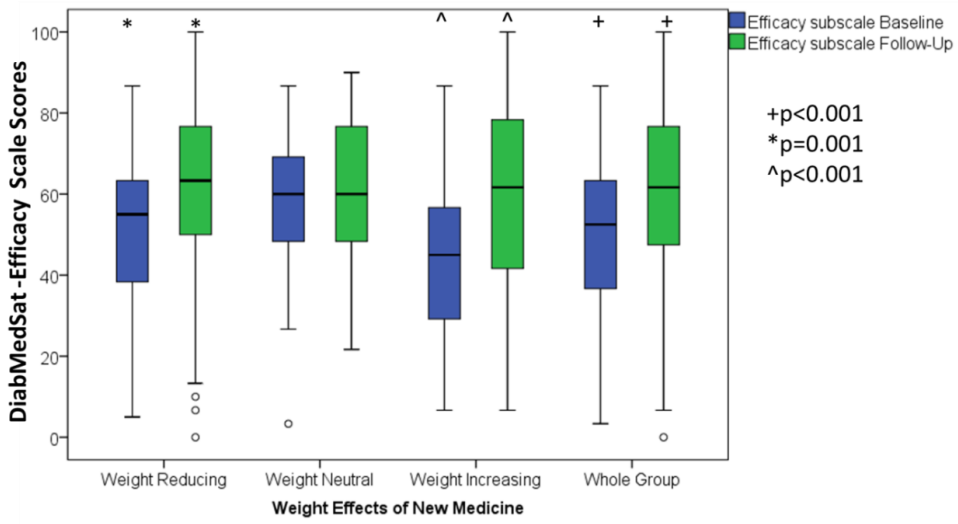

Figure 5.35: Total Satisfaction, efficacy scale, about diabetes medicines (DiabMedSat-Efficacy) at baseline and follow-up. +Indicates significant difference between baseline and follow-up for the whole group,* Indicates significant difference between baseline and follow-up in the WR group, ^ Indicates significant difference between baseline and follow-up in the WI group

However, there was no difference in their satisfaction about the symptoms experienced with their diabetes medicines before (median=68) or after (median=72) new treatment, p=0.139, (Figure 5.36, Table 5.5).

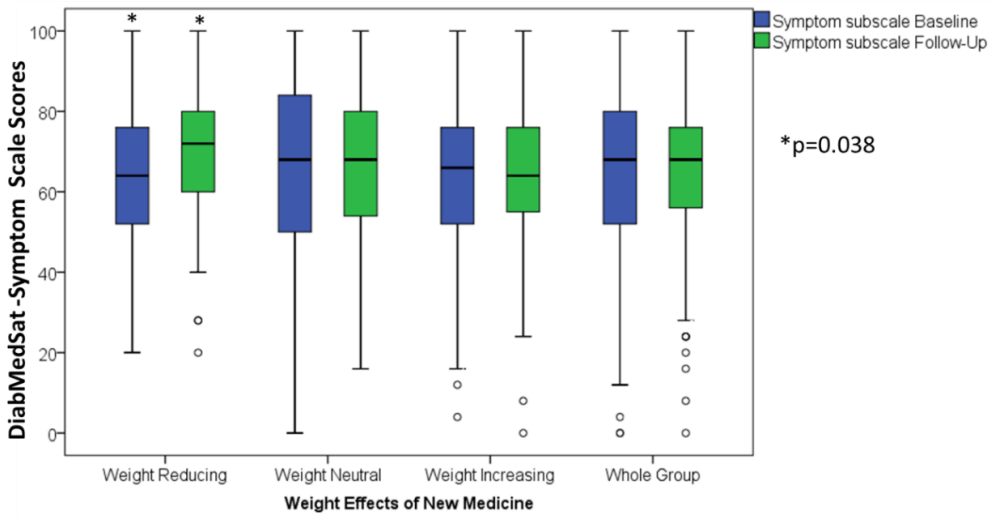

Figure 5.36: Total Satisfaction, symptom scale, about diabetes medicines (DiabMedSat-Symptom) at baseline and follow-up. * Indicates significant difference between baseline and follow-up in the WR group

Overall, almost half (48%, n=80) of participants' satisfaction levels with their new diabetes medicine improved at 3-month follow-up (Figure 5.37), particularly in relation to efficacy (49%, n=83) (Figure 5.38). In contrast, satisfaction levels for burden (49%, n=82) and symptoms (46%, n=76) did not change over time (Figures 5.39-5.40) except for a third of participants where an improvement was seen (burden 32%, n=53, and symptom 31%, n=51), (Figures 5.37-5.40, Appendix 5.8). A smaller proportion of patients showed a decrease in satisfaction levels over time (efficacy 19%, n=31, burden 19%, n=32, and symptom 24%, n=40).

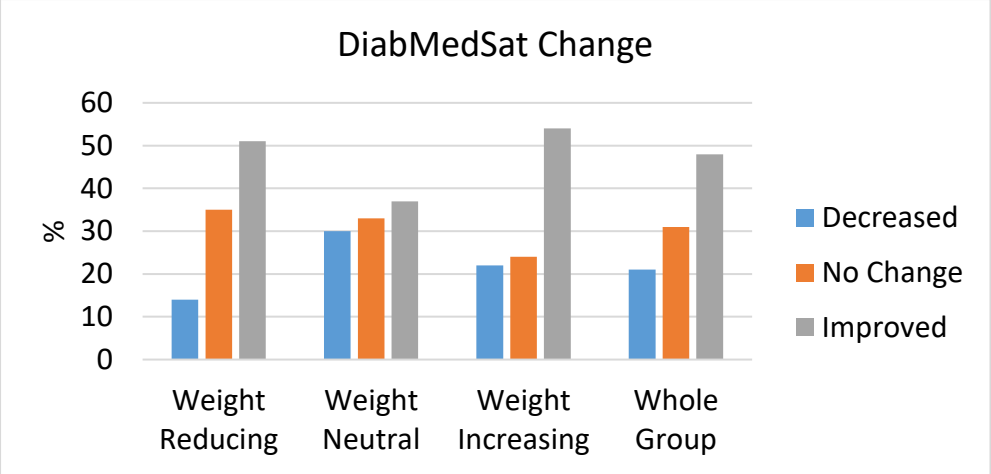

Figure 5.37: Percentage of participants who showed improvement, no change or reduction in satisfaction of new medicine (DiabMedSat)

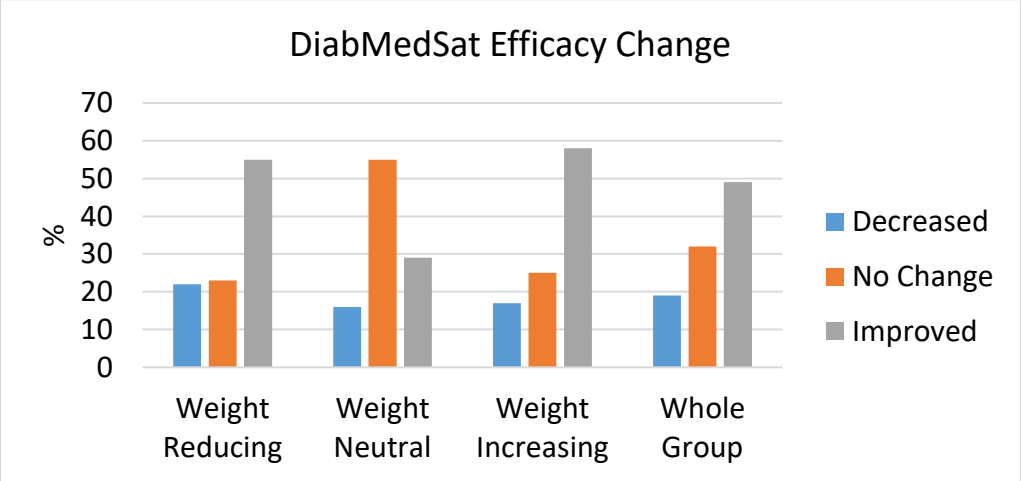

Figure 5.38: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the efficacy of new medicine (DiabMedSat-Efficacy)

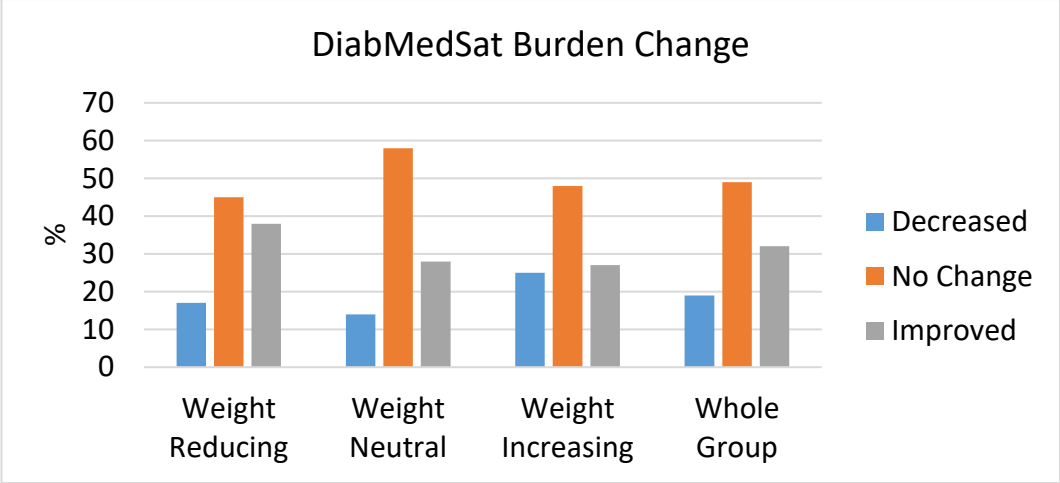

Figure 5.39: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the burden of new medicine (DiabMedSat-Burden)

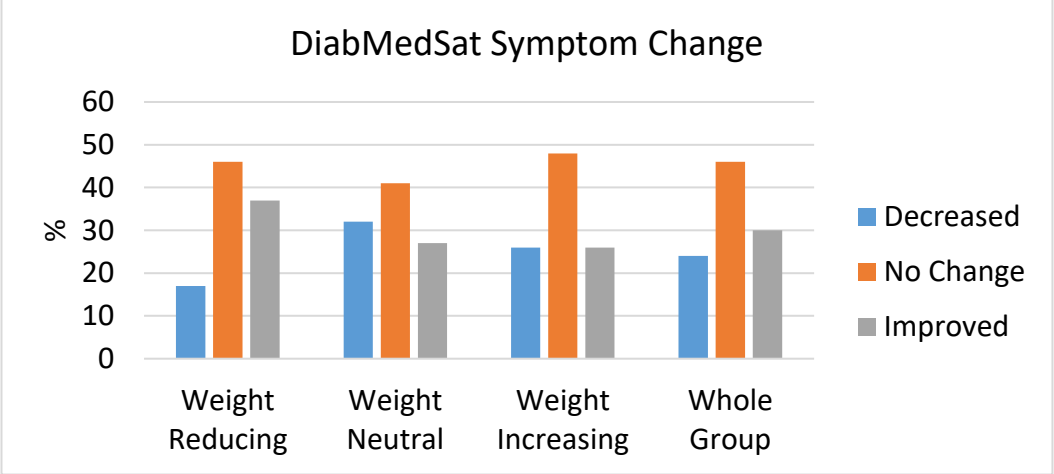

Figure 5.40: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the symptoms of new medicine (DiabMedSat-Symptom)

5.5.4.2 Weight-Effect Groups – Baseline Versus Follow-up

Weight Reducing Group

The WR group was significantly more satisfied with their diabetes medicines overall at follow-up (median=73.6 vs median=66.7, **p<0.001**). In addition, at follow-up, they found their diabetes medicines less burdensome (median=87.1 vs median=86.4, p=0.011), less symptomatic (median=72 vs median=64, p=0.038), and more efficacious (median=62.5 vs median=55, **p=0.001**) (Figures 5.33-5.36).

When inspecting single items, significantly more participants at follow–up were satisfied with the ease and convenience of their diabetes medicines (p=0.005) (Appendix Figure 5.6). Also, more participants either did not have weight gain as a side effect (29%) or they were not bothered by unwanted weight gain (32%) due to their diabetes medicines at follow-up (p=0.002) (Appendix Figure 5.7).

A significant shift was seen towards better satisfaction with their diabetes medicine's ability to keep blood sugars stable (avoid highs and lows) (p=0.006) (Appendix Figure 5.8), as well as a significant shift in the distribution towards being more satisfied that the medicine helped them feel less tired and lacking in energy over time (**p=0.001**) (Figure 5.41).

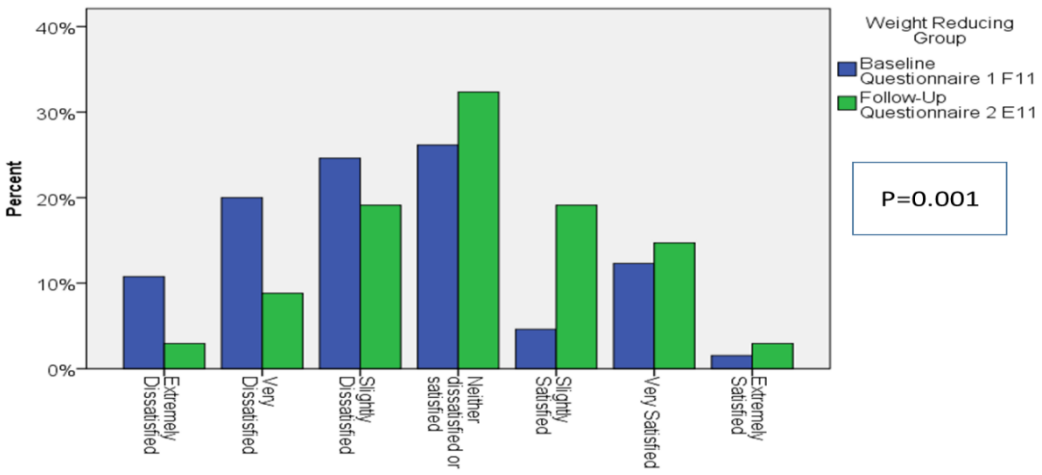

Figure 5.41: Percent agreement to DiabMedSat item "How satisfied or dissatisfied have you been with your diabetes medicine(s) ability to help you from feeling tired and lacking energy" at baseline and follow-up for WR group.

Furthermore, significantly more people in the weight reducing group were satisfied at follow-up with the impact of their diabetes medicines on their physical well-being (**p=0.001**) (Figure 5.42) and on their emotional well-being (p=0.007) (Appendix Figures 5.9).

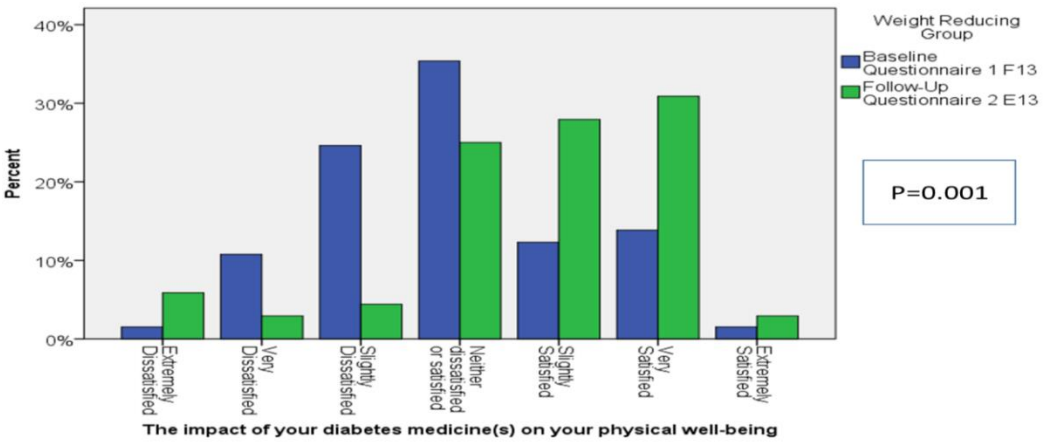

Figure 5.42: Percent agreement to DiabMedSat item "How satisfied or dissatisfied have you been with the impact of your diabetes medicine(s) on your physical well-being" at baseline and follow-up for WR group.

Weight Neutral Group

There were no statistical differences between baseline and follow-up scores for the WN group in any of the scales (DiabMedSad p=0.293, Burden Scale, p= 0.386, Efficacy Scale p=0.088, Symptom Scale p=0.954). Although, at baseline, 52% were not bothered at all by how their medicine interfered with their daily life, and this increased to 75% at follow-up (p=0.022) (not shown). More participants (53% in total) at follow-up indicated that their medicine never interfered with their ability to follow their recommended diet compared to 32% at baseline (p=0.036) (not shown). In addition, there was a significant increase in participants who at follow-up were extremely or very satisfied with their diabetes medicines' ability to keep blood sugars stable (avoid highs and lows) (p=0.024) (not shown). Finally, more participants at follow-up were satisfied with their diabetes medicines' ability to help them feel less tired and lack energy (18% at baseline and 40% at follow-up), although just over a third (36%) were neither satisfied nor dissatisfied (p=0.027) (not shown).

Weight Increasing Group

The WI group was also more satisfied with their diabetes medicines overall at follow-up (median=68.5) compared to baseline (median=63.1), **p=0.004** (Figure 5.33), and this was related to how efficacious they found their diabetes medicines at follow-up compared to baseline (median=61.7 vs median=45), **p<0.001**) (Figure 5.35). Yet,

there were no statistical differences between baseline and follow-up scores in the Burden (p=0.46) and Symptom Scales (p=0.801).

When inspecting single items, there was a significant shift in participants who indicated that their medicine never or rarely interfered with their ability to be flexible with planning meals (when you eat and what you are able to eat) (p=0.007) (Appendix- Figure 5.10). In addition, significantly more participants at follow-up were extremely or very satisfied with their diabetes medicine ability to keep blood sugars stable (avoid highs and lows) (**p<0.001**), and were extremely or very satisfied with their diabetes medicine ability to help them from feeling tired and lacking in energy (**p=0.001**) (Figures 5.43-5.44). Furthermore, significantly more people in this group were satisfied at follow-up with the impact of their diabetes medicines on their physical well-being (p=0.01) (not shown) and on their emotional well-being (p=0.023) (not shown).

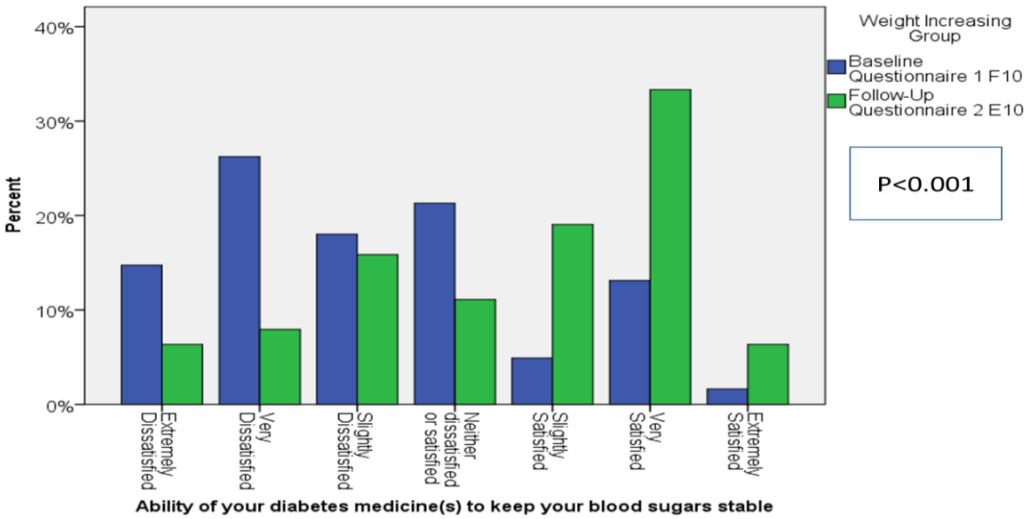

Figure 5.43: Percent agreement to DiabMedSat item "How satisfied or dissatisfied have you been with your diabetes medicine(s) ability to keep your blood sugars stable (avoid highs and lows" at baseline and follow-up for WI group.

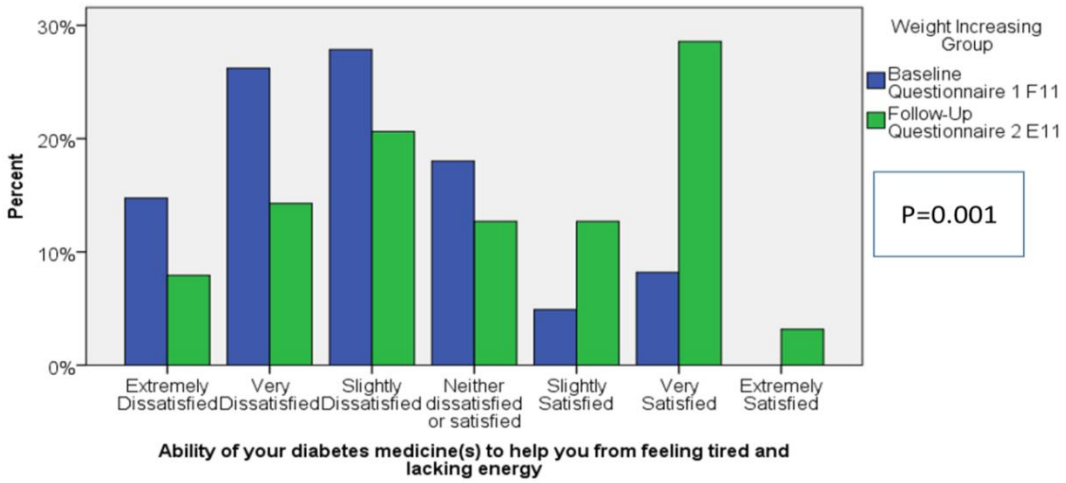

Figure 5.44: Percent agreement to DiabMedSat item "How satisfied or dissatisfied have you been with your diabetes medicine(s) ability to help you from feeling tired and lacking energy" at baseline and follow-up for WI group.

5.5.4.3 Weight-Effect Groups – Comparison between groups

There was no statistical difference between the three weight-effect groups on the overall satisfaction about their diabetes medicines (Table 5.5), however there was a significant difference between groups in the burden (p=0.027) and efficacy (p=0.003) subscales. The WR group found their diabetes medicines less burdensome (median=87.1) than the WI group (median=79.5) at follow–up, **p=0.01** (Figure 5.45). The WN group found their diabetes medicines more efficacious at baseline (median=60) than the WI group (median= 45), **p=0.001** (Figure 5.45).

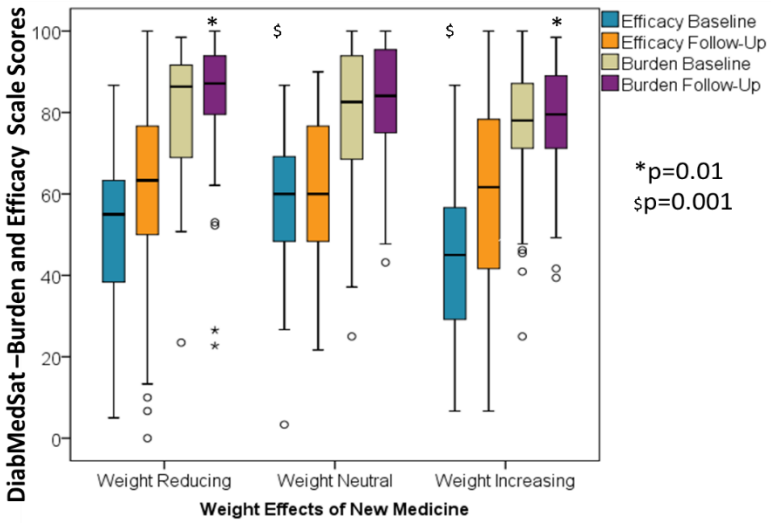

Figure 5.45: Differences in satisfaction about burden (DiabeMedSat-Burden) and efficacy (DiabeMedSat-Efficacy) of diabetes medicines at baseline and follow-up. * Indicates significant difference between WR and WI groups for follow-up scores, $ Indicates significant difference between WN and WI groups for baseline scores

Generally, overall satisfaction levels with the new diabetes medicine for the majority of participants in the three weight-effect groups improved (WR 51%, n=33; WN 37%, n=16; WI 53%, n=31), with a smaller proportion whose satisfaction levels decreased over time (14%, n=9; 30%, n=13; 22%, n=13 respectively) (Figure 5.37, Appendix 5.8).

The WR (55%, n=36) and the WI (58%, n=34) groups had higher proportions of patients whose satisfaction levels related to the efficacy of their new medicines increased at 3-month follow-up. However, satisfaction in medication efficacy in 55% (n=24) of the WN group did not change over time (Figure 5.38, Appendix 5.8). For the majority of participants satisfaction levels related to burden and symptoms of new medicines did not change over time. However, the WR group had a higher proportion of patients whose satisfaction levels regarding the burden (39%, n=25) and symptoms (37%, n=24) of new medicine increased compared to the other two groups (WN: burden 28%, n=12, symptoms 27%, n=12; WI burden, 27%, n=16, symptoms 26%, n=15). Conversely, for a quarter of the WI group, satisfaction levels decreased for burden (25%, n=15) and symptoms (26%, n=15). Satisfaction levels related to symptoms had also decreased for a third of the WN group (32%, n=14) (Figure 5.39-5.40, Appendix 5.8).

5.5.5 Satisfaction with Diabetes Medicines -TRIM-Weight

5.5.5.1 Whole Group- Baseline Versus Follow-up

Participants were significantly more satisfied about the impact of their medicines on their daily life after the new treatment (median=75) than before initiation (median=66.7), **p=0.002**, (Figure 5.46, Table 5.5).

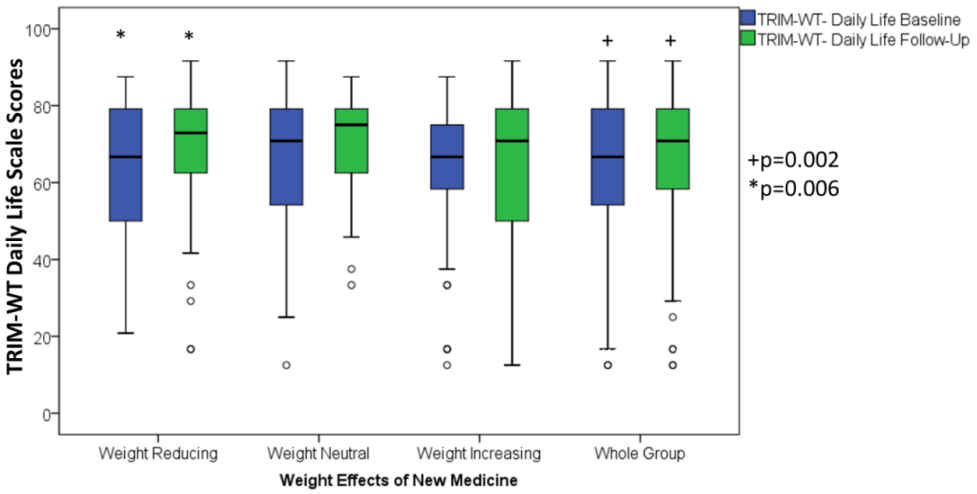

Figure 5.46: Satisfaction with the impact of new medicine on daily life (TRIM-Wt-DL) at baseline and follow-up. + Indicates significant difference between baseline and follow-up in the whole group, * Indicates significant difference between baseline and follow-up in the WR group

Participants were also significantly more satisfied with the impact of their diabetes medicines on managing their weight after new treatment (median=41.7) than before (median=33.3), **p<0.001**, (Figure 5.47, Table 5.5).

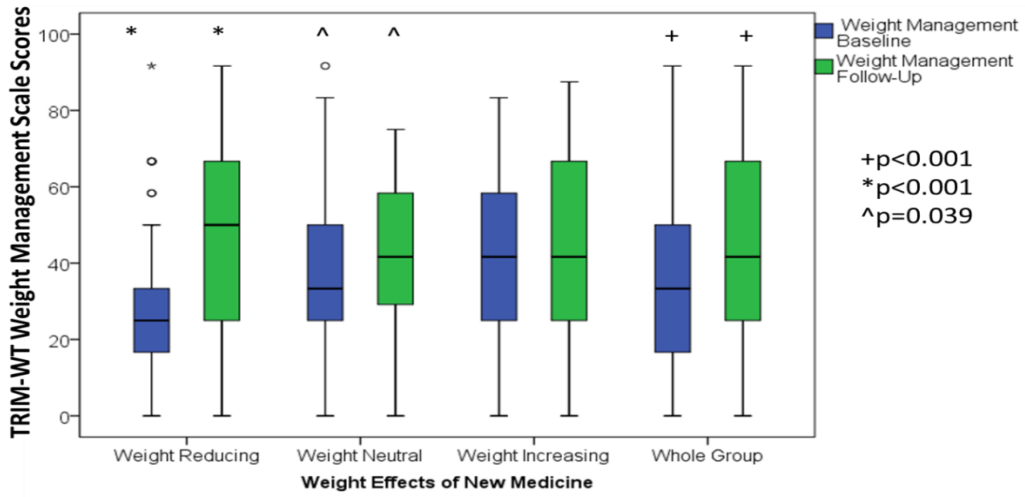

Figure 5.47: Satisfaction with the impact of new medicine on weight management (TRIM-Wt-WM) at baseline and follow-up. + Indicates significant difference between baseline and

follow-up in the whole group, * Indicates significant difference between baseline and follow-up in the WR group, ^ Indicates significant difference between baseline and follow-up in the WN group

There was no statistical difference in participants' satisfaction about the impact of their diabetes medicines on their psychological health before (median=75) and after new treatment (median=75), p=0.335, (Figure 5.48, Table 5.5).

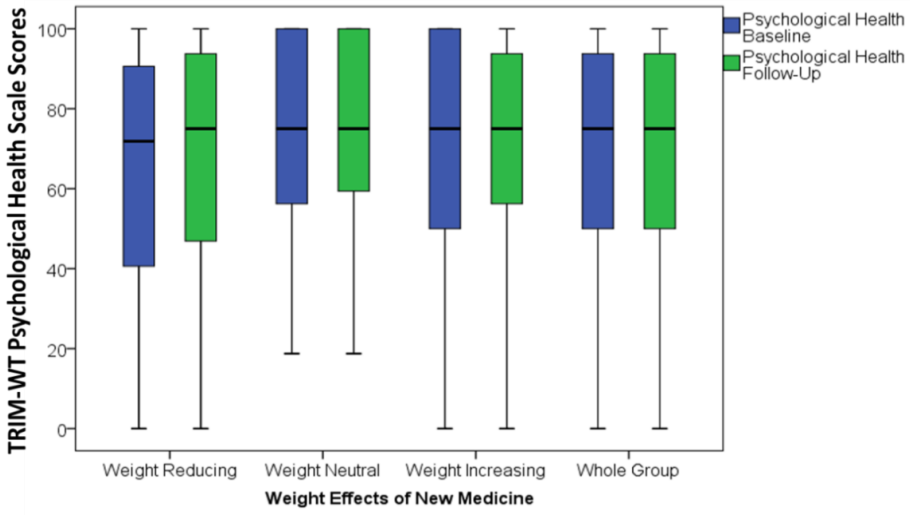

Figure 5.48: Satisfaction with the impact of new medicine on psychological health (TRIM-Wt-PH) at baseline and follow-up.

The majority of the participants' satisfaction levels relating to the impact of the new diabetes medicine on their daily life (63%, n=105), weight management (45%, n=76) and psychological health (51%, n=85) did not change over time. However, for a quarter to a third of participants their satisfaction levels increased (26%, n=44; 39%, n=66; 29%, n=48 respectively) at 3-month follow-up, and a smaller proportion decreased (11%, n=19; 16%, n=26; 21%, n=35 respectively) (Figures 5.49-5.51, Appendix 5.9).

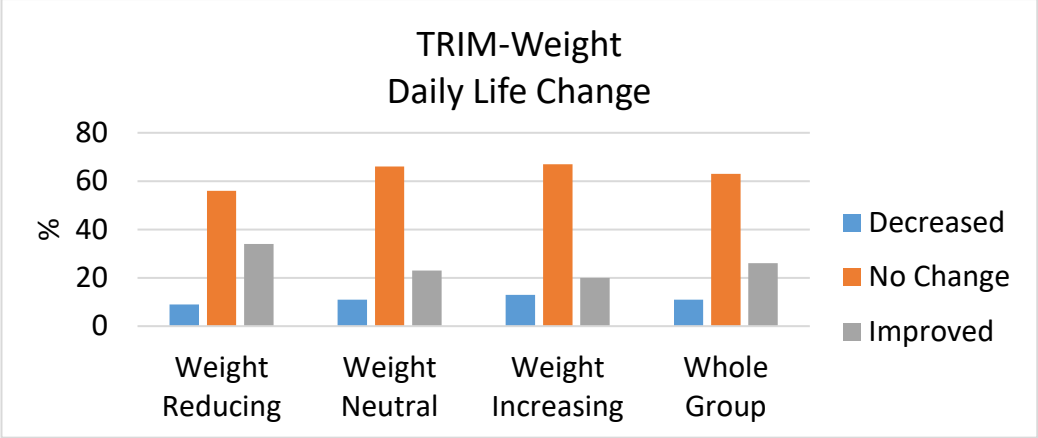

Figure 5.49: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the impact of new medicine on daily life (TRIM-Wt-DL)

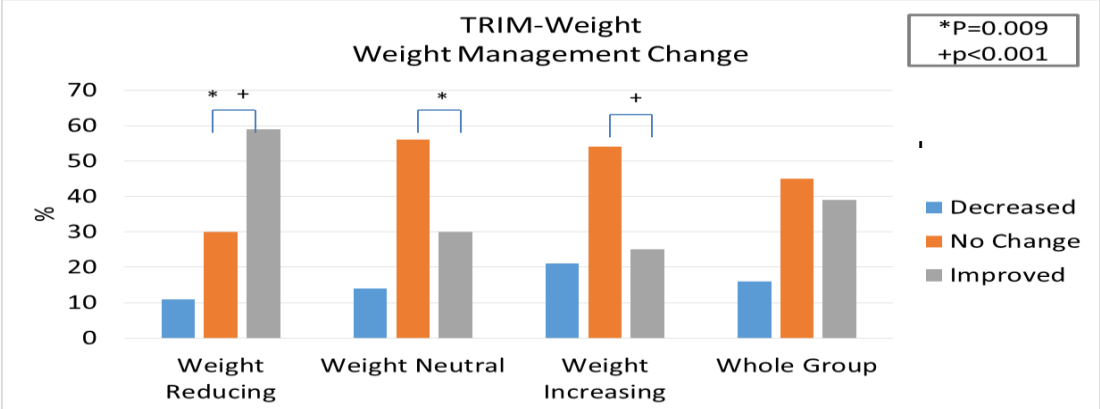

Figure 5.50: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the impact of new medicine on weight management (TRIM-Wt-WM)

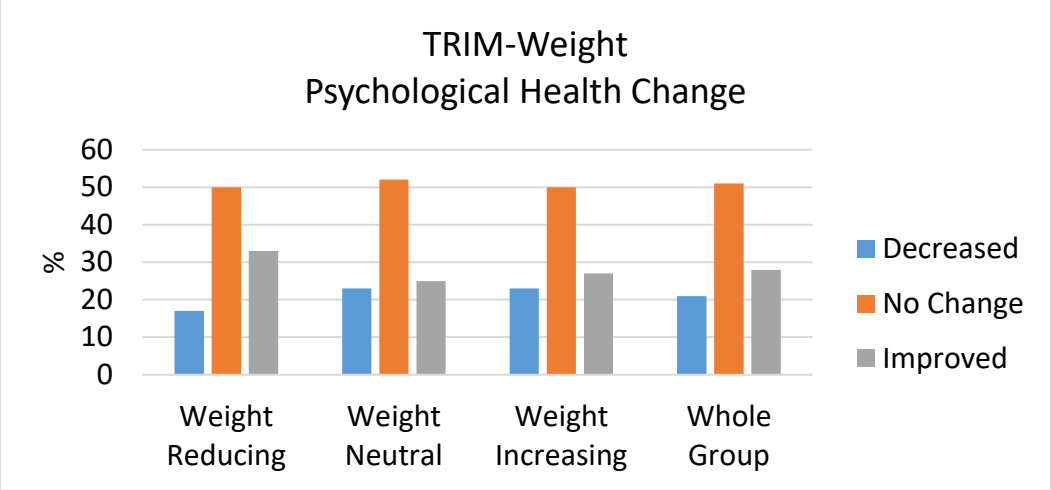

Figure 5.51: Percentage of participants who showed improvement, no change or reduction in satisfaction related to the impact of new medicine on psychological health (TRIM-Wt-PH)

5.5.5.2 Weight-Effect Groups – Baseline Versus Follow-up

Weight reducing group

The WR group was more satisfied with their medicine's impact on their daily life (baseline median=66.7 Vs follow-up median=72.9, **p=0.006**), and on managing their weight (baseline median=25 Versus follow-up median=50, **p<0.001**) at three months (Figures 5.46-5.47). However there was no significant difference in their satisfaction with their medicine's impact on their psychological health (p=0.079)

On inspecting the single items within the three subscales, significantly more people indicated that it is never or rarely a problem for them to be as active as they would like because of their medicine (p=0.015) (not shown), and that their medicine never or rarely interferes with being as productive as they would like (either at home or work) (p=0.038) (not shown). Additionally, more people in this group indicated that they are little or not at all bothered by being tired or drowsy because of their medicine (**p=0.001**) (Figure 5.52).

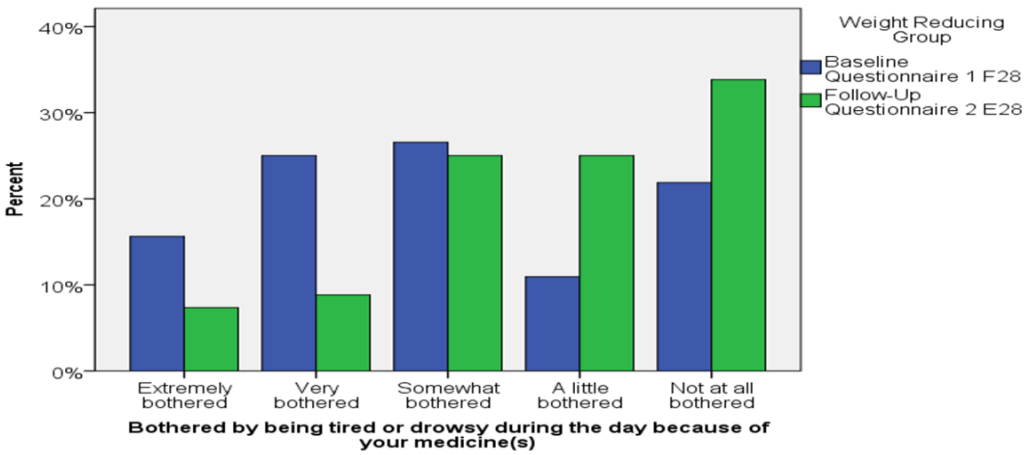

Figure 5.52: Percent agreement to TRIM-Weight item "How bothered or not bothered are you by being tired or drowsy during the day because of your medicine(s)" at baseline and follow-up for WR group.

Furthermore, more people appeared to be satisfied (somewhat to extremely) at follow-up with how well their medicine helps them to lose weight (**p<0.001**) and with their medicines' ability to control appetite (**p<0.001**) (Figures 5.53-5.54). Despite this improvement in satisfaction, a quarter of participants were not at all satisfied with the above aspects. Also, more people at follow-up indicated that they never (almost never) or rarely feel stressed because of their diabetes medicines (p=0.048) (not shown). Nevertheless, almost half (44%) indicated that they sometimes, often or always (almost always) feel stressed because of their diabetes medicines.

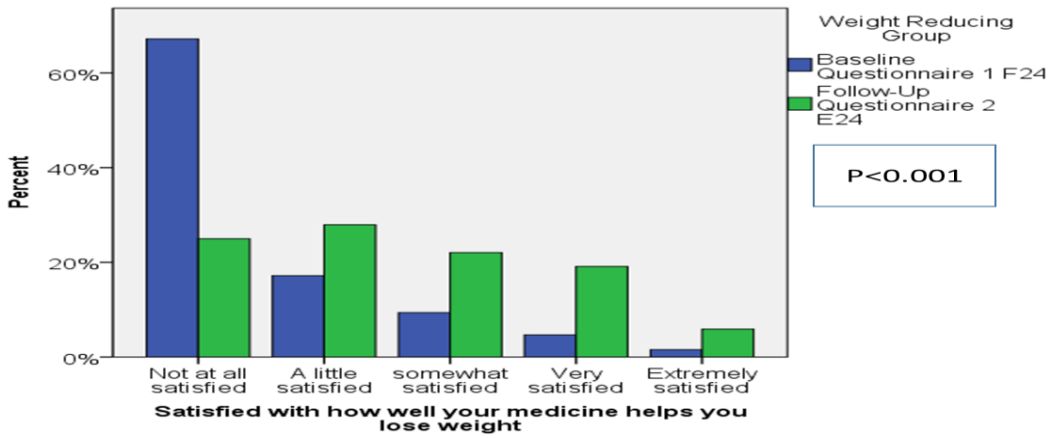

Figure 5.53: Percent agreement to TRIM-Weight item "How satisfied or dissatisfied are you with how well your medicine helps you lose weight" at baseline and follow-up for WR group.

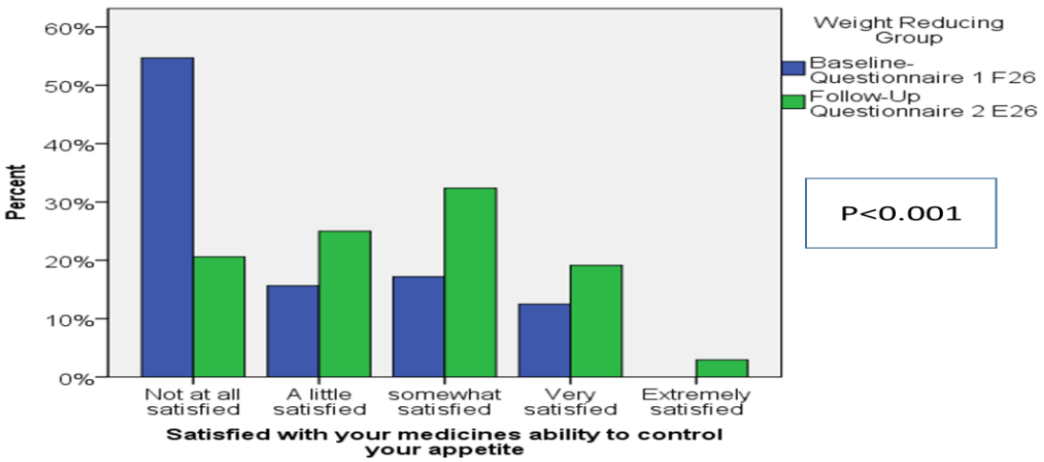

Figure 5.54: Percent agreement to TRIM-Weight item "How satisfied or dissatisfied are you with your medicine's ability to control your appetite" at baseline and follow-up for WR group.

Weight neutral group

The WN group was also more satisfied with the impact of their diabetes medicines on managing their weight after new treatment (median=41.7) than before (median=33.3), **p<0.039** (Figure 5.47). Yet, there were no significant differences in their satisfaction with their medicine's impact on their daily life (p=0.055) and their psychological health (p=0.708). Single items showed that significantly more people at follow-up indicated that it is never or rarely a problem for them to be as active as they would like because of their medicine (p=0.04) (not shown) and they are not at all bothered by weight loss plateaus (periods of no weight loss) (p=0.038) (not shown). However, over half of the group (53%) responded that they were still "a little" to "extremely" bothered about weight loss plateaus.

Weight increasing group

Although the WI group did not show any significant differences overall between baseline and follow-up on the three subscales relating to daily life (p=0.567), weight management (p=0.421) and psychological health (p=0.974), significantly more people in this group indicated at follow-up that they were little or not at all bothered by being tired or drowsy because of their medicine (p=0.004) (Appendix Figure 5.11). Still, a substantial proportion of patients (44%) indicated that they were "a little" to

"extremely" bothered by it. Furthermore, significantly more people indicated at follow-up that they are not at all bothered by weight loss plateaus (periods of no weight loss) (p=0.025) (not shown), but over half of the group (56%) responded that they were still a "little" to "extremely" bothered.

5.5.5.3 Weight-Effect Groups – Comparison between groups

When the three weight-effect groups were compared, differences were found only on the weight management scale (Table 5.5). The WR group was less satisfied with the impact of their diabetes medicines on managing their weight at baseline (median=25) compared to the WI group (median=41.7), **p=0.001** (Figure 5.55).

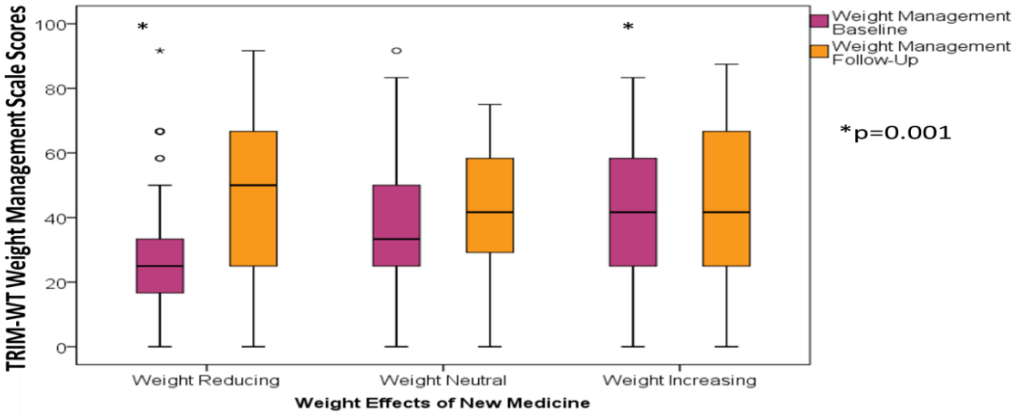

Figure 5.55: Differences in satisfaction about impact of new medicine on weight management (TRIM-Wt-WM) at baseline and follow-up. * Indicates significant difference between WR and WI groups for baseline scores

For most of the weight-effect groups there was no change in satisfaction levels relating to impact of their new diabetes medicine on daily life, weight management and psychological health over time. Nevertheless, the WR group had a significantly higher proportion of participants (59%, n=38) whose satisfaction levels increased in relation to impact of their new diabetes medicine on weight management compared to the other two groups (WN 30%, n=13 **p=0.009**; WI 25%, n=15, **p<0.001**) (Figure 5.50, Appendix 5.9). The WR group also had a significantly lower proportion of participants whose satisfaction levels did not change compared to WN (**p=0.009**) and WI (**p<0.001**) groups (Appendix 5.9).

5.5.6 Medication adherence (MMAS-8)

5.5.6.1 Whole Group- Baseline Versus Follow-up

There was no significant difference in reported adherence levels before (median=6.75) and after (median=7.0) initiation of new treatment in the medication adherence scale, p=0.637 (Figure 5.56, Table 5.5).

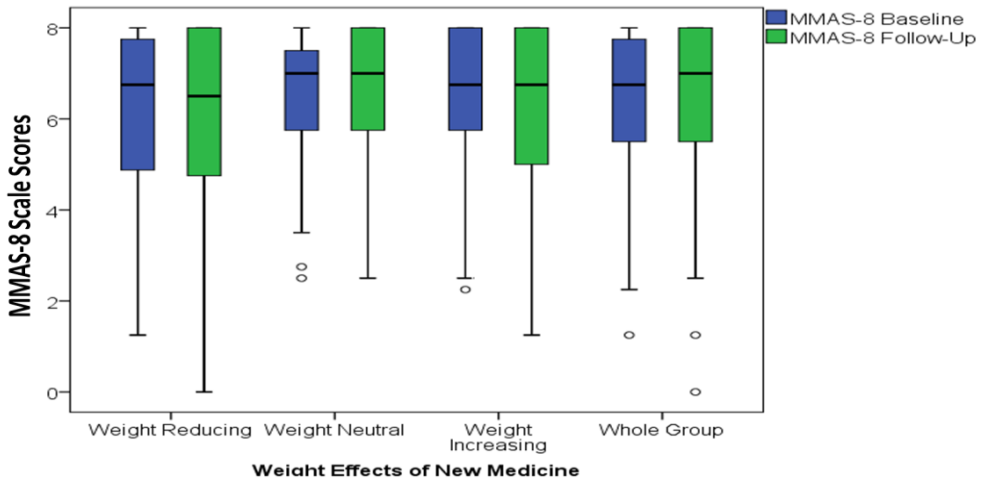

Figure 5.56: Medication adherence (MMAS-8) at baseline and follow-up.

Medication adherence varied across the whole group. The majority of participants were classified as medium adherent both at baseline (44%, n=75) and at three month follow–up (37%, n=71) (Figure 5.57).

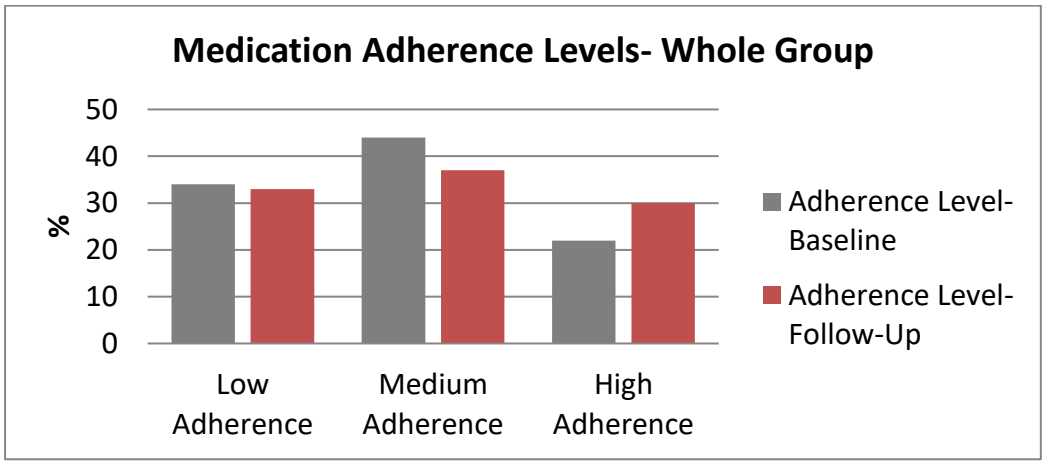

Figure 5.57: Level of adherence with diabetes medicines prior and 3 months after new medicine prescription for the whole group

Almost half of participants (49%, n=84) reported stable adherence levels over the three-month period, whereas 23% (n=39) decreased their adherence levels and 28% (n=47) increased their adherence levels (Figure 5.58, Appendix 5.10).

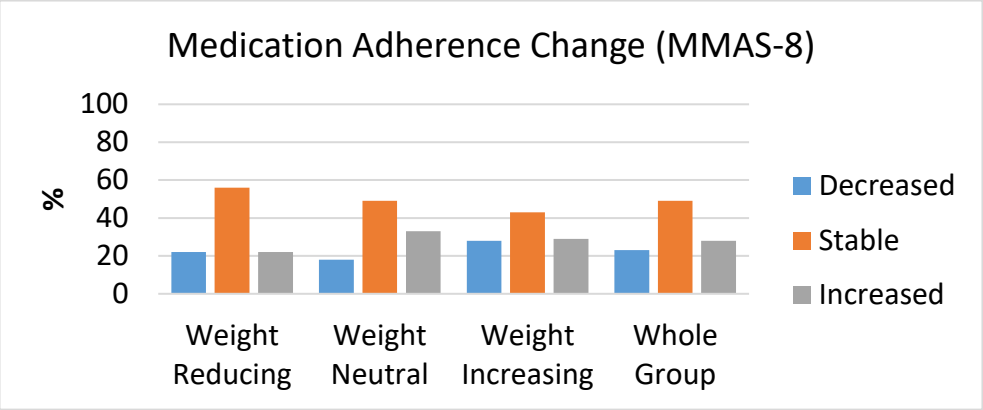

Figure 5.58: Percentage of participants whose levels of medication adherence (MMAS-8) increased, remained stable or decreased over time

5.5.6.2 Weight-Effect Groups – Baseline Versus Follow-up

There were no statistical differences for either weight-effect groups between baseline and follow-up on the medication adherence scale (Figure 5.56, WR p=0.730, WN p=0.147, WI p=0.946), neither was there any significant difference in the single items of the scale. Although there is a trend in proportions for lower and medium adherence groups to decrease overtime, and high adherence groups to increase over time; the WI group is the only group which had higher proportions of low adherence levels at 3 months (34%, n=22) compared to baseline (28%, n=17); an increase of 6% (Figure 5.59).

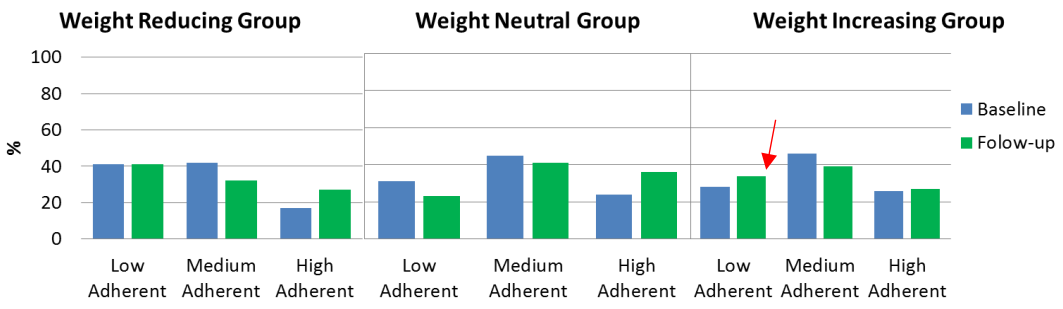

Figure 5.59: Medication adherence levels between baseline and follow-up for each weight-effect group.

5.5.6.3 Weight-Effect Groups – Comparison between groups

There were no statistical differences between groups when their adherence levels were compared (Table 5.5). Amongst the three weight groups, the WR group had the highest proportion of low adherence (41%, n=26) which appeared to remain high at follow–up (41%, n=28). This group also had the lowest proportion of high adherence levels before and after new medicine (17%, n=11 and 26%, n=18 respectively) compared to the other two groups (Figure 5.60). Despite the WI group having the highest adherence levels of the three weight-effect groups at baseline (26%, n=16), it was the WN group which had the highest proportion of high adherence levels at 3-month follow-up (36%, n=21).

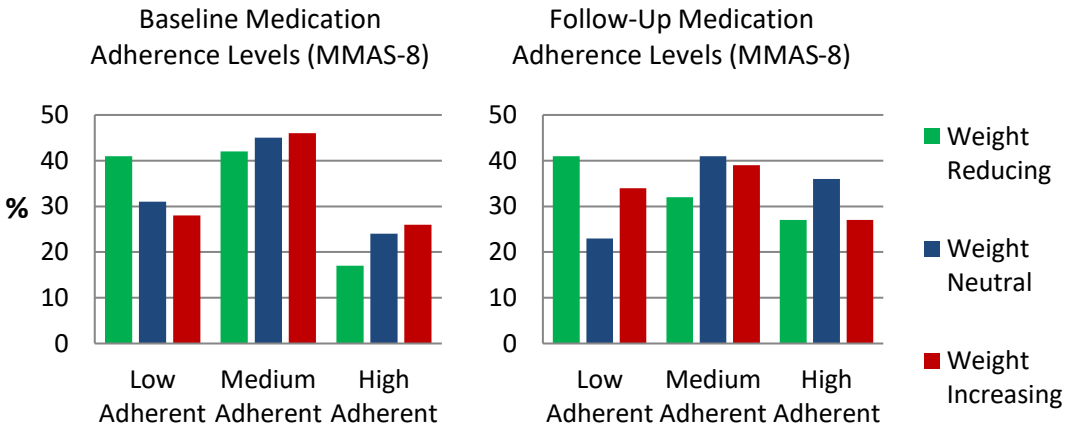

Figure 5.60: Percentage of baseline and follow-up medication adherence levels (MMAS-8) for each weight-effect group

Adherence levels in the majority of the participants (43-56%) in each weight-effect group remained stable over time. However, adherence levels increased in 22-33% and decreased in 18-28% (Figure 5.58, Appendix 5.10).

5.5.7 Self-Efficacy with Medication (SEAMS)

5.5.7.1 Whole Group- Baseline Versus Follow-up

There was no significant difference in overall self-efficacy with taking the new medicine before (median=3.69) or after (median=3.84) initiation of the new treatment, p=0.088, (Figure 5.61, Table 5.5).

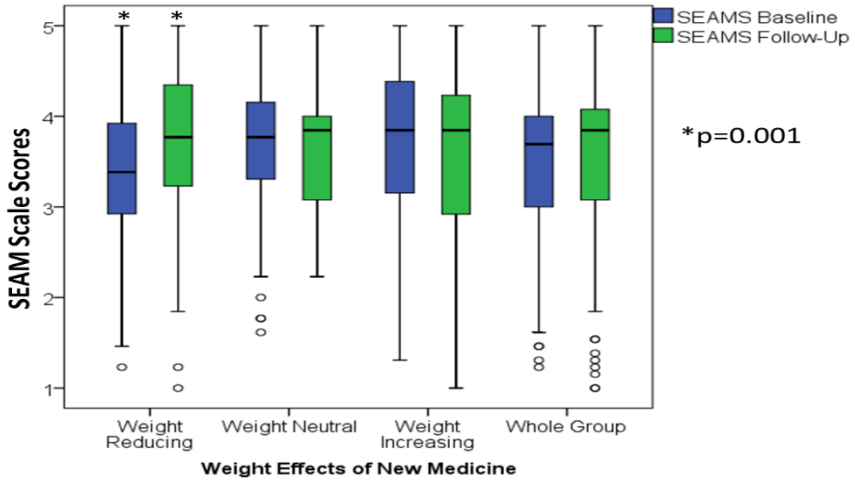

Figure 5.61: Self efficacy with taking medication scale (SEAMS) at baseline and follow-up.
* Indicates significant difference between baseline and follow-up in the WR group

Participants were, however, significantly more confident in taking their new medicine under circumstances of uncertainty at follow-up (median=3.7) than at baseline (median=3.5), **p=0.011** (Figure 5.62, Table 5.5).

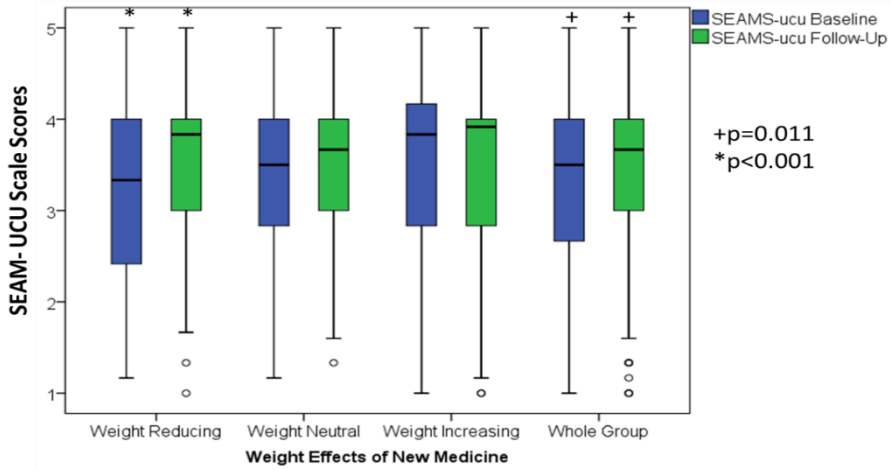

Figure 5.62: Self efficacy with taking medication under conditions of uncertainty (SEAMS-UCU) at baseline and follow-up. + Indicates significant difference between baseline and follow-up in the whole group,* Indicates significant difference between baseline and follow-up in the WR group

Participants' confidence in taking their new medicine under difficult circumstances did not change at follow-up (median=4.0) from baseline (median=3.8), p=0.568 (Figure 5.63, Table 5.5).

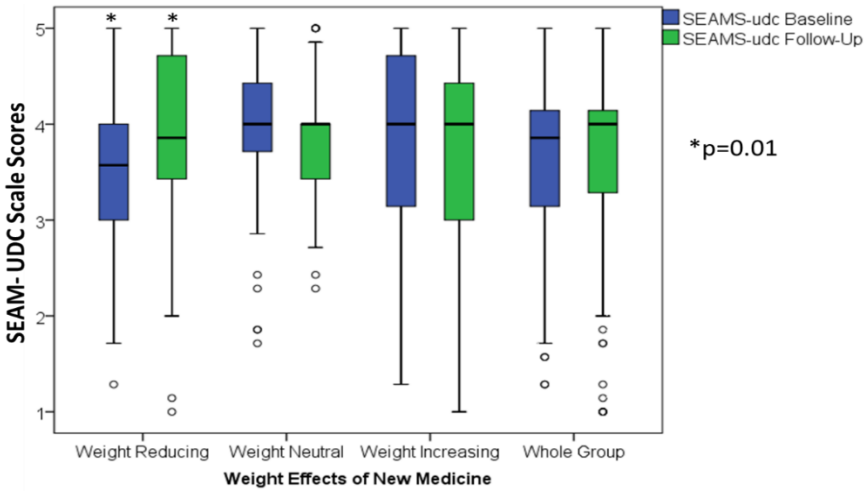

Figure 5.63: Self efficacy with taking medication under difficult circumstances (SEAMS-UDC) scale at baseline and follow-up. * Indicates significant difference between baseline and follow-up in the WR group

For the majority, their overall self-efficacy in taking their new medicine improved over time (41%, n=76), followed by those whose levels decreased (31%, n=57) and those who did not change (29%, n=53) (Figure 5.64, Appendix 5.11).

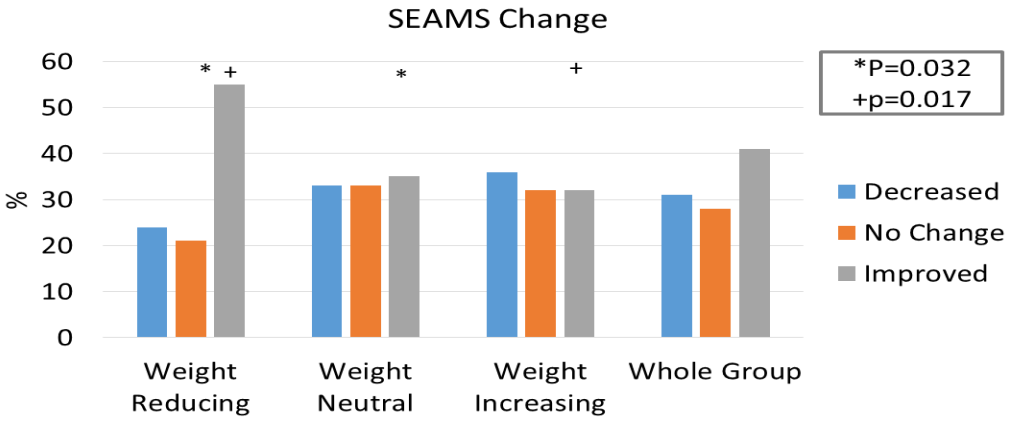

Figure 5.64: Percentage of participants who showed improvement, no change or reduction in self-efficacy of appropriate use of new medicine (SEAMS)

A similar pattern can be seen in relation to self-efficacy under difficult circumstances (Figure 5.65, Appendix 5.11).

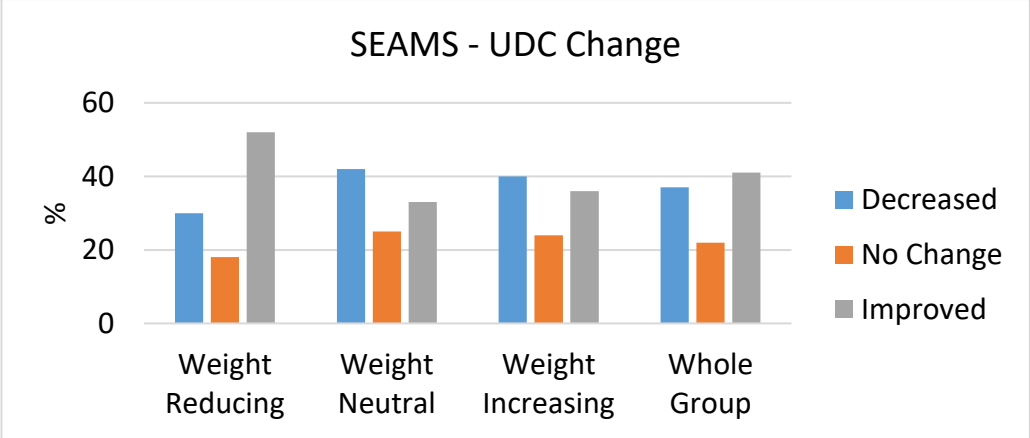

Figure 5.65: Percentage of participants who showed improvement, no change or reduction in self-efficacy under difficult circumstances (SEAMS-UDC) of appropriate use of new medicine

Whereas, over time, 41% (n=77) of participants improved their self–efficacy levels in relation to taking their new medicine under conditions of uncertainty, 31% (n=57) did not change, and 28% showed a decrease (n=52) (Figure 5.66, Appendix 5.11).

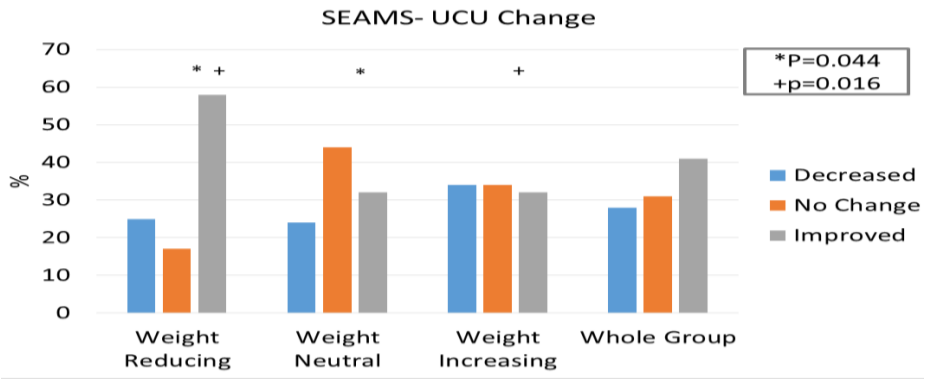

Figure 5.66: Percentage of participants who showed improvement, no change or reduction in self-efficacy under conditions of uncertainty (SEAMS-UCU) of appropriate use of new medicine

5.5.7.2 Weight-Effect Groups – Baseline Versus Follow-up

Weight Reducing Group

The WR group was significantly more confident in taking their medicine at follow-up (median=3.7) than at baseline (median=3.4), **p=0.001** (Figure 5.61). In addition, they were confident about taking it under conditions of uncertainty (median=3.9 Vs

median=3.3, **p<0.001**), and under difficult circumstances (median=3.9 Vs median=3.6, **p=0.01**) (Figures 5.62- 5.63).

When inspecting the single items, again only the WR group showed significant differences in responses to certain items. Significantly more people at follow-up were very or extremely confident that they could take their medicines correctly when they took several different medicines each day (p=0.005) (Appendix Figure 5.12), when they took medicines more than once a day (p=0.012) (not shown), when they were away from home (p=0.047) (not shown) and when their normal routine was messed up (p=0.024) (not shown). Although, a third (35.3%) of the group was somewhat confident with the latter item at follow-up.

Furthermore, significantly more people in this group at follow-up were very or extremely confident to take their medicine when they were not sure how to take it (p=0.003), when they were not sure what time of the day to take it (p=0.002) (Appendix Figures 5.13-5.14), when they were feeling unwell (like having a cold or flu) (**p<0.001**), when they got a refill of their old medicine and some of the pills looked different than usual (**p=0.001**) (Figures 5.67-5.68) and when they caused some side effects (p=0.015). Although, still a quarter of the group (25%) at follow-up were somewhat confident in taking their medicine correctly with the latter aspect.

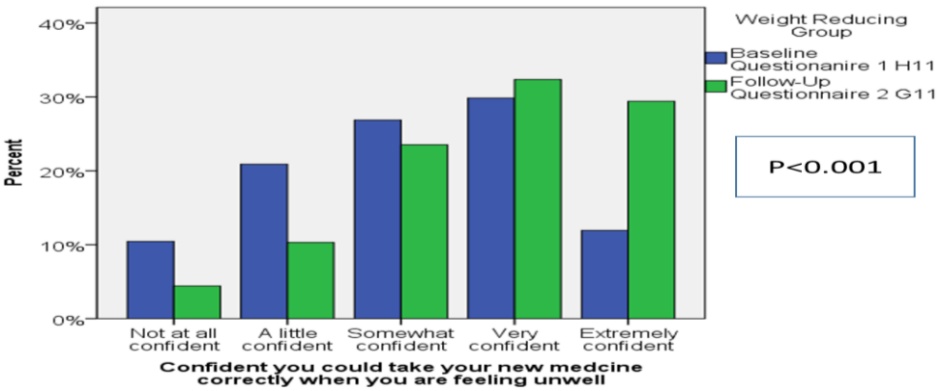

Figure 5.67: Percent agreement to SEAMS item "How confident are you that you could take your new medicine correctly when you are feeling unwell (you know like having a cold or the flu)" at baseline and follow-up for WR group.

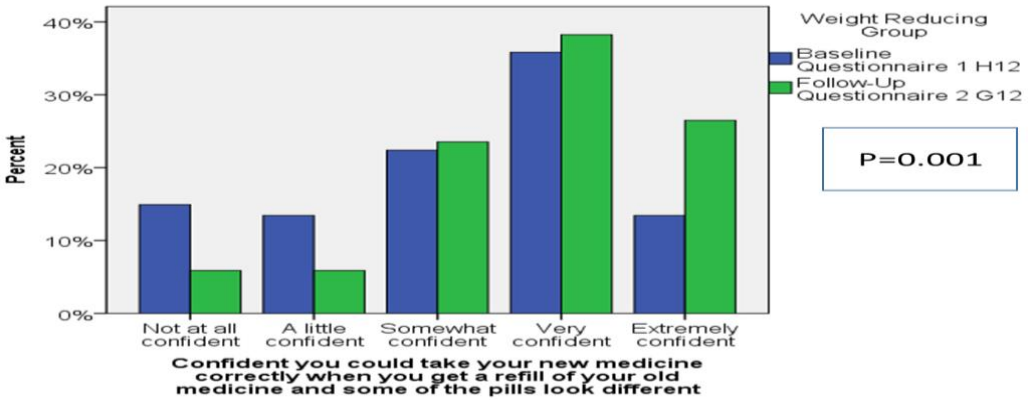

Figure 5.68: Percent agreement to SEAMS item "How confident are you that you could take your new medicine correctly when you get a refill of your old medicine and some of the pills look different than usual" at baseline and follow-up for WR group.

Weight Neutral and Weight Increasing Groups

There were no significant differences in the WN (SEAMS p=0.827, SEAMS-UCU p=0.548, SEAMS-UDC p=0.368) and the weight increasing groups (SEAMS p=0.573, SEAMS-UCU p=0.746, SEAMS-UDC p=0.376) in either of the scales at baseline and follow up.

5.5.7.3 Weight-Effect Groups – Comparison between groups

When the three weight-effect groups were compared, the WR group was less confident (median=3.6) than the WN group (median=4.0) in taking their medicine under difficult circumstances at baseline, **p=0.012** (Figure 5.69, Table 5.5).

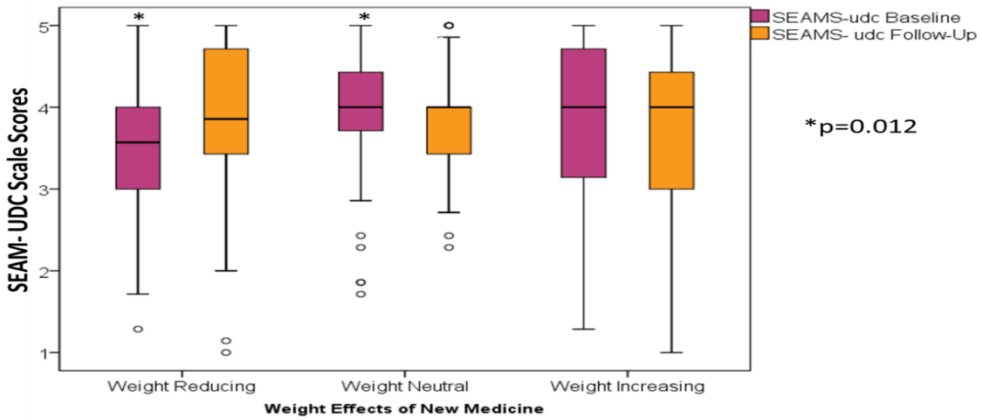

Figure 5.69: Differences in self-efficacy of taking new medicine under difficult circumstances (SEAMS-UDC) at baseline and follow-up. * Indicates significant difference between WR and WN groups for baseline scores

Despite the WR group being less confident in their self-efficacy in taking their new medicine correctly at baseline, it is the only group where self-efficacy levels improved over time in over half of participants (55%, n=37), compared to the WN (33%, n=19) and WI groups (32%, n=20, p=0.017). This difference was significant between the WR and WI groups, following Bonferroni correction p<0.017 (Figure 5.64, Appendix 5.11). In contrast to the WR group, where over half (52%, n=35) had improved their self-efficacy levels under difficult circumstances, 42% (n=24) of the WN and 40% (n=25) of the WI groups decreased their levels over time (Figure 5.65, Appendix 5.11). The WR group had a higher proportion of patients whose self-efficacy levels improved (58%, n=39) under conditions of uncertainty (Figure 5.66, Appendix 5.11) and a lower proportion of patients whose levels did not change over time (16%, n=11). This pattern was significantly different from the WI group, for whom only 32% (n=21, p=0.016), improved their self-efficacy levels, and 34% (n=21, p=0.016), did not change over time.

5.5.8. Weight Related Quality of Life (OWLQOL)

5.5.8.1 Whole Group- Baseline Versus Follow-up

There was a significant improvement in overall weight related quality of life between baseline (median=65.7) and follow-up (median=72.0), **p<0.001** (Figure 5.70, Table 5.5).

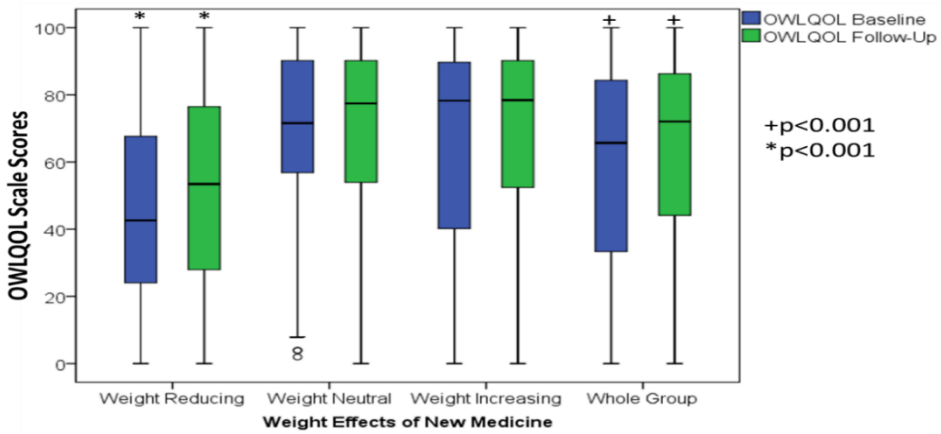

Figure 5.70: Obesity and weight loss quality of life (OWLQOL) scale at baseline and follow-up. + Indicates significant difference between baseline and follow-up in the whole group,* Indicates significant difference between baseline and follow-up in the WR group

Overall, weight related quality of life improved for most of the participants (43%, n=81) over time, whereas 35% (n=66) of the group did not change and 22% (n=43) decreased (Figure 5.71, Appendix 5.12).

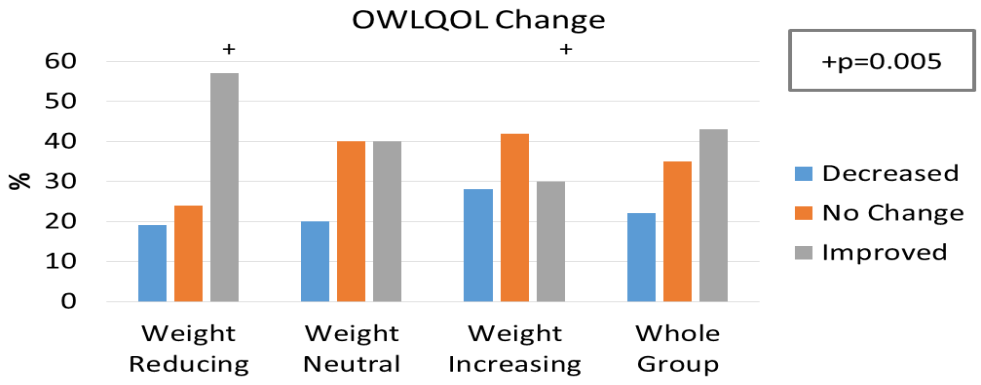

Figure 5.71: Percentage of participants who showed improvement, no change or reduction in weight related quality of life (OWLQOL)

5.5.8.2 Weight-Effect Groups – Baseline Versus Follow-up

Weight Reducing Group

The WR group showed improvement in weight related quality of life over 3 months (baseline: median=42.6, follow-up: median=53.4, **p<0.001)** (Figure 5.70). There was a statistical improvement in eight items within the quality of life scale in this group (Figures 5.72-5.74, Appendix Figures 5.15-19). In spite of this improvement, there was still a large number of individuals (varied from 34%-57% in items) who were bothered about these aspects from a 'good deal' to 'a very great deal', as shown in the figures.

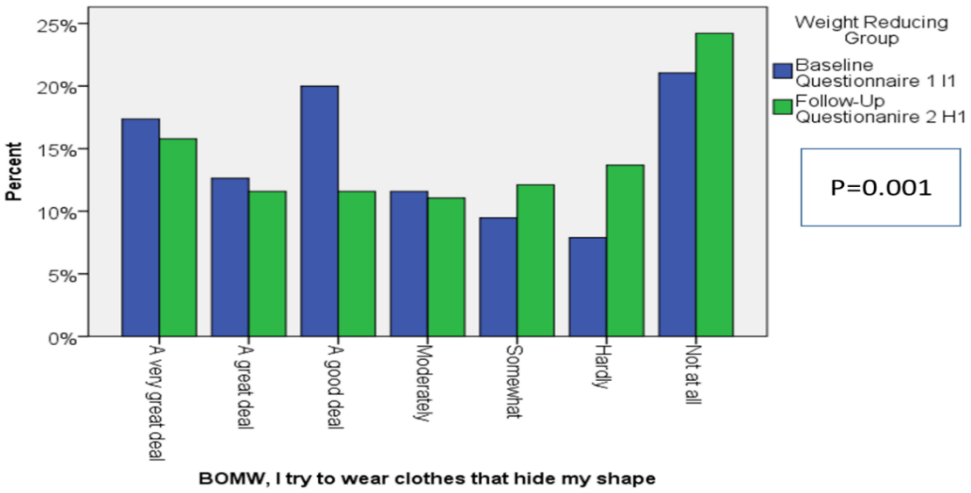

Figure 5.72: Percent agreement to OWLQOL item "Because of my weight, I try to wear clothes that hide my shape" at baseline and follow-up for WR group.

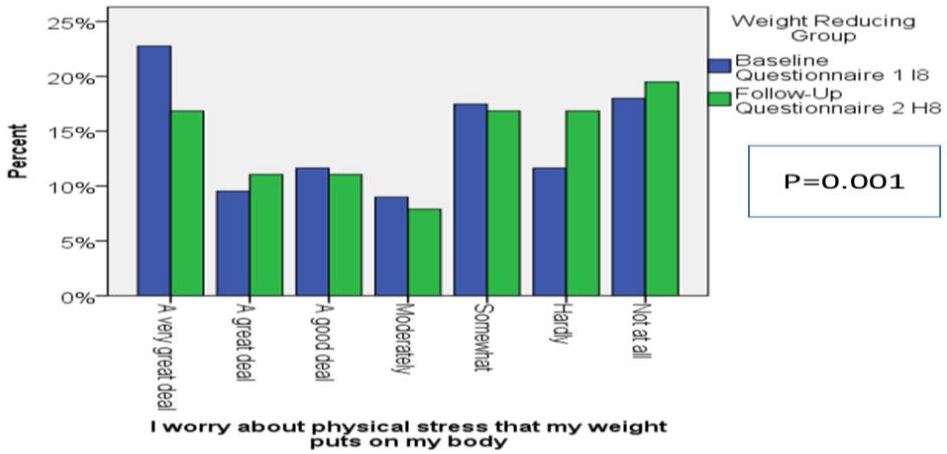

Figure 5.73: Percent agreement to OWLQOL item "I worry about physical stress that my weight puts on my body" at baseline and follow-up for WR group.

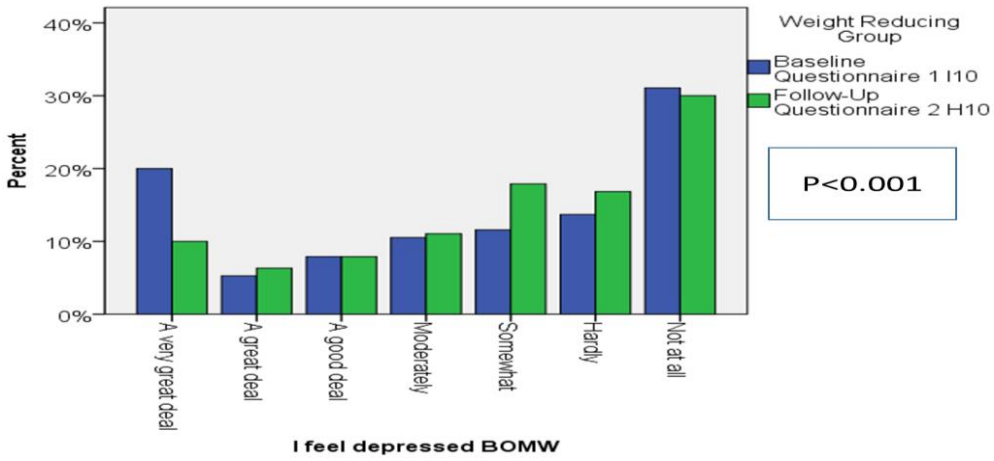

Figure 5.74: Percent agreement to OWLQOL item "I feel depressed because of my weight" at baseline and follow-up for WR group.

Weight Neutral and Weight Increasing Groups

There were no significant differences in the WN and the WI groups (p=0.114 and p=0.650 respectively) in this scale from baseline and follow up.

5.5.8.3 Weight-Effect Groups – Comparison between groups

The WR group had a lower score on quality of life (median=42.6) at baseline compared to the WN group (median=71.6, **p<0.001**) and the WI group (median=78.3, **p<0.001**). The score on quality of life for the WR group remained statistically lower at follow-up (median=53.4) compared to the WN (median=77.4, **p=0.001**) and WI groups (median=78.4, **p=0.002**). (Figure 5.75)

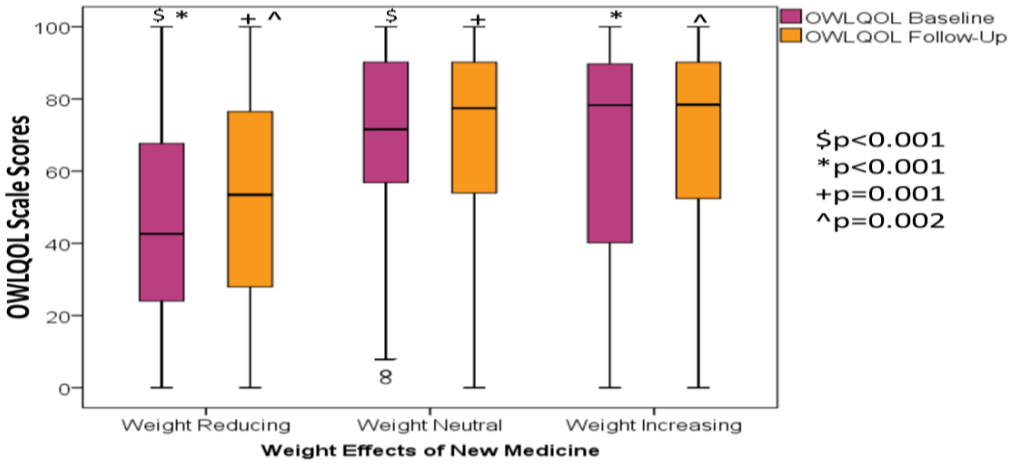

Figure 5.75: Differences in obesity and weight loss quality of life (OWLQOL) at baseline and follow-up. $ Indicates significant difference between WR and WN groups for baseline scores * Indicates significant difference between WR and WI groups for baseline scores, + Indicates significant difference between WR and WN groups for follow-up scores, ^ Indicates significant difference between WR and WI groups for follow-up scores

Despite the WR group having lower quality of life at both baseline and follow-up compared to the other two groups, it was the only group in whom quality of life improved over time (57%, n=39). This was statistically different from the WI group where only 30% (n=19) improved (**p=0.005**) (Figure 5.71, Appendix 5.12).

5.6 Impact of expectations, beliefs and attitudes on adherence

There are three adherence groups classified according to the MMAS-8 score; these are low (score<6), medium (score=6-7) and high (score=8) adherence groups. Table 5.6 presents the baseline and follow-up clinical, scale scores and other characteristics for each of the three adherence level groups. Also, the table presents statistical significant differences (Bonferroni correction p<0.017) between groups at both baseline and follow-up. Those classified as high adherent at baseline and follow-up were significantly older (baseline p=0.016, follow-up p=0.002), had less concerns over the potential adverse effects of their medicines (BMQ-Concerns; baseline p=0.04, follow-up p<0.001), were very confident about taking their medicines correctly (SEAMS, SEAMS-UCU, SEAMS-UDC; p<0.001 for all comparisons), whereas those classified as low adherent had strong beliefs about the medicines being harmful (BMQ-Harm; p=0.03) and were less satisfied with the burden of their diabetes medicines (DiabMedSat-Burden; baseline p<0.001, follow-up p=0.01) and their impact on their psychological health (TRIM-Wt-PH; baseline p=0.004, follow-up p=0.01). In addition, at follow-up, those classified as high adherents were more satisfied with the information they received about their new medicine in relation to the potential problems with them (SIMS-PPM; p=0.03), whereas those classified as low adherents had stronger beliefs that medicines are overused by doctors (BMQ-Overuse; p=0.005).

Furthermore, the high adherents had a higher score on necessity–concern differential indicating that the necessity of taking the medication was stronger than their concern about potential adverse effects from taking it (BMQ Necessity-Concern Differential; p=0.02), yet it appears that the beliefs about necessity of their medicines (BMQ-Necessity; median=3.7, p=0.5) were not as strong as those classified low (median=4.2) and medium (median=4.0) adherents. A closer look at the four diabetes medicines belief groups (sceptical, ambivalent, indifferent and accepting- see section 5.5.3.1 and figure 5.22) showed that the sceptical group was significantly less adherent than the indifferent group at baseline, and the ambivalent group was significantly less adherent than the accepting group at follow-up, Bonferroni

correction p<0.013 (Figure 5.76). The ambivalent and sceptical groups were generally less adherent than the accepting and indifferent groups because of their high concerns over potential adverse effects of their medicines (BMQ-Concerns) (Table 5.6). On the other hand, accepting and indifferent groups had similar adherence levels, but these were higher than the sceptical and ambivalent groups, because these two groups had lower concerns over the potential adverse effects of their medicines (BMQ-Concerns).

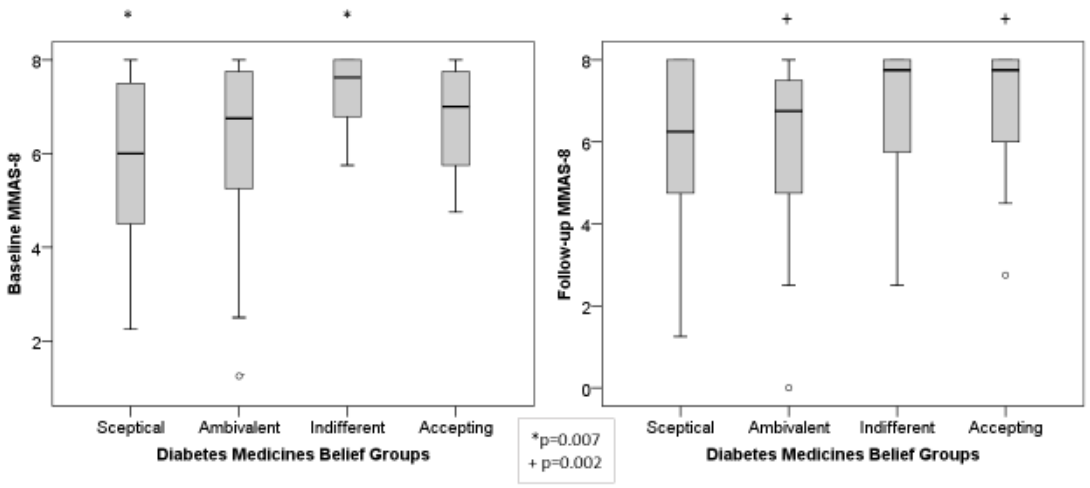

Figure 5.76: Baseline and follow-up adherence levels for the four diabetes medicines belief groups.

Overtime, there was a change in patients' adherence levels with three distinct changes; those who had a *decrease* in adherence levels from baseline, those who remained *stable* and those who *improved* their adherence levels (Appendix 5.4 and 5.10). Table 5.7 presents the baseline and follow-up clinical, scale scores and other characteristics for each of the above three groups. Also, the table presents statistical significant differences (Bonferroni correction p<0.017) between these groups at both baseline and follow-up.

Those who remained stable in their adherence levels over time had significantly lower scores at baseline on beliefs about medicines are overused by doctors (BMQ-Overuse; p=0.014) than the other two groups. Also, they were less satisfied with the impact of their diabetes medicines on their weight (TRIM-Wt-WM; p=0.03) than

those who had a decrease in their adherence levels. It should be noted that the group who had stable adherence levels over time, these levels were generally medium to high (median (Q1-Q3)=7(5.8, 8.0) according to the MMAS-8 classification (Morisky et al., 2008) (table 5.7). Those who remained stable in their adherence levels over time were significantly more confident in taking their medicines correctly (SEAMS; p=0.025) at three months after initiation of a new treatment than those who had a decrease in their adherence levels. A similar finding can be seen for self-efficacy levels under conditions of uncertainty (SEAMS-UCU; p=0.006) between the stable group and the other two groups. As expected those who improved their adherence levels over time had significantly lower adherence levels at baseline (MMAS-8; p<0.001) compared to the other two groups and they had significantly higher adherence levels at follow-up (MMAS-8; p<0.001) than those who had a decrease in their adherence.

Table 5.6: Baseline and Follow-up scores for low, medium and high adherents (MMAS-8)

Whole Group	Baseline				Follow-up			
Medication Adherence Level	Low	Medium	High	P value	Low	Medium	High	P value
Total N	49	70	35		35	48	27	
Age(yrs)	55.0(48.0,64.0)*****	58.5 (51.8, 69.3)	66.0 (54.0, 71.0)*****	**0.016**	*		*	**0.002**
Diabetes Duration(yrs)	8.0 (4.0, 13.0)	7.5 (3.8, 13.0)	10.0 (6.0, 16.0)	0.16				
BMI(kg/m^2)	34.1 (30.3, 40.7)	35.5 (31.9, 40.6)	35.3 (29.8, 41.7)	0.57	33.6 (30.8, 40.5)	35.2	37.3	0.81
HbA1c(mmol/mol)	84 (67, 96)	79 (67, 89)	74 (62, 87)	0.43	74 (60, 88)	63 (52,81)	62 (56, 70)	0.11
Total Medication Burden	6 (4, 9) (range 1-19)	8 (5, 11) (range 1-21)	9 (6, 11) (range 2-17)	0.04	6 (5, 11) (range 2-16)	8 (6, 11) (range 2-21)	8 (5, 10) (range 3-16)	0.99
Total diabetes medication burden	2 (range 0-3)	2 (range 0-4)	2 (range 1-4)	0.27	2 (2, 3) (range 1-5)	2 (2,3) (range 1-4)	2 (2,3) (range 1-4)	0.17
No of Diabetes complications	1 (0, 1)	1 (0, 1)	1 (0, 2)	0.43	1 (0, 1)	1 (0, 2)	0 (0, 2)	0.52
Total N	56	74	38		60	69	56	
EITQ (baseline)/ PITQ (Follow-up)	5.5 (5.0, 6.0)	5.5 (4.9, 6.0)	5.7 (5.1, 6.0)	0.80	5.6 (5.1, 6.1)	5.6 (5.1, 6.0)	5.7 (5.3, 6.0)	0.41
SIMS	11 (8, 16)	13 (9, 17)	14 (11, 18)	0.06	14 (9, 17)	14 (9, 17)	16 (11, 18)	0.05
SIMS-AU	7.5 (6, 9)	8 (6, 9)	8.5 (7, 9)	0.09	8 (7, 9)	8 (6, 9)	8 (7, 9)	0.24
SIMS-PPM	4 (1, 8)	5 (2, 9)	6 (4, 9)	0.13	6 (3, 8)*	6 (2, 9)	8 (4, 9)*	**0.03**
BMQ-Concerns	3.0 (2.7, 3.7)*****	2.9 (2.3, 3.2)	2.8 (2.4, 3.1)*****	**0.04**	3.1 (2.4, 3.4)+	2.9 (2.4, 3.4)*	2.3 (2, 2.7)*+	**<0.001**
BMQ-Necessity	4 (3.6, 4.2)	4 (3.6, 4.4)	4 (3.6, 4.7)	0.72	4.2 (3.8, 4.8)	4 (3.4, 4.5)	3.7 (3.2, 4.4)	0.5

BMQ Necessity – Concern Differential	0.8 (0.2, 1.4)	1.0 (0.5, 1.9)	1.2 (0.6, 1.5)	0.04	0.9 (0.3, 1.4)*	0.9 (0.3, 1.7)	1.2 (0.6, 1.9)*	**0.02**
BMQ-Overuse	3.0 (2.3, 3.7)	2.7 (2.3, 3.1)	2.8 (2.0, 3.3)	0.32	3.0 (2.7, 3.7)+	3.0 (2.7, 3.7)*	2.7 (2.0, 3.3)*+	**0.005**
BMQ-Harm	2.5 (2.1, 3.0)*	2.5 (2.0, 2.8)	2.3 (2.0, 2.5)*	**0.03**	2.5 (2.3, 2.8)	2.5 (2.3, 2.8)	2.3 (2.0, 2.8)	0.25
BMQ-Benefits	4.0 (3.5, 4.8)	4.0 (3.8, 4.5)	4.0 (4.0, 4.5)	0.04	4.0 (3.8, 4.4)	4.0 (3.8, 4.4)	4.0 (3.8, 4.3)	0.92
MMAS-8	4.8 (3.8, 5.5)*^	7.0 (6.8, 7.0)*+	8.0 (8.0,8.0)+^	**<0.001**	4.8 (4.0, 5.8)*^	7.0 (6.8, 7.0)*+	8.0 (8.0,8.0)+^	**<0.001**
SEAMS	3.1 (2.3, 3.7)*+	3.9 (3.1, 4.2)*	4.0 (3.8, 4.7)+	**<0.001**	3.3 (2.5, 3.9)*^	3.7 (3.2, 4.1)*+	4.0 (3.9, 4.8)+^	**<0.001**
SEAMS-UCU	2.8 (2.0, 3.7)*+	3.8 (2.8, 4.0)*	3.9 (3.5, 5.0)+	**<0.001**	3.2 (2.2, 4.0)*^	3.5 (3.0, 4.0)*+	4.0 (3.7, 4.7)+^	**<0.001**
SEAMS-UDC	3.3 (2.4, 3.8)*+	4.0 (3.3, 4.2)*	4.1 (4.0, 5.0)+	**<0.001**	3.4 (2.7, 4.0)*^	4.0 (3.4, 4.1)*+	4.0 (4.0, 5.0)+^	**<0.001**
OWLQOL	51.5 (21.6, 74.8)	69.6 (30.9, 88.7)	71.6 (40.2, 89.5)	0.02	65.2 (33.1, 84.6)	70.6 (35.3, 87.3)	76.0 (52, 90.9)	0.18
Total N	57	73	36		63	70	54	
DiabMedSat	59.3 (53.4, 70.2)	67.6 (58.0, 75.9)	69.0 (57.6, 78.8)	0.008	71.4 (54.2, 79.4)	71.3 (62.7, 79.3)	75.5 (65.6, 82.9)	0.03
DiabMedSat-Efficacy	45.0 (32.5, 58.3)	55.0 (39.2, 66.7)	58.3 (42.1, 70.8)	0.016	60.0 (45.0, 76.7)	60.0 (46.7, 75.4)	69.2 (50.0, 84.2)	0.07
DiabMedSat-Burden	57.0(64.8,85.2)*	86.4(72.7,93.9)*	84.1 (75.6, 91.7)	**<0.001**	79.6(68.9,91.7)*	84.1 (75, 87.5)	88.3(78.0,96.6)*	**0.01**
DiabMedSat-Symptoms	60 (48, 78)	68 (52, 78)	68 (52, 80)	0.5	72 (52, 76)	68 (56, 80)	72 (63, 77)	0.4
TRIM-Wt-DL	62.5 (50.0, 70.8)	70.8 (56.3, 79.2)	66.7 (58.3, 79.2)	0.02	70.8 (58.3, 79.2)	75.0 (58.3, 79.2)	75.0 (58.3, 83.3)	0.2
TRIM-Wt-WM	33.3 (16.7, 50.0)	33.3 (25, 50)	33.3 (25, 50)	0.53	41.7 (25, 58.3)	41.7 (25, 66.7)	50 (33.3, 66.7)	0.3
TRIM-Wt-PH	62.5 (34.4, 84.4)*	7.05 (50.0, 100)	87.5 (64.1, 100)*	**0.004**	68.8(50.0,87.5)*	75.0 (48.4, 95.3)	81.3 (67.2, 100)*	**0.01**

Values are Median (Q1, Q3), Significant difference between adherence groups, Bonferroni correction *p<0.017, +p<0.017, ^p<0.017

Table 5.7: Baseline and Follow-up scores for those who improved, decreased or remained stable in adherence levels

Whole Group	Baseline				Follow-up			
Change in Medication Adherence Level	Decreased	Stable	Improved	P value	Decreased	Stable	Improved	P value
Total N	38	80	41		27	55	28	
Age(yrs)	58.0 (49.0, 67.0)	59.0 (51.0,66.0)	63.0 (53.5, 69.5)	0.17				
Diabetes Duration	9.0 (4.0, 14.5)	8.0 (5.0, 13.0)	10.0 (3.0, 14.0)	0.63				
BMI	34.6 (29.9, 41.3)	35.9 (31.7, 40.7)	35.5 (31.3, 40.7)	0.7	35.0 (31.4, 41.4)	36.5 (32.7, 40.9)	33.6 (30.5, 40.5)	0.66
HbA1c(mmol/mol)	86 (70, 98)	76 (64, 86)	75 (67, 93)	0.05	74 (61, 90)	67 (56, 80)	62 (56, 79)	0.11
Total Medication Burden	9 (4, 11) Range (1, 21)	7 (5, 11) Range (2, 17)	7 (5,9) Range (1, 19)	0.42	9 (6, 11) Range 2-17	7 (5, 10) Range 2-19	7 (5, 10) Range 2-21	0.21
Total diabetes medication burden	2 (1, 2) Range 0-3	2 (1, 2) Range 1-4	2 (1, 3) Range 0-4	0.76	3 (2, 3) Range 2-4	2 (2, 3) Range 1-4	1 (0, 3) Range 1-5	0.63
No of Diabetes complications	1 (0, 2)	1 (0, 1)	1 (0, 1)	0.73	1 (0, 2)	1 (0, 1)	0 (0, 1)	0.41
Total N	39	82	46		39	82	46	
EITQ (baseline)/PITQ (Follow-up)	5.6 (5.2, 5.9)	5.5 (5.1, 6)	5.6 (4.6, 6.1)	0.82	5.5 (5.1, 5.9)	5.5 (5.1, 6)	5.8 (5.3, 6.1)	0.34
SIMs	15 (9, 17)	13 (9, 16)	12 (8, 18)	0.73	15 (13, 17)	15 (10, 17)	13 (7, 18)	0.33
SIMS-AU	8 (7, 9)	8 (6, 9)	8 (5.8, 9)	0.30	8 (7, 9)	8 (6, 9)	7.5 (5, 9)	0.08
SIMS-PPM	6 (2, 9)	5 (2, 8)	5.5 (1.8, 9)	0.86	7 (5, 8)	7.5 (3, 9)	5 (2, 9)	0.39
BMQ-Concerns	2.7 (2.3, 3.3)	2.9 (2.5,3.3)	3.0 (2.3, 3.4)	0.32	2.7 (2.4, 3.3)	2.7 (2.1, 3.3)	2.6 (2.3, 3.3)	0.53
BMQ-Necessity	3.8 (3.4, 4.2)	3.9 (3.6, 4.2)	4.0 (3.6, 4.6)	0.44	3.7 (3.1, 4.1)	4.0 (3.4, 4.6)	3.8 (3.4, 4.4)	0.13

BMQ Necessity – Concern Differential	0.93 (0.54, 1.54)	0.99 (0.45, 1.46)	0.94 (0.46, 1.97)	0.97	0.77 (0.28, 1.38)	1.10 (0.45, 1.86)	1.14 (0.40, 1.86)	0.11
BMQ-Overuse	3.0 (2.3, 3.7)*	2.7 (2.3, 3.0)*+	3.0 (2.3, 3.7)+	**0.014**	3.0 (2.7, 3.7)	2.7 (2.3, 3.3)	3.0 (2.7, 3.7)	0.09
BMQ-Harm	2.5 (2.3, 3.0)	2.3 (2.0, 2.8)	2.5 (2.3, 2.8)	0.10	2.5 (2.3, 3.0)	2.3 (2.0, 2.8)	2.5 (2.0, 3.0)	0.08
BMQ-Benefits	4.0 (3.8, 4.5)	4.0 (3.8, 4.5)	4.0 (3.8, 4.0)	0.15	4.0 (3.8, 4.5)	4.0 (3.8, 4.5)	4.0 (3.8, 4.0)	0.48
MMAS-8	7.0 (5.8, 8.0)+	7.0 (5.8, 8.0)*	5.8 (4.5, 7.0)* +	**<0.001**	5.3 (3.9, 6.8)*^	7.0 (5.8, 8.0)*	7.8 (6.5, 8.0)^	**<0.001**
SEAMS	3.8 (3.1, 4.2)	3.8 (3.1, 4.4)	3.4 (2.6, 4.0)	0.08	3.4 (2.8, 4.0)*	4.0 (3.5, 4.3)*	3.7 (2.9, 4.2)	**0.025**
SEAMS-UCU	3.9 (2.8, 4.0)	3.7 (3.0, 4.2)	2.8 (2.3, 4.0)	0.06	3.3 (2.5, 4.0)*	4.0 (3.5, 4.0)*+	3.4 (2.8, 4.0)+	**0.006**
SEAMS-UDC	4.0 (3.3, 4.2)	4.0 (3.3, 4.6)	3.7 (3.0, 4.0)	0.16	3.6 (3.0, 4.0)	4.0 (3.5, 4.3)	4.0 (3.1, 4.3)	0.13
OWLQOL	71.1 (32.8, 85.3)	63.7 (30.2, 85.5)	58.8 (31.7, 87.3)	0.92	65.2 (43.6, 85.5)	69.6 (35.3, 85.3)	75.5 (40.2, 91.2)	0.59
Total N	38	80	45		38	80	45	
DiabMedSat	67.8 (54.8, 74.4)	64.0 (57.4, 75.8)	61.8 (47.8, 74.9)	0.33	73.1 (58.3, 77.2)	72.3 (62.0, 80.3)	71.9 (55.6, 81.5)	0.62
DiabMedSat-Efficacy	50.8 (36.3, 63.3)	51.7 (40.0, 62.9)	53.3 (31.7, 62.5)	0.84	60.0 (46.7, 75.4)	62.5 (48.3, 76.7)	68.3 (40.0, 80.0)	0.59
DiabMedSat-Burden	86.7 (72.7, 93.9)	81.8 (73.5, 88.6)	73.5 (65.2, 89.4)	0.16	84.5 (72.9, 92.6)	85.2 (77.3, 92.9)	84.1 (71.2, 92.8)	0.42
DiabMedSat-Symptoms	64 (52, 81)	68 (52, 80)	64 (44, 78)	0.44	64 (59, 77)	68 (56, 76)	72 (52, 80)	0.92
TRIM-Wt-DL	70.8 (54.2, 79.2)	66.7 (54.2, 79.2)	66.7 (47.9, 77.1)	0.54	72.9 (50, 79.2)	70.8 (62.5, 79.2)	75.0 (58.3, 79.2)	0.86
TRIM-Wt-WM	33.3(31.3,58.3)*	25.0(16.7,41.7)*	33.3 (16.7, 50.0)	**0.03**	45.8 (31.3, 58.3)	41.7 (18.8, 66.7)	50.0 (25.0, 66.7)	0.50
TRIM-Wt-PH	71.9 (50.0, 100)	75.0 (56.3, 93.8)	68.8 (37.5, 96.9)	0.42	71.9 (50.0, 93.8)	75.0 (62.5, 93.8)	62.5 (43.8, 93.8)	0.13

Values are Median (Q1, Q3), Significant difference between (two) adherence groups, Bonferroni correction *p<0.017, +p<0.017, ^p<0.017

To examine the impact of participants' expectations, beliefs and attitudes on adherence as well as participants characteristics, demographics and clinical values, a univariate analysis was conducted to assess which variables were significant predictors of medication adherence. The analysis was split into four separate analysis: i) using baseline values to predict three-month adherence status, ii) using change values from baseline to follow-up to predict three-month adherence status, iii) using baseline values to predict change in adherence and iv) using change values from baseline to follow-up to predict change in adherence. Multivariate analysis was conducted based on the significant predictors from univariate analyses. All analyses was done separately for whole group and weight-effect groups (sections 5.6.1-5.6.2).

5.6.1 Whole Group

5.6.1.1 Predicting medication adherence at 3-month follow-up from baseline and change values

The univariate analyses showed a number of individual variables significantly predicted medication adherence at follow-up, using the three adherence level groups (low, medium, high) derived from MMAS-8 scale score as the dependent variable (Table 5.8). Results of analyses for all other variables can be found in Appendices 5.13-5.14. However, the multivariate ordinal analysis showed that only seven variables significantly predicted medication adherence at follow-up when entered together in the analysis (Table 5.9). The model fit chi-square statistic indicates that this full multivariate model (Model 1 or 2 in Table 5.9) is performing better ($p<0.001$) than the baseline intercept-only model (no independent variables) at predicting cumulative probability for medication adherence. The goodness of fit tests (both Pearson chi-square and Deviance) suggest that the observed data are good fit for the model ($p>0.05$). The pseudo R^2 statistics suggest that the variables in the model explain 56% of the variance in medication adherence level. However, the test of parallelism is rejected as $p<0.05$ (although only marginal), implying that the effects of the explanatory variables are not the same across the different thresholds, therefore the assumption of *proportional odds*, is violated. Hence, separate binary logistic regressions were undertaken to explore how the odd ratios or the explanatory variables vary at the different thresholds (Table 5.10).

Table 5.8: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the whole group

Variable	β	significance	Test for parallelism
Age	0.041	0.001	0.149
Full time	-0.822	**0.021**	0.308
Part time	-0.200	0.697	
Unemployed	-0.758	0.095	
Other	-0.200	0.637	
Retired	Reference		
SIMS	0.058	0.041	0.546
SIMS-PPM	0.107	0.013	0.550
BMQ-Concerns	-0.477	0.023	0.299
Baseline Necessity-Concern Differential	0.427	0.007	0.650
DiabMedSat	0.023	0.019	0.914
DiabMedSat-Burden	0.021	0.028	0.505
DiabMedSat-Efficacy	0.017	0.024	0.869
Trim-Wt-PH	0.012	0.021	0.937
Baseline MMAS-8	1.022	<0.001	0.840
SEAMS	0.848	<0.001	0.750
SEAMS-UDC	1.046	<0.001	0.549
SEAMS-UCU	0.556	<0.001	0.865
Baseline HbA1c	-0.019	0.015	0.396
Weight-Effects of New Medicine:			0.561
Weight Increasing	0.177	0.582	
Weight Neutral	0.673	**0.043**	
Weight Reducing	Reference		
Expectation Perception Difference (EITQ-PITQ Change)			
Expectations Exceeded by Experience	Reference		
Expectations Unmet	-0.805	0.707	0.505
Expectations Met	-0.119	**0.019**	
BMQ-Concern Change			
Stronger	Reference		0.138
No Change	0.457	0.203	
Decreased	0.933	**0.013**	
BMQ-Necessity Change			
Stronger	Reference		0.964
No Change	0.439	0.205	
Decreased	0.847	**0.019**	
SEAMS-UDC Change			
Improved	Reference		0.378
No Change	1.365	**<0.001**	
Decreased	-0.232	0.454	

Table 5.9: Multivariate Ordinal Analysis predicting adherence at follow-up

	Whole Group			Whole Group with Weight-Effect Variable		
	Estimate β (95% CI)	p value	Cumulative Odds (95%CI) Exp (Cumulative Logit)	Estimate β (95% CI)	p value	Cumulative Odds (95%CI) Exp (Cumulative Logit)
Threshold						
Adherence Level=1 /MMAS-8≥6	10.903 (6.054, 11.434)			10.966 (7.828, 14.105)		
Adherence Level=2/MMAS-8=8	13.578 (8.217, 14.080)			13.685 (10.225, 17.145)		
Variables						
Age	0.034 (0.003, 0.063)	0.031	1.03 (1.00, 1.06)	0.30 (-0.002, 0.061)	0.064	1.03 (1.00, 1.06)
Baseline MMAS-8	0.912 (0.570, 1.192)	<0.001	2.49 (1.77, 3.29)	0.926 (0.602, 1.250)	<0.001	2.52 (1.83, 3.49)
Baseline SEAMS-UDC	1.975 (0.790, 2.357)	<0.001	7.20 (2.20, 10.56)	1.939 (1.085, 2.792)	<0.001	6.95 (2.96, 16.31)
Baseline SEAMS-UCU	-1.118 (-1.778, -0.487)	0.001	0.33 (0.17, 0.61)	-1.108 (-1.785, -0.431)	0.001	0.33 (0.17, 0.65)
BMQ-Concerns Change Stable Vs Stronger	1.111 (0.194, 2.028)	0.018	3.04 (1.21, 7.60)	1.174 (0.222, 2.125)	0.005	3.23 (1.25, 8.37)
BMQ-Concerns Change Decrease Vs Stronger	1.458 (0.494, 2.423)	0.003	4.30 (1.64, 11.28)	1.604 (0.609, 2.600)	0.002	4.97 (1.84, 13.46)
SEAMS-UDC Change Decrease Vs Improvement	-1.399 (-2.159, -0.639)	<0.001	0.25 (0.12, 0.53)	-1.440 (-2.211, -0.670)	<0.001	0.24 (0.11, 0.51)
Weight Neutral Vs Weight Reducing				0.475 (-0.392, 1.341)	0.283	1.61 (0.68, 3.82)
Weight Increasing Vs Weight Reducing				0.359 (-0.460, 1.179)	0.390	1.43 (0.63, 3.25)

Model Statistics	Model Fit: χ^2 (7)=114.658, p<0.001, Goodness of Fit (327)= 293.922, p=0.905, Nagekerke R^2=0.557, Test of Parallelism χ2(7)=15.014, p=0.04	Model Fit: χ^2 (9)=116.409, p<0.001, Goodness of Fit (327)= 297.346, p=0.879, Nagekerke R^2=0.561 , Test of Parallelism χ2(9)= 17.195, p=0.05
Multivariate Model 1 for Whole Group: 10.903-0.912(Baseline MMAS-1)–0.034(Age)-1.975(Baseline SEAMS-UDC)+1.118(Baseline SEAMS-UCU)+1.399 (SEAMS-UDC Change Decrease)-1.458(BMQ-Concern change decrease)-1.111 (BMQ-Concern Change –no change) **Multivariate Model 2 for Whole Group:** 13.578-0.912(Baseline MMAS-8)–0.034(Age)-1.975(Baseline SEAMS-UDC)+1.118(Baseline SEAMS-UCU)+1.399 (SEAMS-UDC Change Decrease)-1.458 (BMQ-Concern change decrease)-1.111(BMQ-Concern Change –no change) Model 1 compares participants with low adherence with those scored as medium and high adherent combined. Model 2 compares those participants who scored as low and medium adherent with those who scored as high adherent (the odds of being high adherent).		

Table 5.10: Separate binary logistic regressions for high adherents and, medium and high adherents for key explanatory variables from ordinal regression

	B co-efficient		**Relative Odds/ Odds Ratios (95%CI)**		
	High	Medium-High	High	Medium-High	Test for parallelism
Intercept	-17.293	-10.093			
Age	0.25	0.039*	1.026 (0.981, 1.072)	1.040 (1.0, 1.081)	0.149
Baseline MMAS-8	0.727**	1.027***	2.068 (1.231, 3.473)	2.793 (1.857, 4.2)	0.840
SEAMS-UDC	2.885***	1.924**	17.895 (3.590, 89.207)	6.850 (2.208, 21.254)	0.549
SEAMS-UCU	-1.044*	-1.370**	0.352 (0.134, 0.927)	0.254 (0.099, 0.655)	0.865
BMQ-Concern Change Decrease (Vs Stronger)	3.247***	0.530	25.701 (4.240, 155.791)	1.699 (0.501, 5.757)	0.248
BMQ-Concern Change- Stable (Vs Stronger)	2.878**	0.154	17.775 (3.027, 104.389)	1.167 (0.3387, 3.519)	0.774
SEAM-UDC Change Decrease (Vs Improvement)	-1.749*	-1.366*	0.174 (0.046, 0.656)	0.255 (0.077, 0.841)	0.213
SEAM-UDC Change No Change (Vs Improvement)	0.581	-0.485	1.789 (0.473, 6.759)	0.616 (0.148, 2.560)	0.203
R^2 (Nagelkerke) Model Chi-squared Hosmer & Lemeshow test	0.58 85.675*** 4.5 (p=0.81) 86.7% Correct (70.2% of high adherers)	0.54 81.72*** 6.8 (p=0.56) 81.3% Correct (88.9% of medium and high adherers)			

*p<0.05, **p<0.01, ***p<0.001, ns= not significant

The logistic regressions indicated that age predicts only those who are medium to high adherents, whereas a change in beliefs over concerns of the potential adverse effects of the new medicine (BMQ-Concerns Change) predicts those who are high adherents. All other explanatory variables predict both those who are medium to high adherents and those who are only high adherents (MMAS-8, SEAMS-UDC, SEAMS-UCU, SEAM-UDC Change). The p values for the test of parallel lines for all the individual variables are above 0.05. In addition, the direction of beta co-efficients is the same as in the original ordinal regression model (Table 5.9), as well as the relative odds and odds ratios are proportionally across the two groups, with the exception of SEAMS UDC, and BMQ-Concern change, which are much higher for the high adherence group compared to the medium to high adherence group. Therefore, it is reasonable to conclude that the ordinal model (Table 5.9) is a fair summary of the patterns of the research data in relation to predicting medication adherence.

Hence, both ordinal models (Table 5.9) suggest that a unit increase in one individual predictor variable when all the other predictor variables remain constant increases or decreases the odds of becoming highly adherent dependent on whether the estimate β (or predicted cumulative logit) has a positive or negative value. The odds of becoming highly adherent is calculated by using the exponential value of the predicted cumulative logit (Table 5.9). Hence, a unit increase in baseline medication adherence score (MMAS-8) increases the odds of becoming highly adherent at follow-up after new treatment by 2.49 times $p<0.001$ (Table 5.9), while a unit increase in age increases the odds of becoming highly adherent by 1.03 times, $p=0.031$. Likewise, a unit increase in self-efficacy under difficult circumstances (SEAMS-UDC) increases the odds of becoming highly adherent after new treatment by 7.2 times, $p<0.001$, whereas a unit increase in self-efficacy under conditions of uncertainty (SEAMS-UCU) decreases the odds of becoming highly adherent after new treatment by a third, $p=0.001$. Similarly, if there is a decrease in confidence levels under difficult circumstances over time (SEAMS-UDC Change) then the odds of becoming high adherent decreases by a quarter ($p<0.001$). Finally, if individuals become less concerned over their new diabetes medicines or there is no significant

change in concerns as opposed to become more concerned over time (BMQ-Concerns Change), then this increases the odds of becoming highly adherent by 3-4 times ($p \leq 0.018$).

The weight-effect of the medicine was an important comparison in this study and it was found that those prescribed a WN medicine were more likely to be adherent at follow-up compared to those prescribed a WR medicine (Table 5.8). Therefore, the weight-effect variable was forced into the final multivariate model. However, in this case, age was not a significant predictor of high adherence, neither were the weight-effect medicines (WN, WR, WI), perhaps suggesting there is an interaction between these two explanatory predictors in relation to medication adherence (Table 5.9). As seen in Table 5.4, the weight reducing group was significantly younger than the weight neutral group ($p<0.05$), whilst age was significant predictor for those who are medium to high adherent than those who are low adherent (Table 5.10). All other predictor variable remained statistically significant and the test of parallel lines was met. Furthermore, after a sensitivity analysis controlling for other demographic and clinical variables (gender, education status, age, marital status, total medication burden, total diabetes medication burden, BMI, HbA1c), the self-efficacy for both under difficult circumstances (SEAMS-UDC) and under conditions of uncertainty (SEAMS-UCU) ($p<0.001$ and $p=0.008$ respectively), the change in confidence levels under difficult circumstances (SEAMS-UDC Change) ($p<0.001$) and the change in beliefs over concerns of potential adverse effects of medicines (BMQ-Concerns Change) ($p=0.002$) remained highly significant (results not shown). Collinearity diagnostics were checked and no issues were found (Appendix 5.15).

Tables 5.11 shows how the predicted probability of being low, medium and high adherent at follow-up changes with various predictors scores identified in multivariate analysis. For example, the probability of being high adherent, if scored highly adherent (MMAS-8) at baseline, is 61%, whereas the probability of being low adherent, when scored low at baseline, is 75%. Because the effects of the predictor variables in this multivariate model are the same across the different thresholds, according to the assumption of proportional odds (O'Connell, 2006), even though this

assumption was only met marginally (p=0.04), it can be concluded that the overall probability for being high adherent following initiation of new diabetes treatment is 28%, whereas the probability of being low adherent is 35% (Table 5.11, final row).

Table 5.11: Predicted probability for Follow-up adherence levels with various baseline scores and age for key variables from multivariate analysis

Predicted probability at various scores/ Age(yrs)	**Adherence Level Low**	**Adherence Level Medium**	**Adherence Level High**
Baseline MMAS-8<6 (Score=5.0)	0.75	0.22	0.03
Baseline MMAS-8<6 (Score=6)	0.32	0.51	0.17
MMAS-8 Score=7	0.18	0.47	0.35
MMAS-8 Score=8	0.07	0.32	0.61
Age=36	0.99	.01	0.00
Age=45	0.36	0.40	0.24
Age=55	0.23	0.39	0.38
Age=65	0.26	0.48	0.26
Age=75	0.06	0.34	0.60
Baseline SEAMS-UDC Score=2	0.95	0.04	0.01
Baseline SEAMS-UDC Score=3	0.53	0.34	0.13
Baseline SEAMS-UDC Score=4	0.13	0.46	0.41
Baseline SEAMS-UDC Score=5	0.14	0.35	0.51
Baseline SEAMS-UCU Score=2	0.52	0.32	0.15
Baseline SEAMS-UCU Score=3	0.36	0.43	0.20
Baseline SEAMS-UCU Score=4	0.29	0.46	0.25
Baseline SEAMS-UCU Score=5	0.19	0.47	0.34
BMQ-Concerns change: Increase Higher concerns	0.38	0.38	0.25
BMQ-Concerns no change	0.33	0.39	0.29
BMQ-Concerns change: Decrease Lower concerns	0.29	0.36	0.36
SEAMS-UDC change: Increased self-efficacy over time	0.31	0.36	0.33
SEAS-UDC change: Decreased self-efficacy over time	0.41	0.39	0.20
Total Predictor score	***0.35***	***0.37***	***0.28***

5.6.1.2 Predicting a change in medication adherence from baseline and change values

A univariate analysis was conducted to assess what predicted change in medication adherence over the 3-month period. Table 5.12 shows the results of the multinomial regression which uses "stable" medication adherence over 3 months as reference. The table shows only significant variables that predict medication change, the results for all other variables can be found in appendices 5.16-5.17.

Table 5.12: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the whole group

Variable	**β Decreased Adherence**	**significance**	**β Increased Adherence**	**Significance**
Single	0.201	0.735	0.000	1.0
Married	Reference		Reference	
Widowed	1.299	0.167	1.946	**0.019**
Divorced	0.488	0.476	-0.405	0.631
IMD				
20% Least Deprived	0.329	0.728	0.580	0.495
61%-80%	-20.497		-0.113	0.849
41%-60%	1.245	**0.030**	0.868	0.141
21%-40%	-0.875	0.198	-1.030	0.127
20% Most Deprived	Reference		Reference	
SIMS–AU	0.020	0.846	-0.174	**0.035**
BMQ-Overuse	0.662	**0.013**	0.647	**0.01**
BMQ-Harm	0.336	0.337	0.743	**0.027**
DiabMedSat-Burden	-0.003	0.807	-0.030	**0.012**
baseline MMAS-8	0.052	0.736	-0.532	**<0.001**
SEAMS	-0.082	0.707	-0.451	**0.026**
SEAMS-UCU	-0.040	0.841	-0.446	**0.016**
Baseline HbA1c	0.025	**0.021**	0.006	0.591
BMQ-Overuse Change				
Stronger	Reference		Reference	
No Change	0.097	0.835	0.420	0.376
Decreased	0.687	0.282	1.344	**0.026**
DiabMedSat-Burden Change				
Improved	Reference		Reference	
No Change	-0.205	0.664	-0.959	**0.023**
Decreased	0.746	0.186	-0.148	0.783
SEAMS Change				
Improved	Reference		Reference	

No Change	-0.221	0.686	-0.266	0.532
Decreased	1.080	**0.021**	-0.351	0.455
SEAMS-UDC Change				
Improved	Reference		Reference	
No Change	-0.047	0.934	-0.550	0.243
Decreased	0.533	0.239	-0.925	**0.036**
SEAMS-UCU Change				
Improved	Reference		Reference	
No Change	0.667	0.190	-0.271	0.536
Decreased	1.383	**0.006**	0.097	0.832

The final multivariate analysis (Table 5.13) showed that if individuals have a high HbA1c level and they live within the 20% least deprived boundary (as opposed to the third most deprived; i.e.-41-60%) prior to initiation of new diabetes treatment, then they are more likely to have a decrease in adherence levels at three months than remain stable. In addition, if they live within the second most deprived (21-40%) boundary (as opposed to 20% most deprived boundary) then it is less likely medication adherence levels to increase at follow-up than remain stable. If they have high adherence levels at baseline, their adherence levels are more likely to remain stable than increase at follow-up. However, medication adherence levels at 3 months are more likely to increase (than remain stable) after initiation of new treatment if individuals are widowed (as opposed to being married). Furthermore, individuals whose confidence levels in taking medicines correctly (SEAMS Change) decreased over time, then their adherence levels are more likely to decrease over time than remain stable. Whilst those individuals whose confidence in taking medicines under difficult circumstances (SEAMS-UDC Change) decreased (than improved) over time, their adherence levels are more likely to remain stable than increase over time.

The multivariate model also showed that strong beliefs that medicines are overused by doctors prior to initiation of a new diabetes medicine can either increase or decrease the adherence levels than remain stable. Table 5.7 shows that both groups who had a decrease and an increase in adherence levels over time had significantly stronger baseline beliefs about the overuse of medicines (BMQ-Overuse) compared to those who remained stable. Their beliefs also remained stronger at follow-up compared to the stable group.

Although the weight-effect of the medicine was not a significant predictor in the univariate analyses for a medication adherence change (appendix 5.16), it was forced in the final multinomial regression analysis, as it was an important comparison in this study. The results of this analyses (Table 5.13) show that the weight-effect of the medicine remained insignificant in predicting medication adherence change, whereas there was no change in any of the other variables.

Table 5.13: Multinomial Analysis predicting change in adherence over time following initiation of new diabetes medicine

	Whole Group		**Whole Group with Weight-Effect Variable**	
	Wald β (SE)	Odds Ratio (95%CI)	Wald β (SE)	Odds Ratio (95%CI)
Decreased Adherence Vs Stable Adherence				
Intercept	-7.36 (2.11)***		-7.73 (2.20)***	
Baseline MMAS-8	0.22 (0.19)	1.25 (0.87, 1.79)	0.26 (0.19)	1.29 (0.89, 1.89)
Baseline BMQ-Overuse	**0.77 (0.31)***	2.16 (1.17, 3.97)	**0.75 (0.31)***	2.12 (1.16, 3.90)
Baseline HbA1c	**0.03 (0.01)***	1.03 (1.0, 1.06)	**0.04 (0.01)***	1.04 (1.0, 1.07)
Single (Vs Married)	0.90 (0.75)	2.47 (0.57, 10.77)	0.89 (0.76)	2.43 (0.55, 10.74)
Widowed (Vs Married)	1.44 (1.07)	4.21 (0.52, 34.07)	1.48 (1.09)	4.38 (0.52, 37.30)
Divorced (Vs Married)	0.39 (0.83)	1.47 (0.29, 7.48)	0.38 (0.84)	1.46 (0.28, 7.51)
20% Least deprived (Vs 20% most deprived)	0.75 (1.15)	2.12 (0.22, 20.03)	0.75 (1.15)	2.11 (0.22, 20.03)
IMD 61-80 (Vs 20% most deprived)	-19.94 (0.0)	2.18E (2.18E-2.18E)	-19.89 (0.0)	2.31E (2.31E, 2.31E)
IMD 41-60 (Vs 20% most deprived)	**1.59 (0.67)***	4.93 (1.34, 18.12)	**1.75 (0.69)***	5.74 (1.49, 22.16)
21-40 (Vs 20% most deprived)	-1.09 (0.84)	0.34 (0.06, 1.75)	-0.92 (0.87)	0.40 (0.07, 2.18)
SEAMS Change Decrease (Vs Improvement)	**2.17 (1.03)***	8.79 (1.17, 65.92)	**2.34 (1.07)***	10.39 (1.28, 84.48)

SEAMS Change Stable (Vs Improvement	-0.06 (0.84)	0.94 (0.18, 4.90)	-0.05 (0.87)	0.95 (0.17, 5.22)
SEAMS-UDC Change Decrease (Vs Improvement)	-1.38 (1.01)	0.25 (0.03, 1.82)	-1.32 (1.04)	0.27 (0.04, 2.07)
SEAMS UDC Stable (Vs Improvement)	-0.83 (0.87)	0.44 (0.08, 2.40)	-0.80 (0.88)	0.45 (0.08, 2.50)
Weight Neutral (Vs Weight Reducing)			-0.54 (0.67)	0.58 (0.16, 2.18)
Weight Increasing (Vs Weight Reducing)			-0.50 (0.64)	0.61 (0.17, 2.11)
Increased Adherence Vs Stable Adherence				
Intercept	1.19 (1.94)		1.33 (2.00)	
Baseline MMAS-8	**-0.65 (0.17)*** **	0.52 (0.37, 0.73)	**-0.68 (0.18)*** **	0.51 (0.36, 0.72)
Baseline BMQ-Overuse	**0.69 (0.31)***	1.99 (1.08, 3.67)	**0.68 (0.32)***	1.97 (1.05, 3.67)
Baseline HbA1c	0.01 (0.01)	1.00 (0.98, 1.03)	0.01 (0.02)	1.00 (0.97, 1.03)
Single (Vs Married)	-0.05 (0.77)	0.95 (0.21, 4.33)	0.03 (0.78)	1.03 (0.23, 4.74)
Widowed (Vs Married)	**2.55 (0.98)****	12.80 (1.87, 87.67)	**2.48 (1.00)***	11.88 (1.68, 84.23)
Divorced (Vs Married)	-0.75 (1.10)	0.47 (0.06, 4.11)	-0.67 (1.08)	0.51 (0.06, 4.25)
IMD 20% least deprived (Vs 20% least deprived)	0.86 (1.08)	2.35 (0.28, 19.61)	0.86 (1.10)	2.37 (0.28, 20.28)
IMD 61-80 (Vs 20% most deprived)	0.43 (0.77)	1.53 (0.34, 6.90)	0.34 (0.80)	1.40 (0.29, 6.75)
IMD 41-60	0.93 (0.76)	2.53 (0.57, 11.19)	0.94 (0.77)	2.56 (0.56, 11.63)

(Vs 20% most deprived)				
IMD 21-40 (Vs 20% most deprived)	**-2.02 (0.94)***	0.13 (0.02, 0.83)	**-2.08 (0.97)***	0.13 (0.02, 0.83)
SEAMS Change Decrease (Vs Improvement)	1.87 (1.01)	6.51 (0.89, 47.36)	1.87 (1.07)	6.49 (0.80, 53.02)
SEAMS Change Stable (Vs Improvement	0.68 (0.71)	1.98 (0.49, 7.99)	0.59 (0.75)	1.81 (0.42, 7.83)
SEAMS-UDC Change Decrease (Vs Improvement)	**-2.46 (0.96)***	0.09 (0.01, 0.56)	**-2.58 (0.99)****	0.08 (0.01, 0.53)
SEAMS UDC Stable (Vs Improvement)	-0.56 (0.74)	0.57 (0.13, 2.45)	-0.59 (0.75)	0.55 (0.13, 2.42)
Weight Neutral (Vs Weight Reducing)			0.94 (0.60)	2.55 (0.79, 8.27)
Weight Increasing (Vs Weight Reducing)			0.42 (0.66)	1.52 (0.42, 5.55)
Model Statistics	Nagelkerke R^2=0.50; Model x^2 (28)=92.16, p<0.001, Goodness of Fit (292)= 279.301, 68% Correct		Nagelkerke R^2=0.52; Model x^2 (32)= 96.68, p<0.001, Goodness of Fit (288)= 276.574, 65% Correct	

*p<0.05, **p<0.01, ***p<0.001

5.6.2 Weight-Effect Groups

A similar approach to identifying significant predictors was conducted for each weight-effect group.

5.6.2.1 Weight Reducing Group

As the WR group is a small group (n=68), multivariate regression analysis was not performed as the data are not sufficient. The following sections present the univariate analysis for both predicting medication adherence and a change in medications adherence levels at follow-up.

5.6.2.1.1 Predicting medication adherence at 3-month follow-up from baseline and change values

The univariate ordinal analysis (Table 5.14) indicated that for the WR group, the older individuals are, the less concerns they have about how harmful or addictive are medicines (BMQ-Harm) and, if these beliefs remain stable over time (BMQ-Harm Change), they are more like to be adherent after initiation of a new medicine. Furthermore, individuals already highly adherent with their medicines (baseline MMAS-8) and confident in taking medicines correctly (SEAMS); particularly under difficult circumstances (SEAMS-UDC) and under conditions of uncertainty (SEAMS-UCU), then for each individual aspect, they are more like to be adherent after initiation of a new medicine.

Table 5.14: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the WR group

Variable	β	significance	Test for parallelism
Age	0.072	0.008	0.620
BMQ-Harm	-1.132	0.012	0.408
BMQ-Harm Change	-1.666	0.019	0.064
Baseline MMAS-8	1.104	<0.001	0.415
SEAMS	0.999	0.001	0.829
SEAMS-UDC	1.521	<0.001	0.779
SEAMS-UCU	0.544	0.024	0.870

5.6.2.1.2 Predicting a change in medication adherence from baseline and change values

The univariate multinomial analysis (Table 5.15) which examined what predicts a change in adherence levels showed that for women, adherence levels are more likely to decrease over time than remain stable, and individuals with beliefs that medicines are harmful (baseline BMQ-Harm), are more likely to either decreased or increase their adherence levels. Individuals who are highly satisfied with their diabetes medicines overall (DiabMedSat), including with how burdensome they are (DiabMedSat-Burden) and medicine related symptoms (DiabMedSat-Symptoms) prior to initiation of a new treatment then their adherence levels are more likely to remain stable than increase.

Individuals satisfied with the impact of their medicine on their weight (TRIM-Wt-WM) prior to a new medicine are more likely to decrease their adherence levels over time than remain stable. Individuals satisfied with the impact of their diabetes medicines on their psychological health (TRIM-Wt-PH), and who are confident in taking medication under conditions of uncertainty (SEAMS-UCU) prior to initiation of a new treatment, then their adherence levels are more likely to remain stable than increase. However, individuals whose beliefs about prescribed medicines are overused by doctors (BMQ-Overuse Change) decrease over time then their adherence levels will increase over time than remain stable.

Table 5.15: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the WR group

Variable	**β Decreased Adherence**	**significance**	**β Increased Adherence**	**Significance**
Women	Reference		Reference	
Men	-1.792	**0.032**	-0.916	0.136
BMQ-Overuse Change				
Stronger	Reference		Reference	
Stable	-0.379	0.609	18.466	
Decreased	0.118	0.911	19.299	**<0.001**
BMQ-Harm	1.352	**0.032**	1.293	**0.039**
DiabMedSat	-0.003	0.907	-0.064	**0.012**

DiabMedSat- Burden	0.001	0.957	-0.047	**0.035**
DiabMedSat-Symptom	-0.018	0.324	-0.059	**0.003**
TRIM-Wt-WM	0.038	**0.032**	-0.013	0.524
TRIM-Wt-PH	0.004	0.731	-0.023	**0.045**
SEAMS-UCU	-0.330	0.310	-0.775	**0.026**

5.6.2.2 Weight Neutral Group

As the WN group is a small group (n=58), multivariate regression analysis was not performed as the data are not sufficient. The following sections present the univariate analysis for both predicting medication adherence and a change in medications adherence levels at follow-up.

5.6.2.2.1 Predicting medication adherence at 3-month follow-up from baseline and change values

The univariate analysis for the WN group (Table 5.16) indicated that individuals highly adherent with their medicines (baseline MMAS-8) and confident in taking them correctly (SEAMS); particularly under difficult circumstances (SEAMS-UDC) and under conditions of uncertainty (SEAMS-UCU), then for each individual aspect, they are more like to be adherent after initiation of a new medicine. Individuals who have lower HbA1c at baseline, have less amount of diabetes medications at follow–up and have a positive change in their HbA1c levels (HbA1c Change) at follow-up, as well as their expectations are exceeded by experience (EITQ-PITQ Change) (instead of just being met) then they are more likely to be adherent.

Table 5.16: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the WN group

Variable	**β**	**significance**	**Test for parallelism**
Baseline HbA1c	-0.046	0.004	0.405
HbA1c Change	0.053	0.026	0.155
Baseline MMAS-8	0.895	0.001	0.242
SEAMS	0.769	0.014	0.215
SEAMS-UDC	0.766	0.02	0.442
SEAMS-UCU	0.633	0.018	0.082
Diabetes Medication Burden F-up	-0.972	0.009	0.663

Expectation Perception Change (EITQ-PITQ)			0.266
Expectations Unmet	-.135	.815	
Expectations Met	-1.362	**.042**	
Expectations Exceeded by Experience	Reference		

5.6.2.2.2 Predicting a change in medication adherence from baseline and change values

The univariate analysis examined what predicts change (Table 5.17) showed that for individuals who are married or are single than widowed, then their adherence levels are more likely to decrease over time than remain stable. Those in full-time employment or unemployed, compared to those on benefits (reference "other"), are more likely to increase adherence levels than remain stable over time. Those with high concerns that prescribed medicines are overused by doctors (BMQ-Overuse) and strong beliefs that medicines are harmful (BMQ-Harm) prior to new treatment are more likely to increase adherence levels than remain stable over time. On the other hand, individuals with strong beliefs about the benefits of medicines (BMQ-Benefits) prior to new treatment are more likely to remain stable than increase adherence levels over time. Those who are highly satisfied with diabetes medicines (DiabMedSat) prior to new treatment, then, are more likely to have stable adherence levels than increase over time. Individuals with high adherence levels (Baseline MMAs-8) before a start of a new treatment are more likely to remain stable than their adherence levels increased. Individuals whom satisfaction levels with diabetes medicines remain stable over time (than improve) (DiabMedSat Change) and, those whose satisfaction with symptoms remains stable than improve (DiabMedSat-Symptoms Change), are more likely to remain stable in their adherence levels than increase.

Table 5.17: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the WN group

Variable	β Decreased Adherence	significance	β Increased Adherence	Significance
Single	18.081	**<0.001**	-1.099	0.472
Married	18.081	**<0.001**	-.223	0.835
Widowed	Reference		Reference	
Divorced	19.180		-19.086	0.998
Full time	0.00	1.0	19.185	**<0.001**
Part time	-19.260		-0.545	1.0
Unemployed	-0.693	0.638	17.393	**<0.001**
Other	Reference		Reference	
Retired	-1.540	0.137	17.845	
BMQ-Overuse	0.993	0.152	1.369	**0.024**
BMQ-Harm	-0.247	0.759	1.953	**0.019**
BMQ-Benefits	-0.730	0.445	-2.029	**0.027**
DiabMedSat	-0.034	0.202	-0.045	**0.05**
DiabMedSat Change				
Improved	Reference		Reference	
Stable	-1.504	0.154	-1.792	**0.048**
Decreased	-1.386	0.191	-1.674	0.067
DiabMedSat Symptoms Change				
Improved	Reference		Reference	
Stable	-1.061	0.341	-2.719	**0.008**
Decreased	-0.288	0.803	-1.030	0.262
Baseline MMAS-8	0.267	0.540	-0.727	**0.011**
BMI Follow-up	0.194	**0.048**	0.016	0.811

5.6.2.3 Weight Increasing Group

As the WI group is a small group (n=64), multivariate regression analysis was not performed as the data are not sufficient. The following sections present the univariate analysis for both predicting medication adherence and a change in medications adherence levels at follow-up.

5.6.2.3.1 Predicting medication adherence at 3-month follow-up from baseline and change values

The univariate analysis for the WI group (Table 5.18) indicated that, individuals who are already highly adherent with their medicines (Baseline MMAS-8), satisfied with the information they received about a new medicine in relation to potential problems with it (SIMS-PPM), their satisfaction with the impact of the new medicine on daily life (TRIM-Wt-DL) improves (as opposed to decrease, or remain stable) and the impact of their diabetes medicines on their psychological health at baseline (TRIM-Wt-PH) is high, then for each individual aspect, they are more like to be highly adherent after initiation of a new medicine. If beliefs about necessity (BMQ-Necessity) remain stable over time (as opposed to become stronger), and if beliefs about medication benefits (BMQ-Benefits) decrease (as opposed to become stronger) then individuals are more likely to be adherent. Individuals with high self-efficacy (SEAMS) at baseline particularly under difficult circumstances (SEAMS-UDC), are more likely to be adherent over time. Individuals whom self-efficacy, particularly with under conditions of uncertainty (SEAMS-UCU), improves over time (as opposed to decrease), are more likely to be adherent. However, those whom self-efficacy under difficult circumstances (SEAMS-UDC) remains stable as opposed to improve, then they are more likely to be adherent. All baseline and follow-up scores indicate that the WI group had strong beliefs about necessity and benefits of medicines, as well as were very confident with taking their medicines under difficult circumstances (Table 5.6).

Table 5.18: Ordinal Regression using single Baseline and Change Predictors for follow-up high medication adherence level for the WI group

Variable	**β**	**significance**	**Test for parallelism**
Baseline MMAS-8	1.055	<0.001	0.643
SIMS-PPM	0.138	0.046	0.770
TRIM-Wt-DL Change **Decreased** **Stable** Improved	 -2.315 -1.257 Reference	 **0.012** **0.049**	0.200
TRIM-Wt-PH	0.021	0.021	0.627

BMQ-Necessity Change			0.942
Decreased	1.148	0.003	
Stable	1.420	**0.203**	
Stronger	Reference		
BMQ-Benefits Change			0.561
Decreased	2.527	.102	
Stable	0.893	**.036**	
Stronger	Reference		
SEAMS	0.713	0.008	0.033
SEAMS-UDC	0.834	0.002	0.034
SEAMS Change			0.052
Decreased	-1.649	**.007**	
Stable	.108	.855	
Improved	Reference		
SEAMS- UCU Change			0.036
Decreased	-1.797	**0.004**	
Stable	-0.503	0.392	
Improved	Reference		
SEAMS- UDC Change			0.037
Decreased	-.590	0.292	
Stable	2.355	**0.001**	
Improved	Reference		

5.6.2.3.2 Predicting a change in medication adherence from baseline and change values

The univariate analysis examining what predicts change in adherence levels over time (Table 5.19) showed that individuals who live in the first [20%], or the second [21-40%] or the third most deprived area [41-60%] than in the fifth deprived area (or 20% least deprived area) then their adherence levels are more likely to remain stable than increase. Individuals with high concerns over the potential adverse effects of the medicine (BMQ-Concerns) prior to starting a new treatment are more likely to remain stable in their adherence levels than increase.

Individuals with strong beliefs about the benefits of taking medicines (BMQ-Benefits), are more likely to remain stable in their adherence levels than decrease. Those satisfied with the impact of their diabetes medicines on their weight (TRIM-Wt-WM) prior to initiation of a new medicine are more likely to increase their adherence levels than remain stable. Individuals highly adherent from the start (Baseline MMAS-8) are

less likely to increase their adherence levels over time than remain stable. Individuals taking many diabetes medicines prior to initiation of a new treatment (baseline medication burden) are more likely to remain stable in their adherence levels than increase).

Those whose satisfaction with diabetes medicines decrease over time (DiabMedSat Change) are more likely to decrease their adherence levels over time. Individuals whose satisfaction levels with the impact of their medicines on psychological health (TRIM-Wt-PH Change) remains stable over time than improve their adherence levels are more likely to remain stable than decrease. Those whose confidence levels decreased over time (SEAMS Change), adherence levels are more likely to decrease over time than remain stable, particularly for under conditions of uncertainty (SEAMS-UCU Change).

Table 5.19: Multinomial Regression using single Baseline and Change Predictors for medication adherence change (MMAS-8 Change) at follow-up for the WI group

Variable	**β Decreased Adherence**	**significance**	**β Increased Adherence**	**Significance**
IMD				
20% Least Deprived	0.057	1.0	-18.630	**<0.001**
61%-80%	-0.491	1.0	-19.061	**<0.001**
41%-60%	0.830	1.0	-18.145	**<0.001**
21%-40%	-16.501	0.999	-18.432	
20% Most Deprived	Reference		Reference	
BMQ-Concerns	-0.603	0.195	-0.938	**0.049**
BMQ-Benefits	-1.569	**0.043**	-0.720	0.298
Trim-Wt-WM	0.014	0.322	0.034	**0.026**
DiabMedSat Change				
Improved	Reference		Reference	
Stable	0.069	0.935	-0.154	0.837
Decreased	1.764	**0.036**	-0.405	0.657
baseline MMAS-8	0.211	0.432	-0.580	**0.010**
Baseline Diabetes Medication Burden	-0.473	0.202	-0.740	**0.048**
HbA1c Follow-up	0.038	**0.048**	0.017	0.371
Trim-Wt-PH Change				
Improved	Reference		Reference	

Stable	-1.686	**0.040**	-0.811	0.287
Decreased	0.511	0.583	0.511	0.597
SEAMS Change				
Improved	Reference		Reference	
Stable	1.022	0.284	-0.231	0.756
Decreased	1.861	**0.044**	0.203	0.785
SEAMS-UCU Change				
Improved	Reference		Reference	
Stable	1.792	0.125	-0.693	0.361
Decreased	2.708	**0.021**	0.223	0.765

5.7. Summary

Participants were generally significantly more positive with their new treatment at 3-months follow-up. Despite one third of the group had their expectations unmet with their new treatment, on the whole, they were more satisfied with the information they have received about their new medicine particularly with the potential problems with medicines (side effects etc.). Therefore, they had less concerns about the potential adverse effects of their new medicine and, they were more satisfied overall with their treatment; including how efficacious and less burdensome this treatment has been, and how it had not impacted their daily life or weight management. Yet, as time progressed trends of ambivalence towards their new treatment was found when inspecting individual scale items. At three months, they had better quality of life in relation to their weight and weight loss. Although their confidence in taking their new medicine correctly only significantly improved for under conditions of uncertainty, they still remained largely low to medium adherent (70%). As it appears, the experience of starting a new treatment and experiencing it, did not affect their beliefs about the necessity and benefits of their diabetes treatment. On the other hand, they had significantly stronger beliefs that prescribed medicines are overused by doctors.

The WR group appears to have the most benefit and positive outcomes of the treatment they have received in this study. The difference in the outcomes between the WR group and the other two groups (WI and WN) perhaps reflected the support they received for the duration of the study or the type of new treatment they were prescribed.

Although unmodifiable factors such as social and marital status appear to have an influence on adherence, the beliefs about medicines (Concerns, Overuse, Harm and Benefits), and self-efficacy in taking medicines correctly are making the most impact on medication adherence levels following initiation of new treatment for T2D. Individuals are seven times more likely to become highly adherent if they are confident in taking a new medicine correctly under difficult circumstances and they are 3-4 times more likely to become highly adherent if they had less concerns about their treatment over time. Moreover, if individuals are highly adherent prior to starting new treatment for their diabetes they are almost 2.5 times more likely to be highly adherent over time, and if they are initiated a treatment before their HbA1c levels reach 75mmol/mol (median HbA1c level for those who improved adherence over time) then their adherence levels are less likely to decrease. On the other hand, if individuals' confidence levels in taking their new medicine correctly decreases over time, then their adherence levels are twice as likely to decrease.

The next chapter will present the findings from the qualitative interviews. The quantitative findings will be further discussed in chapter 7 with the qualitative findings.

CHAPTER SIX: INTERVIEW RESULTS

6.1 Introduction

This chapter presents the results of the analysis of the interviews (pre and post new diabetes treatment) collected in this study. It starts with presentation of the response rates to interview participation, and key demographic characteristics of the participants who completed both interviews. In addition, each section then presents the concepts and themes identified during the analysis. These sections aim to answer two of the research questions:

1. How do the expectations, beliefs and attitudes of people with T2D towards different diabetes treatments that either promote weight loss, are weight neutral or result in weight gain, change over time?

And:

2. What type(s) of intervention(s) promoting treatment options, focusing on effects on body weight, are acceptable to patients in order to increase their understanding of their diabetes treatment and improve adherence?

A summary of the key findings is provided at the end of the chapter.

6.2 Interview Participants

In total, 29 participants completed the first interview and 24 completed the second interview, representing almost 12% of the total sample who completed the questionnaires. Two participants, who did not complete the second interview, did not start their new medicine, and therefore were withdrawn from the study. Three participants, although they completed their second questionnaire, withdrew from the second interview. The final interview sample (n=24) was recruited from both primary and secondary care (Figure 6.1). Whilst the sample contained less from the secondary care (n=5) and the majority from Sefton PCT (n=14), it remained representative of the whole group and, therefore, there was no selection bias. The average interview lasted 41 minutes (range 20-78 minutes).

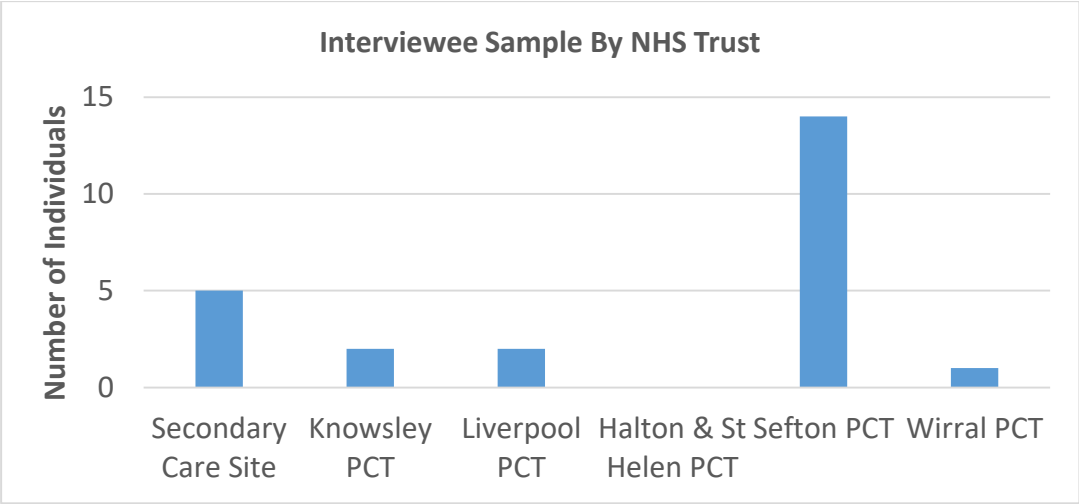

Figure 6.1: Number of participants completing both interviews in each NHS Trust in primary and secondary care

Table 6.1 presents the demographic and clinical characteristics of participants who completed both interviews (n=24). Of those participants who completed the interviews, three had already started taking their medicine prior to their first interview, but they had done so within 24hrs of completing the first questionnaire. Furthermore, at the time of the second interview, only one participant had not started their new medicine, but instead there was an increase in dose of their current medicine (insulin). One participant had changed their new medicine (exenatide) to a medicine in the same class (liraglutide). The interview sample provided a good representation of the questionnaire sample, both in terms of demographic and clinical characteristics, as well as questionnaire scale scores (see Appendix 6.1 and Table 5.1-5.2 for comparison). The results of the questionnaires (Appendix 6.1) were not reviewed prior to interviews to minimise any of the effects that might incur to the patient interview. Data saturation was reached after interviewing these participants, through an iterative process of reviewing transcripts and no new coding or themes emerging (Holloway & Wheeler, 2010).

Table 6.1: Key Characteristics of interview participants (baseline and change data)

Pseudonyms	HCD location	Lives with	Employment status	Age (yrs)	BMI (kg/m^2)	HbA1c (mmol/mol)	T2D Duration yrs	T2D complications	Medicine Type Experienced	New Medicine (Class, Weight-effect)	Total no of meds (all meds, T2D meds)	Adherent (L,M,H)	Adherence Change	HbA1c Change	Weight Change
Keith	SCDC	wife	Retired	63	41	71	12	Neuropathy	Tablets	Exenatide, WR	10, 3	L	↑	N/A	↓
Teresa	SCDC	husband	Retired	63	36	73	19	CVD, ACR	Tablets injections	Exenatide ER, WR	8, 3	M	↑	N/A	↓
Robert	GP	family	Full time	52	32	77	2	None	tablets	Gliclazide, WI	3, 1	M	↑	↓	↑
Kelly+	MDT	family	Un-employed	55	52	54	9	None	tablets	Exenatide, WR	~15, 1	L	↑	N/A	↓
Andrew	MDT	wife	Retired	72	43	83	8	Nephropathy	tablets	Gliclazide, WI	8, 2	H	↔	↓	↑
Vanessa *	SCDC	alone	Un-employed	49	44	84	9	None	Tablets injections inhalers	Liraglutide, WR	20, 3	L	↑	↑	↓
Julie	MDT	husband	Part time	55	36	86	10	None	tablets	Liraglutide, WR	6, 3	M	↑	↓	↓
Edward	MDT	alone	Retired	64	29	92	6.5	Neuropathy Nephropathy Retinopathy	Tablets, injections	Insulin BD, WI	7, 3	L	↑	↓	↑

Daniel	GP	alone	Un-employed	57	32	60	2wks	None	tablets	Metformin, WN	6,0	N/A	N/A	↓	↓
Karen	MDT	family	Full time	46	36	65	2	None	Tablets inhalers	Liraglutide, WR	6, 2	L	↔	↓	↓
Oliver	SCDC	wife	Full time	49	30	98	10	None	tablets	Liraglutide, WR	4, 3	L	↓	↓	↓
Gareth	MDT	partner	Retired	66	28	58	13	None	tablets	Linaglitpin, WN	7, 3	L	↑	↓	↓
Patrick	MDT	alone	Full time	58	42	68	7	Neuropathy Nephropathy Retinopathy	Tablets injections	Linagliptin, WN	16, 2	L	↓	N/A	↓
David	MDT	wife	Retired	76	34	97	1	CVD	tablets	Metformin MR, WN	7, 1	M	↑	↓	↓
James	MDT	wife	Retired	72	31	63	12	None	tablets	Sitagliptin, WN	5, 2	M	↑	↓	↓
Irene	MDT	husband	Retired	71	39	79	19	CVD	tablets	Liraglutide, WR	12, 2	M	↓	↓	↑
Kate**	MDT	son	Un-employed	49	33	110	11	None	Tablets injections	Sitagliptin, WN	3, 2	L	↔	↓	↑
Linda	MDT	family	Retired	64	43	52	10	Neuropathy Retinopathy	tablets	Dapagliflozin, WR	8, 2	M	↓	↓	↓
Alison+	MDT	son	Part time	70	37	87	10	Neuropathy Nephropathy	Tablets, injections	Exenatide, WR	~6, 2	H	↔	↓	↓
Angela	MDT	alone	Retired	74	30	102	13	None	Tablets injections	Insulin BD, WI	6, 4	M	↑	↔	↑
Christo-pher	MDT	family	Retired	57	31	93	12	CVD, ACR Neuropathy	tablets	Insulin OD, WI	9, 2	H	↓	↓	↑

Philip	MDT	wife	Retired	66	35	66	8	CVD Nephropathy	Tablets injections	Exenatide ER, WR	~18, 2	N/A	N/A	↑	↓
Elizabeth	SCDC	husband	Part time	66	38	78	17	Retinopathy	Tablets injections	Insulin BD, WI	14, 1	H	↔	↑	N/A
Adam	SCDC	wife	Retired	65	28	73	13	CVD Nephropathy	tablets	Insulin OD, WI	10, 3	M	↔	↓	↑

HCD=Health Care Delivery, MDT=Multidisciplinary Team, ACR=Albumin- Creatinine Ratio a measurement of microalbuminuria, Adherence Level: L=Low, M=Medium, H=High, HbA1c and Weight Change: ↔=stable, ↑=Increase, ↓=Decrease, N/A=non-applicable due to missing data *Vanessa started at the same time Levemir (once daily insulin) but completed questionnaires based on Liraglutide. Her perceptions on both medicines were explored during the interviews. ** Kate never started sitagliptin, instead her insulin dose and frequency of injections increased. + Alison and Kelly reported type and/or number of medicines taken, so total number was estimated as there were not accurate clinical records at time of study.

6.3 Central Themes

Analysis of the interview transcripts identified the following central themes:

- Diabetes, diabetes medicines and factors influencing perceptions of severity (section 6.3.1)
- Body weight (section 6.3.2)
- Beliefs and perceptions about medicines (section 6.3.3)
- Experience of taking medicines (section 6.3.4) and emotional impact (section 6.3.5)
- Routine and coping mechanisms (section 6.3.6)
- Perseverance and compromise with medicines (section 6.3.7)
- Aspects of helpful and unhelpful support in diabetes management (section 3.6.8)

The themes presented here follow the trajectory of the participants' experiences from when a diagnosis of T2D was confirmed to being prescribed their new medicine(s). This encompasses their understanding of managing their T2D and body weight; their experiences of taking diabetes (and where appropriate other) medications; their beliefs about their prescribed medicines and their perceptions of their effectiveness; and the strategies of adapting (or not) to their prescribed medication. Participants' reflections on their experiences of the support they received for managing their diabetes and their recommendations for service improvement are also presented. The themes are explored separately. Individual participants' key changes between their two interviews can be found in Appendix 6.2. Participants' names have been changed to protect their anonymity. Participants' new pseudonyms are included after each quote, which is tagged with interview round one or two i.e. I1 or I2. The quotes in the following sections aim to give a fair representation of the data.

6.3.1 My Type 2 Diabetes and my medicines

6.3.1.1 Diabetes understanding

Most of participants reported getting diagnosed with T2D by "*accident*" following an infection or other presenting symptoms or a routine test at their GP practice, hospital or opticians. Out of all the participants, even those who did not explain the details of their diagnosis, almost half either had a parent and/or sibling who had T2D, and few had a son, a daughter or a cousin with diabetes. Despite the relative link with diabetes, only a few of them described "*genes*" as a factor for having diabetes. Other reasons for having diabetes were being overweight, lifestyle and age, but most of them did not provide any explanation.

While diabetes was regarded as a serious/"*killer"* disease by all, there were different elements to its description. Diabetes was described as a "*prolific*", but "*you can't catch it*" kind of disease. Although it is a "*silent*" and "*invisible*" condition, it can have an "*aggressive form*", most commonly referring to limb amputations and blindness, with few participants mentioning complications such as heart disease/stroke and diabetic coma (associated with either low or high blood glucose control). Hence, in that sense, it can be "*chronic*" and "*progressive*", but equally an "*inconvenience*", "*a life sentence*" and "*a source of by-products*" such as having high cholesterol, blood pressure and other related conditions. Physically having diabetes means "*[body] organs [are] not functioning*" and emotionally "*body lets me down*" and "*a disease not nice to have*".

6.3.1.2. Perceptions of Blood Glucose and Self-monitoring

Participants regularly made comments about their blood glucose, and their effects on their body when these were either high or low. "*Early warning signs*", when glucose was high, included headaches, feeling "*dizzy*", "*tired*" and "*sleep a lot*", whereas signs when glucose was low included "*shaking like a leaf*", "*queasy feeling in stomach*", body feeling "*weak*", sweating, feeling "*hot*", getting "*agitated*", waking up at night, and a feeling that you "*can't put your finger on it*" or "*something is not quite right*". Although, some participants reported they, too, had headaches, dizziness and tiredness as a result of low blood glucose.

Also, participants discussed actual blood glucose figures and whether they felt these were high, low, stable or unstable. High blood glucose levels were generally in double figures. Most commonly these were reported as anything over 10, but if they were above 20, they were described as "*too high*", "*miles"*, "*dangerously*", or "*sky*" high. Whereas, figures below four were considered low. For example, Elizabeth who experienced blood glucose of 3.1 described it as "*extremely low*". Some participants reported their blood glucose levels were "*all over the place*" or unstable, as Andrew's quote demonstrates:

"And recently my blood sugar has been up and down, like this morning it was 12-something, that's even before I had my breakfast…. And I'm doing nothing different, but it's just going up. I mean it's 15, 16 sometimes and it shouldn't be". (I1)

They all understood that there are acceptable levels for their blood glucose, although not all mentioned what these were. A few participants provided a range, which was between four to seven, or four to eight, whereas, Adam and Edward discussed blood glucose as having to be in "*single figures*". Nevertheless, participants had their own perceptions of what was acceptable for them, for example Kelly said "*But I mean I took my blood sugar today and it was 7.7, which isn't particularly high, but it is high for me*" (I2); whereas Kate said: "*I feel fine, you know, where they say it's got to be under five my sugars or seven, mine's always sort of like 11 or 13 around that, and I feel fine*"(I1). On the other hand, Angela, whose readings were always above 6, said: "*you see I've just taken my reading just before lunch and it was 4.3. Well that's low*" (I2), and Adam who experienced blood glucose of 3.4 said he felt fine even though he knew this figure was low. Keith, on the other hand, adopted his wife's interpretation of glucose levels as he explains in this quote:

"*my wife, she takes insulin and she does her blood sugars a couple of times a day, and over the years if she, if it's five or under, she will not go to bed. Now if it stays about eight, nine, ten, she'll go to bed. Now that's, as she said to me, if it's going sky high,*

like 14 or 15, there's something wrong, or if it goes below five there's something wrong, but say between five and ten or 11, you should be all right." (I2)

During the interview participants provided a number of factors that could influence their blood glucose to go high or low, and how they coped with hypo/hyperglycaemia, as figure 6.2 demonstrates.

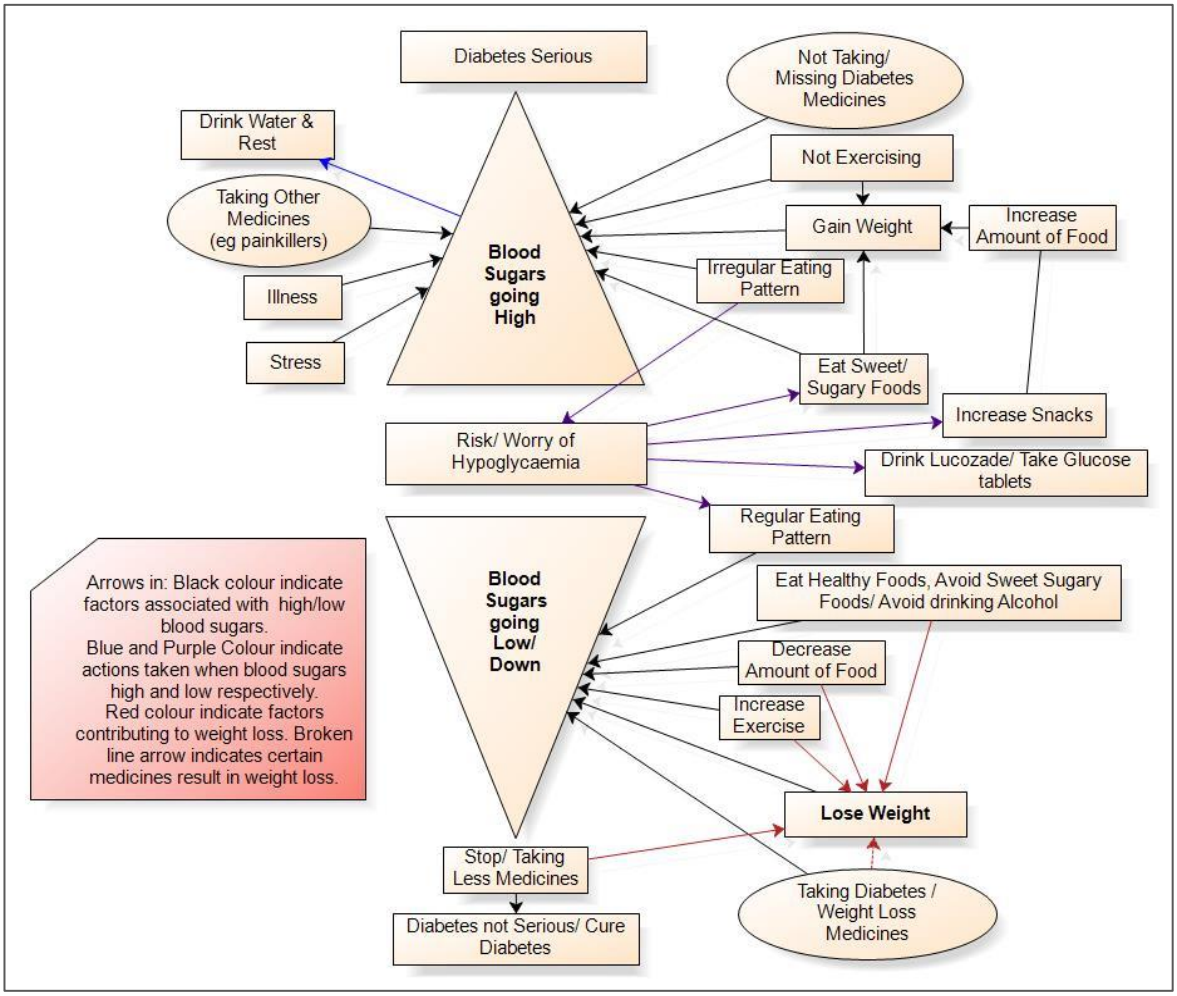

Figure 6.2: Participants' perceptions of factors affecting blood glucose

Very few of the participants were relying solely on HbA1c testing for assessing their diabetes control, whereas the rest of the participants were also familiar with the blood glucose monitor but the frequency of testing their blood glucose varied from person to person. For some participants, SMBG provided reassurance that they could identify certain foods that could cause blood glucose levels to go high, as David explains:

"*I've found if I have a treat, like a jam doughnut, I know what's going to happen when I do my bloods, it's going to go up. So what I've done, I've just got to say no to any sweet stuff, no, none at all*." (David, I2)

Whereas, Adam prior to starting his new medicine (Insulin) found that "*while I was on holiday I treat myself [to apple crumble and custard], and my blood sugars weren't that much different so I wasn't that bothered, because I take my blood sugars every day*". (I1)

Also, SMBG was used by others when symptomatic to ascertain whether their symptoms or actions resulted in high or low blood glucose, whereas Karen said: "*I don't test myself on a daily basis so I wouldn't know if there was any difference really [in my blood sugars]*"(I2), and Julie suggested that not doing the SMBG regularly is like "*head in the sand business, isn't it, because you don't know if you're up, you don't know if you're down*". (I1)

Some participants were aware that their blood glucose had gone *"progressively high"* or "*out of control*", but still, did not monitor their glucose regularly and indicated they felt fine, as the following quotes describe:

"*I don't do it [SMBG] often to be fair because I've had it so long now, my diet's always the same as such, you know, I don't really help myself so I sort of know. I don't get any highs or lows as such, like I never feel anything. I just feel normal no matter what I do.*" (Oliver, I1)

"*But I was doing it twice a week and then they [diabetes staff] said well just do it once a week because… I don't like doing it anyway, so….even doing the blood test I know it's vital but I just hate doing it because it reminds me I've got diabetes and why should I be doing this when I know I'm okay"* (James, I2)

Yet, those participants who were SMBG twice a day or more, often described that they could not rationalise why their glucose levels were either high or "*up and down*", despite not making any changes to their diet, eating patterns or their lifestyle in general.

"*Before my blood sugars were a bit erratic, I was sort of getting six to eight of a morning and the same at lunchtime, but just before the evening meal it was going up to 13 or something. I wasn't eating anything mid-afternoon, I was only having the one sandwich at lunchtime, so no one could see why this was happening."* (Patrick, I2)

Nevertheless, despite the bewilderment by their readings, most of them provided some explanation as to why this was happening, such as stress or illness (Figure 7.2). However, Angela, like others who started on insulin as their new medicine, found that "*It seemed to take a long time to kick in and my readings were very high. But just in the last couple of weeks the readings are so much better, the last say three weeks…"* Therefore, she suggested "*it just took some time to change from my old insulin to my new [insulin regime]*" (I2). This belief was reinforced by HPs who told participants that it could take *months* (Adam, I2) or a *year* (Christopher, I2) before they see any difference in their blood glucose with insulin treatment. Nevertheless, Adam also suggested "*But I've been without two tablets, a water tablet and a cholesterol tablet, and I don't know whether because I've done without them for a week…"* his blood glucose levels have "*gone quite good*" (I2).

On the other hand, Elizabeth, alluded that her husband said "*you wonder whether you've hit a fatty patch there and it's not really going through.",* hence the high blood glucose readings *"…could even be the way [insulin is] going in".* (I2). A belief, also, shared by Philip.

However, SMBG led to negative feelings of frustration, regardless of participants' effort to control their blood glucose. For example, Christopher said:

"It's down heartening when you think, well I think, I've eaten the right things doing this, then you get a 14, and you think where did that come from?" (I2).

Furthermore, when he was advised to self–monitor his blood glucose more often, as a result of initiating insulin, he said:

"*What I got fed up with was the pin pricks in your fingers, I was doing it, like twice a day every day for a month, which is a bit of a pain to be honest. You think, oh shall we go out and have say a pub lunch, oh I can't I've got to do my bloods, because there's got to be a certain gap which I found irritating, annoying really. Because you're using like, in one month I've used 50 strips of testing strips. So that was getting on my nerves a bit I must admit…*" (I2)

6.3.1.3 Diabetes Treatment

Although the first line of treatment for T2D is through lifestyle changes, very few participants stated that they started with exercise and diet control. Although most of the participants said they used to be more active when they were younger or when they were in full-time work, very few participants reported currently doing regular physical activity. Most of them suggested they struggled to engage in exercise because of their lifestyle, their body weight or other health conditions. Some of them said that when it is spring/summer they find it easier to be more active, like gardening, cycling and going out for walks.

Nevertheless, as a result of their diagnosis, some people had to think about making changes to their diet; most commonly referring to avoiding sugar and sweet foods. Other dietary changes included reducing/cutting out alcohol intake and trying to have regular and smaller meals throughout the day. Conversely, only very few people said they were already eating quite healthy at the time of the diagnosis, as Adam explained when his doctor asked about his diet: "*… when he realised what my diet was, I was on a better diet than a diabetic's on, because I didn't eat chips and only mainly ate meat and veg, cereal of a morning and things like that. So I didn't have a problem with adjusting diet-wise because I was already on that type of diet.*" (I1)

Yet, Daniel, who recently had attended a diabetes course, at the second interview said: "*I always thought I had a healthy diet but obviously I wasn't because, but I do tend now to cut out a lot of chocolates, biscuits. I didn't eat a lot of the bacon, you know, but I've more or less cut them out now. I wasn't a great eater of them but I've cut you know like. And I always had brown bread but the last nine months I've tended to have, I'm tending to go back on white bread for the first time in years. …but I've cut that all out again, gone back onto brown bread. But I'm not eating half as much as what I used to*." (I2)

Despite being aware of the dietary changes needed, many participants said they are "*not always 100% on it"* and "*now and again cheat"* because *"you are only human" and "you don't have to suffer".* The following quotes demonstrate how difficult it has been for participants to maintain the dietary changes:

"*At first it was diet control, which they tell you to go and do, and then you do to a certain extent but you go off, you know. I don't think any diabetic can really do diet control, because you're losing so many, leaving out so many foods that you're enjoying.*" (Julie, I1)

"*I haven't tried very hard. The first six months, yeah, you know, I had all the steamed fish and the boiled potatoes and the fresh vegetables and all that lark, and to be honest with you, it probably done me good, you know, I did feel that I was losing a bit of weight. But that's a bit off putting because you struggle to lose it [off the waist], you know, I can lose it off my legs, my arms, everywhere…. Not off the waist, no. But yeah, and then, I suddenly just went back into my old little life, like gradually, like of gluttony."* (Oliver, I1)

Alison reported that her doctor *did not believe in trying to diet* (I1), so she started her medication right away, whereas Teresa was advised to start medicine straight after her diagnosis but she refused to do so, as she explained:

"*… for eight months I, I, I just refused point blank to take [the medication], to diet, to do anything, but you realise that, you know, if you want to feel better you've got to take [the medication]… and when I first went to see the dietitian and…. at that stage it was you can't eat that and you can't eat this, um, so I started to learn that, you know, I couldn't eat all the sweets and, and the rubbish that I was eating and you do change your lifestyle a bit."* (I1)

Most of those on diet control moved on to medicines within weeks/months except Linda who managed to control her diabetes without medicines for 7-8yrs. Participants most usual first drug was Metformin. However, the types and progression to treatment differed for every individual. Nevertheless, their experience of constant change in their diabetes treatment over the months and years was very common. This common change included the types of medicines (tablets and/or injections), strength and frequency of doses, as the following quote explains:

"*…originally they put me on metformin, which was six tablets a day…. A few years back they called me in and they reduced that, they've taken two off, so it was only four a day. Then around that time they'd given me what you call another tablet, gliclazide…and they've given me one [tablet] originally, then a year or so after that they knocked it down to half of one, which was a load of messing actually, given me half [tablet]. Then they put it back up to one. This is over several years now."* (Christopher, I1)

According to participants, most of the changes to their treatment were made because their "*blood sugars were not coming down*". Still, for Patrick and Irene, medication changes were made due to major complications with metformin and their kidney function, whilst David, Elizabeth and Karen reported changes as a result of side effects of their diabetes medicine. Furthermore, Kelly and James reported their medication change was attributed to potential complications of treatment, as James explains:

"*the problem with the tablets I was on at the time was I'd read in magazines and various things in America they were trying to ban it because of the side effects and it was killing a lot of people,… it was about three years ago, got a phone call from the doctor to say we need to speak to you about your medication. So they took me off this tablet and changed it to whatever I'm on now.*" (I1)

6.3.1.4 Acceptance to new medicine

All participants accepted the initiation of their new medicine, and most of them had started and continued taking their new medicine at the time of the second interview. It was evident from participants' first interviews that some of them were already aware of their new treatment prior to prescription, because; it had been suggested in the past, close friends or relatives had been given that treatment or they themselves had read about it on the media. Although, Daniel, as others, felt "*still blasé*"(I1) about being prescribed the new medicine, Angela and Vanessa felt relief, as Vanessa's quote portrays:

"*You know, instead of, as I said, oh carry on doing what you're doing, come back in three months. I felt like they were doing something for me, and I was going forward rather than sitting there and going backwards.*" (Vanessa, I1)

Most were willing and keen to try the new medicine in hope for the potential benefits, which could lead to living a normal life (Appendix 6.2), as Andrew explains:

"*Just want to try and sort myself out. I want to lead a normal life, I'm not a gymnast or skiing or cycling and all that, I just want to live a normal life for my age*." (Andrew, I1)

Nevertheless, starting a new treatment was linked with feelings of scepticism, apprehension, reluctance and disappointment, as the following quotes reveal:

"*I never dreamt I'd be here talking about insulin."* (Christopher, I1)

"*But to me, it wasn't desperate that I needed it... So in some ways I regret coming [to clinic to see consultant]… I'm being honest, because I think well nothing was, major was happening in my life…*" James (I1)

"*I was disappointed, probably in myself. But ultimately, I mean I was glad to change, I've sort of been expecting it so I figured if it's got to be, it's got to be, and if it does me good let's give it a go.*." (Oliver, I1)

Keith was "*a bit sceptical*" (I1) when the doctor suggested exenatide, but because his wife was treated with insulin and understood it is a treatment that she has to have, he hoped this injectable treatment would be "*okay*" for him too.

Consistent with participants' previous experiences with medication changes, the most common reason this time for a new medicine was that their recent HbA1c results showed that their blood glucose was high. Elizabeth, in addition, willingly decided to try her new medicine, as she felt that her symptoms of itchiness may be due to her current insulin. However, according to Patrick, and Gareth, their doctor suggested that their blood glucose was in control, but their kidney function was deteriorating. James, also, was told that his blood glucose was in control, but the new treatment may improve this even more.

Whilst participants were discussing the benefits of their new treatment, it became apparent that the changes to their treatment had a dual purpose, apart from improving their blood glucose. Many of the participants specified that the key motivation to accept the new treatment was they believed it would help them lose weight (see Appendix 6.2).

"…that's my aim; lose weight, er, and then for the clothes I've got they fit, you know, that, that's what I want." (Keith, I1)

"*I'm hoping it'll work towards the weight loss as well*." (Andrew, I1)

Their motivation for weight loss coincided with the type of medicine they were prescribed (i.e. GLP-1 agonist/SGLT-2 inhibitor), except Andrew, who was prescribed gliclazide, a medicine known to result in weight gain (see Table 1.1).

Furthermore, another key motivation was to take less medicines; for some participants this meant taking less tablets (discontinuing or reducing frequency/doses) and for others it meant taking less insulin (dose and frequency of injections).

"*If this one [Bydureon] doesn't make me lose weight, at least I'd gain losing tablets.*" (Philip, I1)

"*so hopefully taking this tablet mean I won't get more insulin*" (Kate, I1)

Finally, as noted before, some participants agreed to the new treatment, as it would preserve their kidney function.

"[the Doctor] explained to me that he thought that the diabetes was under good control, but he thought that the change in this particular medicine, which is called linagliptin… it was a medicine that superseded sitagliptin and was better for me and was more likely not to affect my kidney function than was sitagliptin... I said that's your best opinion is it? And he said yeah. I said fine I'll go along with that…" (Gareth, I1)

Not all participants were given an option for a new treatment, however for those who did, Julie and Teresa opted for an injectable treatment in order to avoid insulin,

"*…the doctor I spoke to said, well, it's either that or its insulin, um, and I really don't want to go onto insulin. I'm big enough already, I don't want to, to get any bigger*." (Teresa, I1)

Instead, Linda who was given three options, opted for a tablet, as she justified:

"*well the first [option to remain on the same treatment] didn't seem reasonable because my level was still higher than they wanted…the second option was this injection, and … because I told him … I was considering asking for a gastric band so I could lose weight, so he said to me this injection, some people have referred to it like a gastric band because they didn't eat as much and it's made them feel full. So I told him that I didn't know if I liked the idea of that one…. Plus giving yourself injections every day is another thing that really, it's not that nice to have to keep doing it…. and I'm on aspirin, so I bruise more easily and all of that. And... I don't know if it was a risk more of cancer or something, I can't remember, I really can't… So then the third option, just the fact sounded simple, it was only one tablet a day anyway… So I thought no that sounds like it might work for me*." (I1)

On the other hand, James mentioned he "*won't even consider*" the second option he was given because "*the doctor said… the second one's got more side effects and weight gain and all that…"*(I1)

Christopher, too, opted for a medicine with less side effects, as he explained: "*Well when I spoke to the doctor he said there's so many options tablet form. One's better than the other and all… or you might get ankle swelling, different things. But they said insulin you will end up on it. So I thought well you might as well start now than later. So it's going to do me more good than harm – that's the way I'm looking at it*." (I1)

Nevertheless, Edward, David, Robert and Daniel were the only participants who did not exhibit a dual purpose to their new medicine during their first interview. Initiating a new medicine for all of them meant that there was an increase in the number of tablets they need to take, except Edward who had an increase in frequency of insulin injections. All, except Edward, were recently diagnosed with diabetes (from 2 weeks to 2 years). Therefore, they were keen to initiate their new treatment to control their diabetes, minimise complications and relieve any symptoms.

Conversely, Edward took some time to consider starting his new medicine as he explained:

"*I've got so used to doing the one insulin jab a day. That becomes second nature. You take that the same time noon, every day, so you knew where you stood. But when they said oh we might think it's for your benefits to go on two insulin jabs a day, I was a bit reluctant at first. But they did persuade me there, it was all for the good like.*" (I1)

6.3.1.5 Perceptions of Seriousness

Despite the acknowledgement of Diabetes as a serious condition and the worry about future potential complications, the level of seriousness appears to change over time depending on several factors (Figure 6.3).

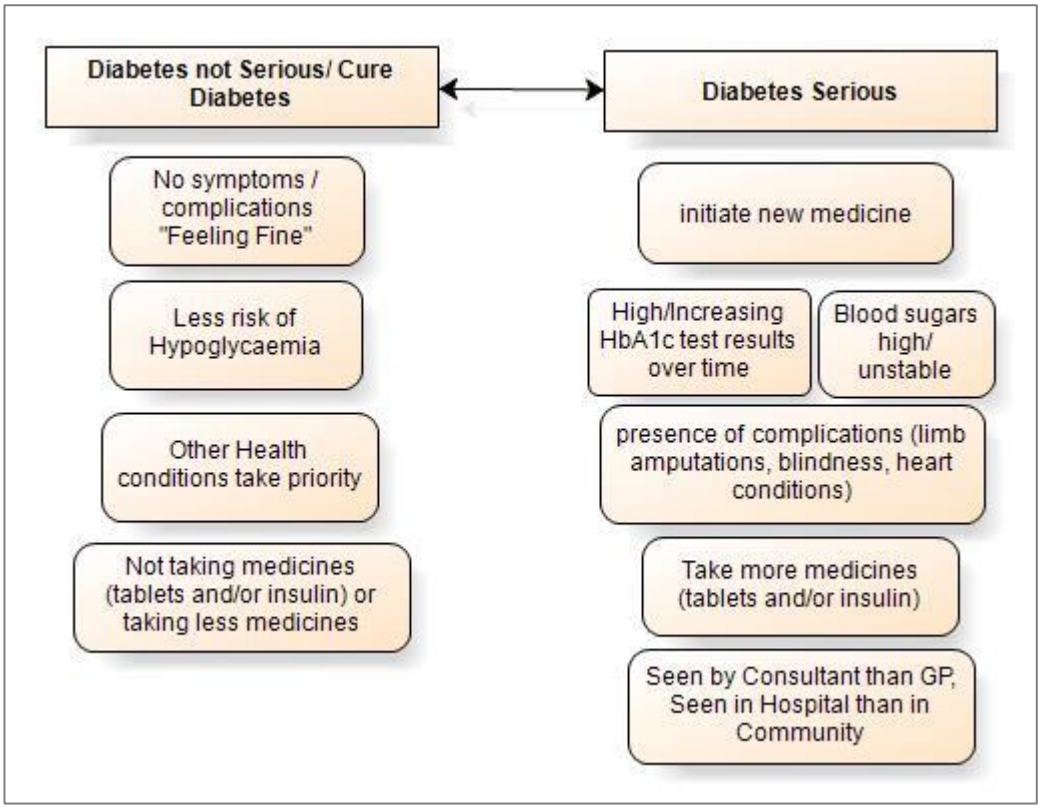

Figure 6.3: Perceptions of Seriousness of Type 2 Diabetes

For some, initiation and/or changes to diabetes treatment together with evidence of high blood glucose or HbA1c results and symptoms, such as "*pins and needles*" in fingers, suggested an increased level of seriousness of participants' condition. Hence, it is no surprise that any changes to blood glucose, either through SMBG or HbA1c

test results, and their own perceptions about blood glucose (section 6.3.1.2) had affected their perceptions of their diabetes seriousness.

At first interview, Philip, Christopher and Irene felt that their diabetes is serious because of their high blood glucose. At second interview, Philip and Christopher were both concerned that their blood glucose was still high. Whereas Irene was more concerned about the risk of hypoglycaemia since her new treatment "*brought my blood sugars right down"* (I2), despite this was less likely with her new treatment (see Section 1.6.7).

James, at the second interview, had seen, through SMBG, that his blood glucose remained stable with his new treatment, he said that *"[the diabetes] hasn't progressed any more, and it might have regressed slightly…Well the only one that sticks in my mind is… I would say [blood sugar is] always 5.3 and used to be 5.5, so it's minimal.*" (I2)

On the other hand, at the second interview, Vanessa expressed that her diabetes team "*because my blood sugars are so high, they're trying to get it down. I think they're more bothered about that than I am.*" (I2). However, Vanessa's reason for being less concerned about her high blood glucose is because she is more afraid of the risk of hypoglycaemia as a result of what happened to her dad, as she explained:

"*Because my dad was diabetic and he had quite a few episodes of hypos, and it wasn't nice... he was on the tablets for years and then as he got older into his 60s he got put on injections, and that's when the hypos started more... and he went into a diabetic coma and he died, and that did frighten me at first when I got told I was diabetic. And I didn't really want to take the injections, because of what happened to my dad." (I1)*

Most participants indicated that their diabetes is not serious at the present moment because they are "*feeling fine*". This means they do not have any symptoms or the symptoms they have can be tolerated, as Daniel explains:

"[I] feel okay myself, don't tend to have any of the side effects of diabetes and that. Well not that I've noticed, do you know what I mean. The only reason I know, is because the doctor said I had diabetes, other than that I've had no [symptoms]… Not really, no, apart from the odd dry mouth now and again, but obviously you can live with that can't you, that's easy solved but other than that no major big complaints over it." (Daniel, I2)

In addition, participants believed that they did not have any complications from their diabetes, even though more than half of them had at least one diabetes related complication (Table 6.1). It was apparent that participants who did have complications, either did not realise their link with their diabetes or focused on unrelated issues and/or complications. For example, Andrew, who has nephropathy, was concerned and wondered about the deterioration to his kidney function, yet he indicated as his "*thyroid is on the borderline, so maybe that's part of it*" (I1), whilst Adam, who has CVD and nephropathy, focused on avoiding "*losing limbs*" (I1), a complication his mother had from her diabetes.

Still, participants felt reassured by the regular monitoring provided by their GP or diabetes team through their regular checks of their feet and their HbA1c test.

"*I mean I go for the yearly checks and touchwood they've never had any changes in me... I just couldn't imagine living my life if I was visually impaired to such a degree, ... I couldn't see where I was going ... I think as soon as something like that was to start, I think then I would just basically live on vegetables or something like, ..., and just change my life completely. But until that happens I probably won't.*" (Oliver, I1)

"*I don't worry about my condition, do you know what I mean, because my doctors have been very helpful with the reviews and that, and checking over me and doing my bloods, and they say look this is you know it's going up. They've kept a good eye on me.*" (Robert, I1)

Some participants compared their health with others, in terms of complications as well as the amount and type of health service contact they have received, such as whether participants are reviewed by a registrar, a consultant or a GP, and whether they are reviewed in hospital or in community:
"[my daughter has diabetes]… hers is bad… she was undiagnosed diabetic until she had to have part of her foot removed, and it had, she'd been missed by different people over the years…. she got cellulitis and iritis in her eyes….She's had heart valves…" (Linda, I1)

"*my sister's a diabetic but she's worse than me, she has fits and that. I mean she goes to the hospital; she doesn't go to the walk in [diabetes clinic]... she has more insulin than me, takes more tablets than me. But more seeing people, appointments, and things like that, so regular check-ups.*" (Kate, I1)

Other participants compared themselves with family or friends in terms of their health conditions and amount of medicines prescribed:

"*It's harder for my wife because she takes a lot more tablets. Because she's got heart failure, so she takes about 13 different medications… and her problems are a lot worse than my problems*" (Robert, I1)

"*I'm taking a lady who is nearly 100 to hospital for an operation tomorrow… She had cancer on her face here. They took it off last week and I've got to pick her up at seven o'clock in the morning. Because they can't change the time she's going in. And they couldn't take her in tonight… So my worries are nothing in comparison to her. She's got no family, she's got nothing, and she lives in a place that doesn't have care or anything*." (Angela, I1)

Furthermore, some participants considered other aspects in their health had priority than their diabetes, or they justified the seriousness of their diabetes based on the amount and/or type of treatment they receive for it:

"*Well health-wise it's not my diabetes that's the problem, at the moment it's my kidneys, so once that's been put to rights I should be fine again*." (Adam, I2)
"*…if it wasn't anything to do with the weight I wouldn't bother about it [increasing dose of insulin], just do it. But they have told me don't worry, some of them are on 100 units a day, yours isn't too bad. No, but it's the weight problem. It's because I've got leg issues."* (Elizabeth, I2)

"*But the way this has been, it's been such a level playing field, I haven't got this dramatic thing of well I've got to get insulin*" (James, I1)

6.3.2 My Body Weight

6.3.2.1 Weight Worry

The majority of participants worried about their current weight, often discussing the difficulties faced in trying to lose weight despite numerous attempts to modify their eating patterns or food intake. In addition, some expressed that due to a physical impairment, heart/breathing conditions, pain, or their age, they were not able to maintain or engage in a regular exercise pattern. These unsuccessful attempts to lose weight were coupled with strong feelings of frustration, embarrassment, disappointment, and self-blame for not looking after themselves when young.

"*I just felt that like it was like a stamp suddenly put on me and it was like saying, you know, yes you are fat, but there was always a possibility you'd lose weight and you were still active, and then you become a diabetic and they give you all these tablets to take then… Makes me feel guilty that I never took care and attention when I was younger about my own weight…. I felt invincible when I was younger, because I was active, I was able to do things, I had good stamina… if I lost weight that I'd actually feel better about myself and so I wouldn't feel so down and things like that. I feel almost like a shadow of my former self*." (Kelly, I1)

On the other hand, Adam, Edward, Gareth, Christopher and Angela stated that they are not worried about their weight, because they do not see themselves as "*terribly overweight*" or their weight has been quite "*stable*". Nevertheless, Christopher and

Angela indicated they would not want to gain any more weight, whereas Adam and Edward felt that they could keep an eye on their weight by regularly checking it at their home or the diabetes clinic.

6.3.2.2 Medicines and effects of body weight

Half of the participants felt that their medicines had either contributed to their weight or prevented them from losing weight, as the following quotes show:

"*anybody on 18 tablets a day at your age is never, ever, ever going to lose weight on diets and it works the opposite…I wouldn't say categorically that they put weight on me but I wouldn't say they help me to lose weight. It's a bit of a catch 22 and then you've got the age thrown in, so you've got three factors."* (Philip, I1)

"Well I think because metformin makes you gain weight… because it was every time you ate you were supposed to have the metformin, and I never used to eat a midday meal. I wouldn't feel like I'd eaten enough to have the metformin, so I'd be eating for the sake of eating, just because I was taking the metformin. (Linda, I1)

Of those with experience of taking insulin, most of them associated this medicine as being responsible for their weight gain. Adam and Christopher, who had only just started insulin for the first time, were also aware of this fact. However, Kate and Angela, although experienced with taking insulin, did not relate insulin with weight gain. They did mention, however, that the injection site could have contributed to weight around their stomachs as Kate's quote illustrates:

*I don't know whether it's because of the tablets or just me putting weight on, I don't know. I mean I do feel… as I said it's just round my belly and that, and that's where I was doing my insulin anyway in my belly, or some at the top of my thighs, but it's mostly my belly I do my insulin ... (*Kate, I2*)*

The participants who did not associate taking medicines with any effects on their body weight, felt that they "*always*" had a weight problem, even before the diagnosis

of diabetes, or that their weight has been stable since they started taking their diabetes (or other) medicines, as Gareth described:

"Nothing that I'd taken so far affects my weight; the only thing that affects my weight is the volume of food that I take and the lack of exercise." (Gareth, I1)

6.3.2.3 My diabetes matters Vs my body weight matters

The balance of keeping the diabetes stable and their body weight manageable can be tipped over depending on whether participants believed their medicine is important for their diabetes or their weight, and as such, the participants can be split into two categories. The first category includes those who adamantly said they would not stop their medicine if they gained weight. In addition, this category includes all those participants who said that they would stop it, or were unsure at first interview, but changed their opinion at the second interview. The second category includes those who said they would stop their medicine if they gained weight. Also, this category includes those participants who said they would not stop their medicine or were unsure about it but changed their mind at the second interview.

Participants, who indicated they would not stop their medicine, even if they gained weight, described their medicine as more important for controlling their blood glucose and preventing diabetes complications, as the following quote reveals:

"*I am overweight but not excessively, I don't think so. And it's more important that the insulin I'm taking is going to control my diabetes rather than my being fat. It's not about being fat it's about controlling it for me so I don't go blind and I don't lose my feet*." (Angela, I1)

Some of them even said they would "*sacrifice*" a couple of pounds extra or did not expect a lot of weight gain with their medicine. This group mostly consisted of people who did not worry about their weight, and felt it had been relatively stable. However, for those who changed their mind, they were all concerned about their weight but they experienced both weight loss and improvements in their blood glucose with

their new medicine at follow-up. Patrick called the weight gain as "*the lesser of two evils*" (I2). Everyone in this group indicated that in order to manage their weight they would look into their diet, possibly by decreasing their portion sizes, and would try to increase their exercise or be more active.

Some participants indicated they would be unlikely to stop their medicines, like Daniel, for instance, who at the time of the second interview believed his medicine had helped him lose weight even though he was unsure if his blood glucose had improved. Moreover, Robert, who thought he gained weight at follow-up, reported he would be unlikely to stop his medicine because he remembers prior to his diagnosis "*it wasn't a nice way of living because I was just constantly on the toilet … I couldn't quench my thirst and I was tired and I was up all night*" (I2). Edward raised concerns about gaining weight because he had already made drastic changes to his diet, and he had seen an improvement in his blood glucose at follow-up. His new medicine was, also, much more convenient than the previous one, and he was more concerned about the consequences of uncontrolled diabetes. Instead, Oliver, who appeared reluctant to make any lifestyle changes (either with diet or exercise), suggested that he would not blame the injection as he knew he could be doing more and "*haven't given it a fair chance*" (I2).

On the other hand, the participants who said they would stop their medicines if they gained weight, were all worried about their weight in terms of wanted to lose more, felt they had tried everything and there was nothing else they could do. They indicated that taking medicines restricted their life. Most of them appeared to grieve following their diagnosis of diabetes by blaming themselves for being overweight and causing their diabetes. As a result, they believed that by losing weight, they could stop taking their medicines and their diabetes might even disappear.

"*Well if I lose weight - type 2 diabetes, most of it's associated with being overweight. So if I get down to my normal weight, which I haven't done for a long time, but if I got down to a normal weight of say nine stone then I would imagine all the things of*

diabetes would disappear with it. So therefore I need less medication and be fitter." (Linda I2)

"*…well I am feeling the benefits of it, and I wouldn't think that I would be on it long term compared to other people who've extra weight, who carry more weight. I mean there must be a cut off time when you say well you're not taking it no more if you've lost the weight.... I'm thinking oh maybe I'll cure myself and I won't be a diabetic at the end of it, but what's the chances of that being like*." (Julie, I2)

Most of the participants in this category were obese and all had lost weight at follow-up. Of those who changed their mind, (even though they had lost weight), David was certain that his diet was healthy and any weight gain would have been as a result of taking his medicine. He therefore appeared confident in asking his GP to change his medicine if he could not tolerate any of the side effects. Alison said she was "*heavy enough*" and although she had put on weight when she started insulin, this had stayed "*fairly stable*" (I2). Karen, who had experienced nausea with her new medicine, said she would rather lose weight naturally than being sick all the time and if the medicine had caused weight gain she would have asked for an alternative.

Keith was the only participant who was not asked what he would do if he gained weight with his medicine. However, he implied that if he continued with the medicine he would like to lose some more weight. At his second interview, he was "*made up*" with his weight loss and was pleased to see that his blood glucose had been stable.

6.3.3 Beliefs and Perceptions about medicines

6.3.3.1 Trust in Doctors to Prescribe Medicines

Although the majority of participants have trust in doctors to prescribe appropriate medicines, as the following quote illustrates:

"*The only medicines I will ever take in conjunction with what… already being prescribed is what will be further prescribed by the doctor. …I've great faith in the British medical profession, at least in my own doctor*." (Gareth, I1)

They accepted that they are not in a position to argue otherwise, when it comes to changes to medication treatment, since doctors are considered experts in this field. However, as Patrick emphasises:

"*It's not something you can decide for yourself what you'll take, so you've just got to say, well, they know what they're doing and I'll take their word for it and hopefully it's the right one*." (I1)

6.3.3.2 Necessity and Benefits of Prescribed Medicines

Most participants agreed that their prescribed medicines are essential for the management of their diabetes because they help to control blood glucose and, therefore prevent complications and keep them '*alive*'. The belief about the necessity of their medicines appeared to be closely related to physical evidence, which reinforced the belief that their medicines are beneficial, as the following quotes illustrate:

"*…I found actually that after I'd started with the Metformin that I had a load more energy.., I was back to normal…I felt really drained leading up to [the diagnosis], and the medicine took away that, and it was positive for me, I felt great…. I know I've got to take them to look after me*." (Robert, I1)

"*The main difference [with the new insulin] is the improving blood levels, which is very promising, so hopefully that will continue… and I've been hitting that [normal blood sugar range] target a lot more recently than I've ever done before, so that's very reassuring. At least you know you're on the right track*." (Edward, 2)

Hence, the benefits of their prescribed medicines mainly included; their effectiveness in controlling their blood glucose and in alleviating diabetes related symptoms. Other benefits to their medicines included the convenience of taking them, and having less concerns about taking them.

6.3.3.3 Effectiveness of Prescribed Medicines

Participants' perceptions of effectiveness of medicines in general and medicines specific to diabetes varied from individual to individual, as well as within an individual over time. Two key factors were identified that changed their perception of effectiveness. These were as a result of evidence from blood tests (i.e. HbA1c, cholesterol), blood–pressure monitoring and/or through SMBG, as well as physical effects on their body in relation to energy levels, and/or body weight (Figure 6.4).

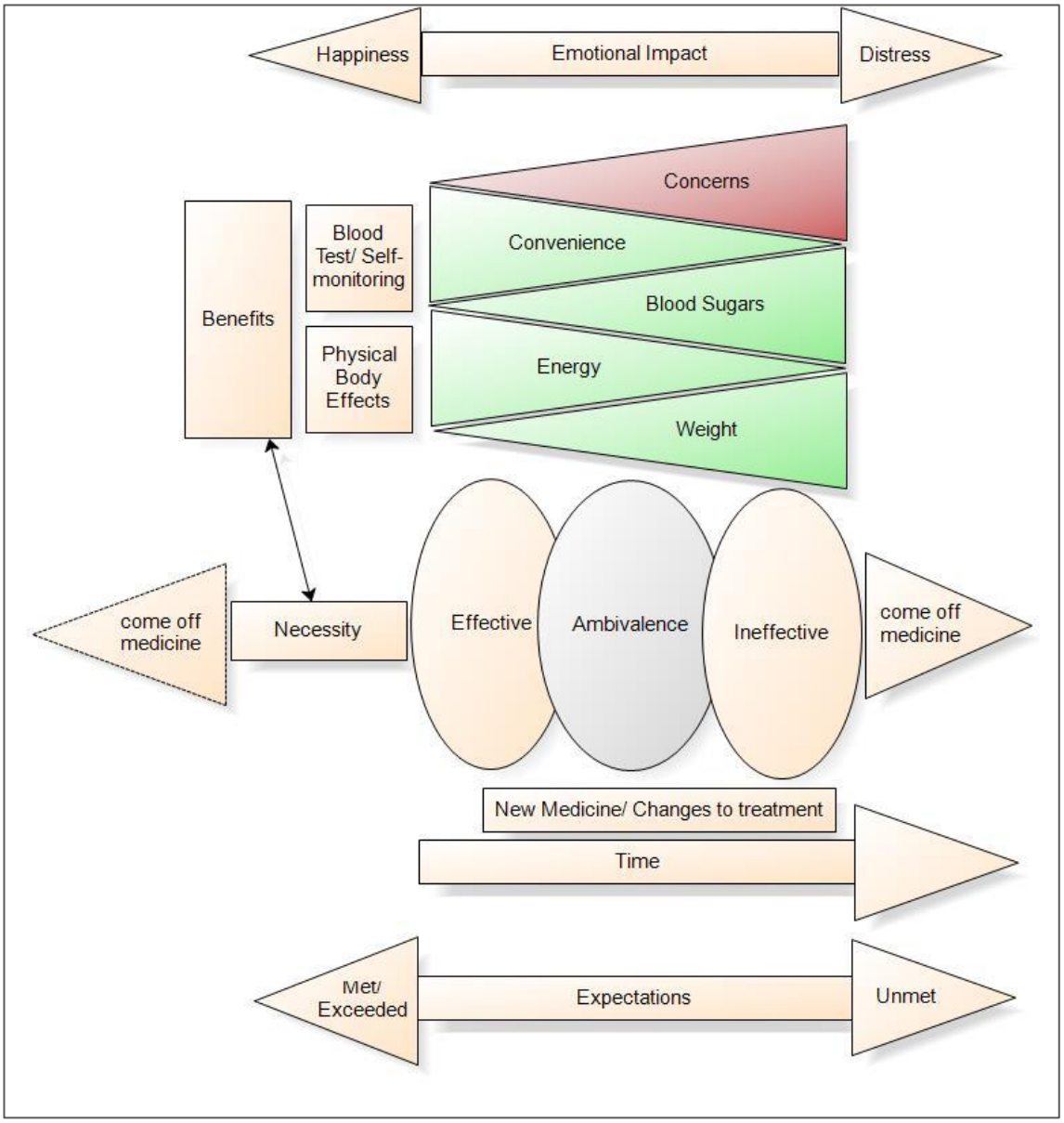

Figure 6.4: Conceptual Model of Participants' Beliefs and Perceptions about their Diabetes Medicines

Thus, medicines were effective if blood glucose levels were improving or becoming more stable, and participants were feeling more energetic or losing weight. Whereas medicines were ineffective if blood glucose was high or unstable and participants were feeling tired and/or were not losing weight as they expected. For example, Irene stated that she "*did very well on the metformin; [as blood sugar] was around 6.1 up until September of last year…"* while *"… the glimepiride, I've really not seen any difference in [blood sugars]… That dosage I've been on for quite a few years. I can't remember how long I've been taking it but it has been quite a few years.*" (Irene, I1) Elizabeth said she tried "*virtually*" most of the diabetes medicines available *"... like gliclazide tablet, Lantus, NovoMix doesn't really suit me, NovoRapid, I've tried them all really."* So when she was asked why these did not suited her, she indicated *"Well just the control isn't good generally. You know, the readings are all over the place. You know, as I said before I can be very low one minute and terrific within a couple of hours.*" (I1)

Philip, out of all his diabetes medicines, found that "…*the metformin wasn't working, my walking wasn't too good and I was just in pain all the time, my energy level's zilch, but I've been off the metformin now for just, it's... About 18 days and I feel better just being off the metformin. Whether it's mind over matter I don't know, but I'm in good spirits, so."* (I1). However, at the second interview, he suggested that "*the Levemir's not doing its duty!"* because he "*…had ten carbs of a morning and I went from 10.1 to 13.7 with two eggs and one lousy piece of bread - I shouldn't have been that figure."* (I2)

Whilst Keith confirmed that "*[Exenatide] seems to be working, because apparently I've lost half a stone… I'm actually refusing food now. I've been on six metformins now about eighteen months, maybe two years. And I can't understand why, because the doctor told me this will help with your diabetes. It hasn't. This injection's helped me more*." (I2)

Yet, some participants showed ambivalence towards the effectiveness of their medicines. Reasons for ambivalence included interactions with HPs, as Alison explains:

"*I'm on Humalog Mix 50, but I had stress eczema and was on steroids. Now since I was on the steroids, my levels have gone so high, my insulin's [dose] gone up and up and up... and [the diabetes team] just said, you know, we are going to have to do something else, was I prepared to try this [exenatide]?…and they've said it will cut then, my Humalog down*." (Alison, I1)

Also, ambivalence was shown when improvements in either blood glucose or body weight, did not meet participants expectations, particularly when they anticipated that the treatment would provide instant results, as Robert, Christopher and Adam explain:

"*I don't know [the benefits of gliclazide] see because I haven't had the review which is tomorrow. I've done my blood [test], I don't know whether it has benefited me by bringing my blood sugar down, and I do feel in a way since I've started it I do feel bloated….I don't think it's been as beneficial in terms of psychologically how I felt. I don't feel, I feel like I have improved but not to the extent I was hoping*." (Robert, I2)

"*Well I know [insulin]…, supposed to be doing good for me, but at the moment I don't feel any different from when I first started… I just feel the same to be honest... It's a slow process, it's like 14 weeks now and I thought it would have been a bit quicker… I mean when I was monitoring myself [blood sugar] was like 19, now the other week it was 14. Yeah, and the readings of teatime and dinnertime are quite good. The mornings and evenings were slightly higher again*" (Christopher, I2)

"*Because I honestly thought I'd take the insulin and my blood sugars would be in-between five and seven, and I was quite shocked…I thought my blood sugars would just go to more or less a normal person overnight… It didn't happen, I was on 12 units… now I'm on 24, so they've doubled the dosage…*" (Adam, I2)

Whereas, Oliver and David said:

"*Well [liraglutide] does appear to be helping to control my weight… I seem to plateau of a morning, around about 12-ish, you know, and I still have plateaus around there, but that's probably more down to me…So I haven't give it enough time I don't think to notice any big differences, but that's down to me more what I would imagine. It's probably helped me to a certain degree because otherwise I probably would have been worse off*." (Oliver, I2)

"*I used to stop and rest. But I did have heart failure and I've had the bypass. But since this [new medicine] I've felt better, a bit better, you know, I can do walking a bit and a bit more without getting tired. I don't know if it's in the mind or it's the tablets but whatever it is I'm not bothered; it's keeping me happy*." (David, I2)

Nonetheless, overtime, the constant changes in participants' medicines has resulted in the belief of them being ineffective, as Karen describes: "*You know, I've tried a couple of things and they haven't worked and it's like we've got to try something else now, and it's a bit like, you know, just keep stopping something and trying something new, all the time..*" (I1)

On the other hand, Oliver suggested: "*I'm not medically trained so I don't know if I'd be any worse if I'd stopped taking them, you know, I just don't… and I have been tempted sometimes just to stop taking them and don't even tell the doctor and then go for my blood test and see if it was any different, just to see if these things work. I mean we're presuming, you know, like one size fits all, you know, these tablets work on everybody like, but I don't think they do, you know, I think it's horses for courses and until you get the right one, maybe I'll begin to feel different.*" (Oliver, I1)

While, others, like Daniel, reported that medicines work "*hand in hand*" (1) with lifestyle measures such as diet, in order to "*reinforce*" (I2) its effectiveness, and Linda clarified that:

"*You've got to take some responsibility, like a lot of people today think a tablet fixes everything. So I'm not like that, I know that I've got responsibility for it too*." (Linda, I1)

Therefore, ambivalence in the effectiveness of their medicines could result in ambivalence in the necessity of their medicines. Some participants, who believed their specific medicines were ineffective, they wished to stop taking them, like Vanessa, who said "…*what's the use of me taking all these? I don't feel like I'm getting any better, I don't feel any different. I wish I could just stop taking them all…*" (I1)

Whereas others believed that if their medicines are effective and are able to reduce their blood glucose or lose weight, then they would come off their medicines, like Daniel: "*But if it works I'll be able to come off it, you know…*" (I2)

6.3.3.4 Concerns about Prescribed Medicines

Participants frequently expressed their concerns over taking medicines (Figure 6.6). These concerns were either for individual medicines (Figure 6.5) or the amount of medicines as a whole.

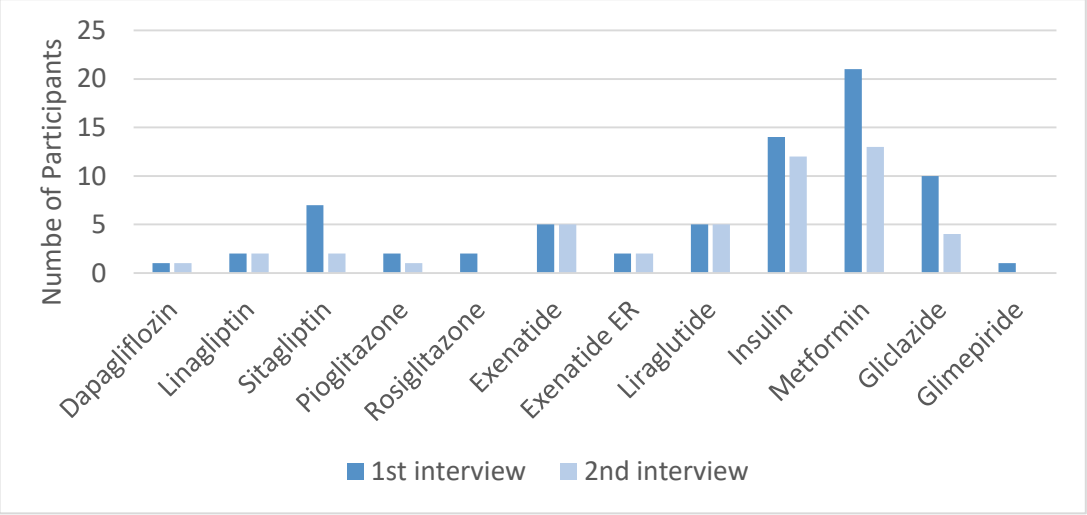

Figure 6.5: Types of medicines participants talked about in their first and second interview.

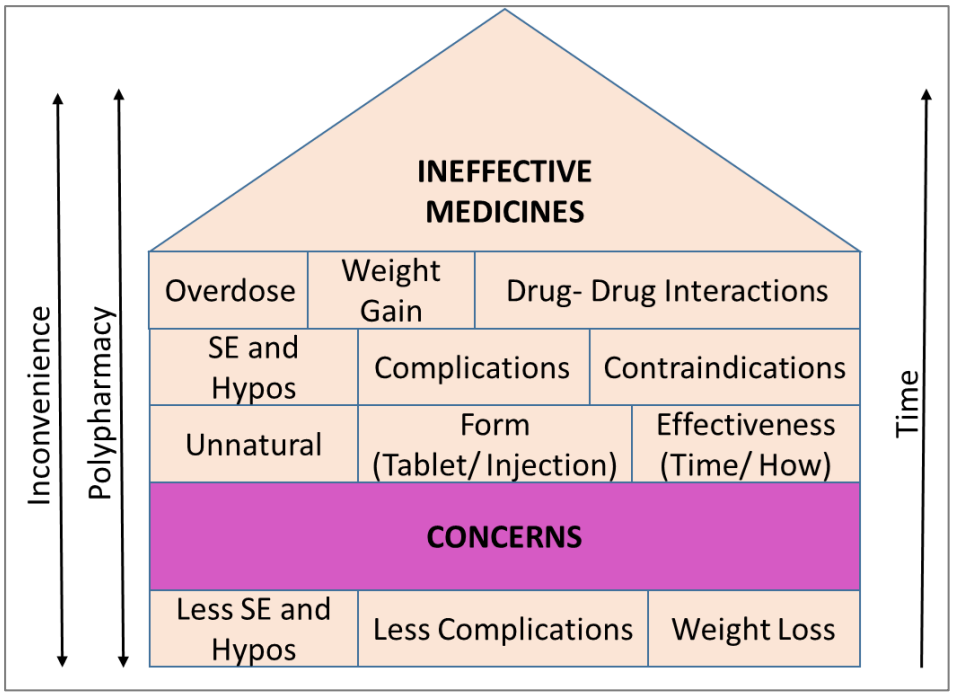

Figure 6.6: Participants' Medicines Concerns and Polypharmacy

Participants described medicines as unnatural as Gareth portrays in his quote:

"*Because any medicine that I take is a foreign body to my body; it's a chemical which the body doesn't produce naturally, unless it's an insulin substitute I suppose. So, no, don't like putting stuff like that in my body, it just goes against the grain*." (I1)

Keith said medicines "*must do something to the inside but I, I don't, I don't understand. You take so many tablets and you swallow them all at once… how do the tablets know which way to go when they get to the inside?*" (I1)

Consequently, participants voiced their worries regarding their medicines' side effects and complications before and after they started taking them, as Julie and James illustrate:

"*Well with everything you worry about new medicines, don't you, because you worry about side effects, and I mean may have more side effects than just the vomiting, you don't know, and what effect will that have getting into my system, will that make me have the runs...*" (Julie, I1)

Often the fear of side effects, particularly those affecting the gastrointestinal tract, was related to past experiences, as Teresa illuminates: "*I was very reluctant to, to go on [exenatide ER], very reluctant because I'd had exenatide when I first started injecting, um, twice daily, and I was very, very, very sick with it, um, very nauseous and, and I thought, I can't, I can't do this again…*" (I1)

Another major concern was the increasing number of medicines participants needed to take for their diabetes and, where relevant, for other conditions. Participants considered having to take medicines as being old or getting "*sicker*". Some were also worried how other people would perceive them if they knew how many medicines they take, as Philip articulated:

"*If it was less it would make you feel better because if you say to people I take four tablets a day and a person who doesn't take tablets, they'll think there's something wrong with you, you're a hypochondriac or something like that. But how many people would stand up and say I take ten tablets in the morning and eight at night? You'd feel like a, well, a phony wouldn't you…"* (I1)

Participants suggested that as a result of taking more medicines to manage their condition(s), there was an even more increased risk of drug-drug interactions, contraindications, and overdosing. Their perceptions about polypharmacy coupled with the increased risk of taking more medicines, made participants believe that overtime, they are at higher risk of getting side effects/complications from their medicines, and these may become ineffective, as Elizabeth suggests:

"*because you've been taking [the medicine] for so long, but I'm wondering whether maybe my system's got tired of it, you know, and it's starting to react now…*" (Elizabeth, I1)

Therefore, any side effects or complications that arise in the future, would make it *harder* for them to know which of the medicines had caused them.

6.3.3.5 Trial and Error when taking Medicines

Despite participants concerns about medicines overall, they recognised that initiating a new medicine is a case of "*trial and error*". This is related to how effective the medicine would be, what side effects/complications it would cause (if any), how they are going to cope with them and whether it would require changes to other medicines. The following quotes demonstrate how participants rationalise the risk of trying something new, and the timeframe they perceived as acceptable for determining whether the medicine causes side effects or its effective.

"*But I do expect once I start taking the tablet for a few days to have some side effect on me, whether, because as I say I don't take tablets, never taken tablets so I assume that there would be some. There might be and I hope there isn't, but I'll give it a week and then if it settles down well I'll just carry on.*" (James, I1)

"the medicines, they seem to be working for me, I don't feel anything [no SE]. But it's only early days, it's only three or four months ain't it, so it again in a couple of years and see how it goes then." (Daniel, I2)

"Well, all it is really, if they get the dose right and the mix, I take about 12/15 different types of tablets a day, and they've all got to work together. I think once they get it right it works, but it does take a few years of trial and error really to get to the situation where it's right. I suppose that my, something happened with me health-wise it would alter it again, probably have to treat me for something else." (Patrick, I2)

6.3.3.6 Tablets versus Injections

Furthermore, participants seemed to have perceptions related to the form of their medicines, whether a tablet or injection. Relative to their past experience with their medicines, participants expressed a preference towards tablet or injection. In general, tablets appeared to have less impact than the injections, as they are "*easy to swallow*" and "*just throw them down, have a drink, its gone that's it*". However, Philip was worried about tablets "*mainly the metformin and the gliclazide and a*

couple of other tablets that they are not coated" because he believed that coated tablets "*go past [liver and kidneys] so they don't affect them*", and blamed these tablets for the polyps found in his bowels (I1). For that reason, he revealed that "*I'll say, give me two injections a day, sooner than have those tablets, sooner than have that*." (I1)

Conversely, those inexperienced with injections but who were prescribed insulin/GLP-1 agonists as new treatment, implied that these types of treatment are more important because they are likely to be more effective and efficient than tablets, as the following quotes illustrate:

"[The diabetes team] put me on [liraglutide] because it's not controlling my blood sugars as in an oral tablet. So this way straight into your blood stream…" (I1), "*I don't know, I probably sound ridiculous saying it's more important doing a needle but no, I think it's just the methodology of the fact that you're doing a needle feels more like you're taking medication that taking a tablet. I don't know, it's just the way I think".* (Karen, I2)

"*I think [insulin] seems like more serious. That's what I say, if you miss a pill you don't double up, you just miss it, but insulin you think is that more serious if you miss insulin than the odd tablet?… I would say so*" (Christopher, I2)

However, both Elizabeth and Christopher, who found that the effect of their insulin on their blood glucose was not as expected, articulated that:
"*You know, I'm waiting for the days to come when they produce a tablet, that would be wonderful, but there you go.*" (Elizabeth, I1)

"*Might be better if it was in tablet form but [insulin] doesn't seem to affect the kidneys as much as tablets.*" (Christopher, I2)

Regardless whether participants had experience with taking injections, most of them discussed about the stigma surrounding injecting in public and how this impacts on

lifestyle. Many said they would not like to inject every day or many times throughout the day. James went on to say that there is no disadvantage in taking tablets because "*It's not as if it's taken in public view*" (I1), whereas Julie said "*Taking a tablet you can do anywhere out and about, no one notices it*" (I1). Those with experience in taking injections discussed about the "*awkwardness*" having to inject outside of home. Vanessa said, whilst in a restaurant, "*I go into the toilet and sometimes if there isn't a cubicle empty I just do it, and if there's people there they're looking at me as if I'm a druggy.*" (I1) Julie, as a result of taking GLP-1 injections, was worried about going on insulin due to "*all that paraphernalia of carrying needles round with you and things for the rest of your life*". This fear was reinforced after going on holidays and realising that she had "*to get letters from people to say you're carrying [needles] like you're a bloody drug dealer… but even that's like I don't want to be doing this, I just want to slip through like everybody else.*" (I2)

Those participants who for the first time were about to experience taking injections talked about being "*nervous*" and "*terrified*" of having to inject. Adam was worried "*because actually I was thinking at first, well, do you have to inject it into your veins…*" (I1). Although some were not afraid of needles because they had relatives who were on insulin, others were "*apprehensive*" about the size of needle like a "*hypodermic*" "*syringe*", but justified it as "*probably similar to the finger prick test, like once you've done it a few times hopefully it will be okay*" (Oliver, I1). Adam explained that after seeing the insulin injection, it has "*shattered a lot of fears*" (I1). Following the experience of learning to inject for the first time, participants described it as "*dead easy*" to do, "*only a little needle*" "*hidden*" in a "*fountain pen*" that takes "*seconds*" or "*minutes*" to do. Edward, who has been using insulin injections for two years, said "*there's no need to worry about it now on reflection, but at the time, I think it's the unknown isn't it, you know… But you just do it now and you don't think anything of it*." (I1)

Nevertheless, some participants said that they still feel the "*soreness*" when they are "*stabbing*" themselves and concerned about the bruises. Karen said "*when I first seen them I thought it was a little bit disturbing because like you look a bit black and blue*

where the bruises are" (I2). Elizabeth usually injects around her navel area, but recently started to inject in her legs, yet she said she would rather not inject in her arms as she "*don't want to get all brown specks; I've got awful brown marks keep coming [in legs]... nobody sees [the legs] do they, and if they do they shouldn't*" (I2).

6.3.4 Experiences of taking medicines

6.3.4.1 Inconvenience and Forgetting to take Prescribed Medicines

Participants discussed the inconvenience of taking their medicines and how this resulted in forgetfulness. Still, only a small number of them were frustrated because they found it hard to remember their medicines, and panicked when they realised they forgot to take them, and blamed themselves if they did. Aspects of convenience were related to how the medicines fit with current lifestyle and routine. In particular, they discussed the frequency of taking medicines, how, when and where to take their medicines, as well as any related dietary adjustments they had to make.

For instance, participants found their medicines to be inconvenient if they interfered with their lifestyle including family, work and social lifestyle, when routine alters, especially when they were going out of the home or when they travelled, as the following quotes show:

"*It's hard to remember to take them, sometimes being, having a busy lifestyle, a mum, I've got a full time job, so sometimes there's a lot going on after school as well, so it's hard to remember to take them especially at the same time.*" (Karen, I1)

"*I mean I've forgot it once or twice, and that's because I rush out and things like that*" (Kate, I2)

"*If you're out you think oh take a tablet with me and little things like that not a great deal, because nine out of ten I'm in the house so they're already there to take. It's just if you do pop out. Possibly if you go on holiday you've got to make sure you've got enough, but that's common sense again, that's all*." (Christopher, I1)

"*I don't like the idea of carrying the needle heads round, and then you've got to dispose of them when you've used them safely…[and if] you're visiting somebody and they've got kids, you've got to be careful you don't put them down or that sort of thing. When you're staying in a hotel or something like that, you've got to dispose of them there because you've got people coming. You can't just throw it in the bin where someone might be emptying the bin and put their hand in…*" (Patrick, I2)

Although different experiences shape what is perceived as inconvenient, in general, having to take medicines more than once per day, which encompasses various different doses through the day, was considered a "*nuisance*". Examples provided below:

"*…I know I've got to take half and half, whether it's one, it'd be easier if it was like 40mg tablets and they're already split. You don't have to split it so it's just one [tablet]*" (Robert, I2)

"*And some tablets I take, the milligram they gave me, it can't be in one tablet, it has to be in two. So I'm trying to like reduce the tablets and taking them, it's like I'm taking twice as many… So if I could just get like them two tablets put into one on a couple of them I'd be all right."* (Vanessa, I1)

"*And it's just a damn nuisance having to take large doses because it means sort of, instead of two injections a day, it's three injections a day...*" (Alison, I1)

Also having to take medicine (with meals or food) at a specific time of the day as well as having to take certain medicines at different times from other medicines, was thought to be problematic. Most commonly participants said that it was difficult to remember to take their medicines in the "*middle of the day*", in the "*evening*" or at "*bedtime*".

Although Gareth said "*Well breakfast you get up and you have your breakfast in the morning but lunchtime with me varies depending on what I'm doing or what I'm not*

doing, whether I'm at home or out somewhere. Just that's the one that I tend to forget if any..." (I2). Linda found the evening more difficult "*…because that's when I'm busier and I'm subjected to getting ten different people wanting me to do different things, and that's when I'd be likely to forget.*" (I2), whilst Patrick indicated that "*… sometimes about nine o'clock if I have to go to the toilet I just don't bother coming back down, I'll just go to bed. And I think that's what I done last night… and I was off to sleep straightaway."* forgetting to take his medicines. (I2)

Furthermore, some participants said that they found it challenging to take their medicines with food, as advised in the instructions, because of their concerns over side effects and/risk of hypoglycaemia. This meant that they would either eat more or avoid eating altogether, as Kelly and Karen suggested:

"*They say they don't give you hypos, but I have definitely had hypos. Whether it's because not a true hypo, whether it's just because my blood sugar's coming down, but I've had to adapt to that. I have to take things like dextrose tablets, so that if I do feel like that way that I can take something. I didn't have to think about that before.*" (Kelly, I1)

"I take my two lots of metformin after my tea of a night. But sometimes if I don't take it immediately, because you have to take it with food, … and then I feel like later on I've got to eat something to remember to take the tablet, do you know what I mean, so… I'd have something to eat, like I like something small to eat to take the tablet, or if it's too late and say I'm going to bed, I just haven't took them, you know, because I'd rather not take them on an empty stomach, so I just haven't took them." (Karen, I1)

Vanesa, however, claimed "*It felt like I was eating all the time because I had to take [my insulin] three times a day and going from that to my new medication I feel like I've gone from eating loads to eating nothing... Whereas before I was eating, I felt like I was eating for the sake of eating. Whereas now I'm made up because I'm not sort of*

tied to, I've got have something to eat now because I've got to take this…So now I can go without either my lunch or my tea so in that way I feel better. (I2)
Patrick, too, reiterated not being "…tied down to mealtimes. So if for some reason you forget [the new medicine], it's easy enough to take it later on" (I2).

A few participants described how Metformin, due to its size, was particularly considered as a *"horse*" or "*elephant*" tablet which was difficult to swallow "*and sometimes get stuck in my throat and I've got to gargle water and all that…*" (Kate, I1). Vanessa said despite taking them for 10 years "*all of a sudden because they're so big I feel sick taking them. I feel like I'm choking. And I don't know why, because it didn't bother me before… [and] it has prevented me from taking them before. The odd time… I just look at them and think I can't swallow you. So I just don't*." (I2)

In addition, some participants felt that they had to adjust their lifestyle and diet as a result of taking their medicines. Especially those on insulin injections who explained how insulin made them to be more aware about their food choices and eating patterns, because of the direct effect on their blood glucose.

For example, Philip described insulin as "*like the weather. You're taking insulin and everything's great if you eat, it's all about food. If you have two Weetabix in the morning it's great. If you have your food at around about 12 o'clock it's good and then you have your food at five o'clock, but if you go past five o'clock you're starting to nosedive…that's all diabetes is, an inconvenience where you've got to be awake all the time to your body*…". He, then, went on to say that when "*my wife's been out shopping… and she'll come in too late and when I say late, only by half an hour, and I'm screaming at her, I live on a clock, I can't live by when you want to come home from the shops. Five o'clock I've got to eat, five o'clock, and that's the part, the inconvenience part, that's all it is."* (I1)

Moreover, insulin injections have an added inconvenience of having to be kept in the fridge, because "*…it says on the instructions… it's best to keep them at a certain temperature. It must affect the insulin*" (Edward, I2), "*…And once they got pushed to*

the back of the fridge and froze. Well they're no good; they've got to be thrown out…." (Alison I2). Also, Angela said "*Because although I've always kept it refrigerated I can't now [fridge broke down] and I can't put it in the freezer, so I'll watch my readings and if they suddenly start going sky high or something I'll know that there's something wrong with the NovoMix, but [the leaflet] does say it can stay up to four weeks [in a dark place].*" (I2)

Furthermore, participants on certain injectable medicines mentioned that they are "*more fiddly*" because you have to "*make sure [the liquid is] well mixed*", and that can be "*a bit of a performance*", in comparison to the pre-mixed insulins.

Also, participants were worried how the injections might affect their driving licence and insurance, but those on non-insulin injections, like Oliver, after searching on the government website, was relieved to find "*they only need to know if you're injecting insulin, unless you're prone to hypos or hypers, which I'm not*". (I1)

6.3.4.2 Experience of side effects

Experience with side effects from medicines varied from participant to participant. Those who reported never having any "*problems*" with taking medicines explained they were "*lucky*" and "*resilient*" in that respect. Those who experienced side effects stated that only certain medicines had a "*bad*" effect on them (most commonly metformin) and that some of the side effects were "*horrible*", "*unpleasant*" and "*embarrassing*" and made them feel "*lousy"/"drained*". Side effects, therefore, had an impact on participants' lifestyle:

"*…I think, if I was at home, if I didn't work it wouldn't be as bad, but I think because I'm working and I've got quite a busy, stressful job, that it's hard when you've got an upset stomach to actually concentrate on your job and what you're doing*." (Karen, I1)

"*…if it's like impacting on my life, like diarrhoea, vomiting, nausea, dizziness. Well you can cope with the dizziness probably, nausea, but diarrhoea, vomiting, that's like,*

you're out and about, I was really bad when I first started taking my Metformin, that didn't agree with me one bit when I first started on that. The diarrhoea, oh my god, I think I knew where every toilet was in [my town], I wouldn't go out unless I was in the car with somebody, wouldn't go on public transport because I just used to, and I'd have to go right away there and then. How embarrassing. That was like for about two, three years that." (Julie, I2)

Hence, past negative experiences of side effects made participants worry and wary when they start new medicines *"…considering that you've got a disease, but the medication you're taking is making you feel worse really…*" (Karen, I1) and "*…because when you're taking a medicine that makes you feel poorly, it's just an added stress to you isn't it?... and you're plodding on every day, and you think oh, this is a bit of a time waste, but obviously you do it*." (Elizabeth, I2).

6.3.5 Emotional Impact of taking Diabetes medicines

It is no surprise that participants' beliefs, perceptions and experience of taking medicines for diabetes and other conditions had an impact on their emotional well-being (Figure 6.4). The majority of participants revealed they do not like taking medicines and wished for "*the less the better*" or "*better off without*" them. David said:

"*I'm not taking them because like I want to, I'm taking them because I have to. That's the way I look at it, you know. See some of them will be heart tablets or gout tablets, and a cholesterol tablet, you know…and I'm scared to go to the doctor's in case he gives me another one.*" (I1)

Many said that they would be more stressed if they thought they had to start taking more medicines, particularly if they felt that these were not reviewed as often as they would like, as Keith indicated

"*And the doctor's left me on … all this medication, he hasn't altered it, apart from two years ago he put it up. I just worry, I'm a terrible worrier, because I know like if*

anything happened to me, how would [my wife] cope on her own, I don't think she would." (I2)

Although Daniel and David felt that there was a lot to learn about their diabetes since they recently got diagnosed, and Robert found it was a positive experience after starting taking his diabetes medicines, other participants were shocked to find that they had to take medicines. Oliver was "*a bit shocked when [the doctor] said I'd never come off it, I mean he said even if I lost weight and got myself as fit as a fiddle, you know… I'd still be on it for the rest of my life. That was a bit, you know, off-putting, to be fair…*" (I1). Alison, too, was shocked with the amount of her medicines as she claimed "*Well I never took anything before I was a diabetic. There was never really anything wrong with me. Few bouts of depression or, you know, not sleeping but that was due to - how can I say it - anxiety. But apart from that I didn't take medicines so it was sort of, you know, gosh, have I got to take all this?*" (I1).

Edward never realised there would be constant changes in his medicines, suggesting that "*When I started off it was only like one or two items, so it has escalated over time… It does make you a bit anxious that to remember what time of the day to take it and that takes some getting used to, you know*." (I1)

On the other hand, Linda who had diabetes for a number of years said that she "*…was a bit upset when I had to start taking metformin, because I've been diet control for so, you know, for quite a long time. So it was like we was going back a step when I had to start taking it*." (I1) Whilst Kate reported she "*…didn't think I'd have to take tablets around my age now, or for when I first started them, because I was about 37, 38 when I started. I didn't think I'd take tablets that early in my life. You know, for every day you've got to have them constantly, I didn't think I'd start that until I was older.*" (I1)

Other participants wished for a wonder drug or cure, so they could come off their medicines. Kelly reported there was no other option but taking her medicines, "*Unless there was some drug that they could give you and they give you it as a time*

capsule thing, almost like a capsule in your arm that emitted this drug out so that you wouldn't have to think about it, because it's a daily reminder for me that I'm overweight and I've got diabetes…" (I1), whilst Gareth implied "*If you give me one of those [pancreas] without having to take all the anti-rejection tablets I'd go for one of those, but apart from that, and that's unlikely, then I'm quite happy with what I've got.*" (I1)

While James had felt relief to find he had diabetes, yet, reported, "*It was explained to me when I first got it, it was like opening a door, once you shut that door, the next stage is and then you shut that door, but you can't go back and open that door… And I keep saying well if someone's drinking, gradually that door's going to shut and then the tablets are going to run out. Whereas to me I'm still at door one. That's the way I think. Okay, the medication's changed but I keep thinking God that door's shut and then I'm regressing, then I'm regressing, isn't, yeah. I give up then, you know. That's why I fight it all the time*." (I2). He also said that no-one in his family (except his wife) knew about his diabetes because "*it's like if you've got a cold or you're not well and people start fussing, you feel worse. You think just go away and leave me, let me sniffle in peace.*" (I2) So it was no wonder that he "*hated*" SMBG because it reminded him he had diabetes.

Participants stated they often blamed their diabetes and their medicines if they were unwell or experienced side effects, as Karen's quote illuminates:

"*Early on in the week I was really quite bad but I put everything down, all the symptoms I get I go, oh it's my needle, oh it's my diabetes, oh it's my medication, and really it could be others things.*" (Karen, I2)

Whereas, Philip stated that his insulin was *"…stopping me from doing what I want, eating what I want and having the energy I want*" (I1) and that "*… I just want to get on with life. I don't want to be taking tablets; I don't want to be doing that. I want to be on boats, planes. I would have been still living abroad only for [the diabetes].*" (I2)

Patrick, as a result of taking insulin, had put weight on: "*…But if you're restricting your diet and you're still not losing the weight or you're putting it on, it does have a bad effect on you because at the end of the day there's not really much more you can do. You've lost a lot of the things that you could do. Like going out, socialising, things like that, you're sort of more confined to being at home, and probably one of the highlights of the day is your evening meal or something like that. So you want to eat what you want to eat, you don't want to be sitting there eating something you don't want to eat*."(I1)

Julie felt guilty about taking her diabetes medicines because: "*…you think oh well I'll have a sandwich, and then you go shall I have a cake, oh yeah I'll have a cake. But then as you're eating it you go oh no, I shouldn't be eating this. But it goes back to like I say because you don't feel it. You think oh well yeah nothing happened [no diabetes complications visible].*" (I1)

While Kelly felt "*a bit disillusioned, you know, and I think then I start to think well I'm taking these medicines and okay and it's good to see that they are stabilising my blood sugar, but I'm not really losing weight. I'm not able to lose weight*." (I1), and whilst she had high expectations of her new medicine, she reported "*it feels like failure of me because I really thought that I would have lost quite a bit of weight by now. And I feel like I've just gone to a plateau. It might not be the drugs fault, but it doesn't seem to be working as I imagined it would.*" (I2)

On the other hand Vanessa had positive experience from her new medicines as she explained: "*It's the freedom of not having to take it [insulin] three times a day. That's the only thing, and because I've lost the weight, my clothes have gone smaller as well. I've gone down a size, so that's made me happy. Although I'm not sort of over-rejoicing too much because I don't know whether I'll stop [taking liraglutide] or I could just put [my weight] back on I don't know*." (I2)

6.3.6 Routine and Coping Mechanisms

6.3.6.1 Medication Routine

Participants were given the opportunity to discuss about how they were managing their medicines on a daily basis or when away from home. Table 6.2 shows that many of them used a number of different methods to help them take their medicines as prescribed. Most participants explained these methods had become "*routine"*/"*habit"*, which was done "*automatically*", "*which doesn't take thinking about*" and gradually was "*ingrained*", "*instilled*" and "*embedded*" in them. Most of them associated taking their medicines with a specific time of the day like when they get up first thing in the morning, during meal time, or when having a drink. In addition, most of them identified a specific location such as their kitchen cupboard or fridge (for injectable treatments) or bedroom as to where most of their medicines are located. Very few associated their medicines with an event, like taking their injectable medicines shortly after they checked their blood glucose, as Alison explains:

"*See I wouldn't forget my injection, because I do my finger prick and my injection. I come downstairs, I wash my hands, put the kettle on, do my finger pricks and my injection, then get my breakfast.*" (I1)

or like James who said:

"*Well on my computer, which I go on everyday anyway, I have the boxes underneath, the box of tablets, this, that and the other. So first thing of a morning I always check my emails so there's the tablets*." (I2)

Most of the participants used plastic boxes to organise their tablets into morning, afternoon, evening and bedtime as appropriate to them. Some of them used large boxes which contained all the original packet of medicines or single strips of their medicines. Some of them used small boxes with compartments where they could place their daily tablets on a monthly, weekly or daily basis. Others methods included

jars or cups, blister packs from chemists, and folders with a medicine checklist. Those on injectable treatments used pencil like cases to store their medicine.

Some participants said they were dependent on others to remind them to take their medicines as the following quote illustrates:

"*If I didn't have him [my husband] I've been a bit fuzzyheaded if you like, nothing to do with diabetes …and so without him even reminding me when we're going on holiday have you got enough tablets to go away with, and so it's good that I've got him*." (Kelly, I1)

Whereas Kate explained "*I just remind myself, if I get hungry I'll get something to eat and then take the insulin*." (I2)

When participants were compared based on their routine practices over time, it became apparent that the amount and type of methods they used influenced their adherence levels (Table 6.2). Participants who were dependent on others to remind them to take their medicines were generally low adherent. Although, Keith's adherence level slightly increased at the time of second interview because his wife was also taking an injectable treatment (insulin) and, therefore, he said "…*it's usually just before we have our tea, I usually get a clip round my ear or whatever, I haven't taken this medication*." (I2)

On the other hand, those who established a routine where they took their medicines in conjunction with other events, such as SMBG, they were more likely to be adherent to their medicines. Often these combination reminders were mainly to specific medicines as Kelly's quote illustrates:

"*What I do is I always do my blood sugar because that's also next to my chair. I do my blood sugars and then straightaway, because I'm going to use the sharp bin, I take the liraglutide*." (I2)

Table 6.2: Routine and coping mechanisms/ strategies

Adherence Levels		Participants	Trigger	Self-monitoring	Storage/ system	Location	Going Out/ Holidays	Negotiation Skills	Treatment Injections	Number of injectable Treatments	Treatment Tablets	Number of tablets/ medicines	Words to describe routine
	Stable Low	Kate	Reminder by friend (I1,I2), Hunger (I2) Orders next prescription after runs out (I1)	When sympto-matic	Little tub with strips	Kitchen cupboard (tablets) Fridge (insulin)	Insulin purse in handbag	SE	BD to TDS	one	BD or TDS	3	
	Increased Low	Keith	Reminder by family (I2) SMBG (I2)	OD	Blister pack	Fridge (GLP-1) (I2)	In little bag		None to BD	None to one	QDS	10	*Automati cally*
	Stable Low	Karen	Place on kitchen table during meal or when cleaning dishes (I2)	Rarely	none	Kitchen cupboard/ work desk/ handbag (tablets)		SE inconve-nience	None to OD	None to one	BD or TDS	6	*Natural instinct, embedde d in brain, Automati cally*

	Increased Low	Edward	Post –it note in blood glucose diary, injects with meals, knows by packet shape and tablet size	*Daily*	Used to write down in diary	bathroom cabinet (tablets) Fridge (insulin)	Takes injection with him (I2)	Inconve-nience	OD to BD	one	*Various times*	6	*Just comes normal now, second nature, gradually ingrained*
	Decreased Low	Oliver	Takes with meals	rarely		cupboard next to dining table	Keeps in car (I1), used to keep in work (I2)	Inconve-nience	None to OD	None to one	TDS	4	
	Decreased Low	Patrick	Takes with meals, orders repeat prescription 1 week in advance	OD	2 Plastic boxes for morning & evening	Kitchen cupboard	Pill box, 2 compartments for morning and evening, spares	SE	BD	one	QDS and 2 tablets weekly	17	*Doing it without thinking, got to get organised*
	Low to Medium	Gareth	Orders next prescription before runs out, takes with morning coffee (I1), takes "*lot*" with meals (I2)	N/A	Weekly pill box, 4 compartments (I2)	Kitchen cupboard/by coffee mug	Pill box	Inconve-nience	N/A	N/A	TDS	7	*Automatically, doesn't take thinking about it*

	Low to Medium	Vanessa	Sets phone alarm but turns off (I1), injections when gets up, SMBG (I2)	OD		handbag			TDS to OD (twice)	two	BD	17	*automatically*
	Low to Medium	Kelly	Reminder by family (I1,I2) Takes before/after meals (I1), SMBG (I2)	random to od	Plastic box and injection on top (I2)	Next to chair usually sits is	Reminder by family for early prescription	Effective-ness	None to BD to OD	None to one	BD or TDS	*From 15 to 14 tablets*	*Will have to be good at my practice and routine*
	Missing to Medium	Philip	Takes when gets up (I1), SMBG (I2), when runs out leaves packages open (I2)	All the time	Monthly pill box, 2 compartments	Bedroom-by bed/ wardrobe	Takes spares/ requests early prescription	Concerns effective-ness	OD to OD and once weekly	One to two	unclear	*18 tablets to 8 tablets*	*methodical*
	N/A to medium	Daniel	Takes with meals, places on kitchen table	N/A					N/A	N/A	OD to BD	2 to 3	*Becomes matter of habit, force of habit*

	Medium Stable	Adam	Place pill box on windowsill- walking past can't help but see (I1), injects when gets up (I2)	BD to QDS	Pill box, 4 compart ments, sorts every 3 days	Wardrobe and dressing table (I1) Injection by bed (I2)	Overcoat/ wife's handbag (insulin), pill box. Checks clock/ adjust watch, writes down new timings	Inconve- nience	None to OD	None to one	BD or TDS	10 to 9	*Get used to it, repeating all the time* (I1), *easier routine* (I2)
	Decreased Medium	Irene	Takes with juice in the morning, coffee or milk in the evening (I1), injects after giving dog food (I2)	All the time	Weekly pill box, 4 compart ments	On shelf by kettle (I1), Shelf opposite fridge (tablets)/ Fridge (GLP-1) (I2)			None to BD	None to one	BD	12 to 11	*Ritual, Habit*
	Decreased Medium	Linda	Takes with meals	Rarely, when sympto- matic	Weekly pill box to 1 large box (I2)		In hand bag	Inconve- nience	N/A	N/A	TDS	8	*Instilled in me, feels like regular routine, don't dock watch*

	Increased Medium	Angela	Injects after morning shower	BD & when sympto-matic	Weekly pill box	Fridge (insulin)	Prio bag (insulin), adjusts timing	Effectiv e-ness	OD to BD	one	BD	4 to 3	*A way of life after a while*
	Medium to High	Robert	Takes with meals or milk or juice	N/A		Kitchen cupboard-out of reach	Never takes to work / when out of home	SE	N/A	N/A	BD or TDS	3 to 4	*Like a ritual, automatic ally* (I1), *more organised* (I2)
	Medium to High	Teresa		1-2 times per week to rarely			Leave at home (I1), takes on holidays-easier (I2)	SE	OD to once weekly	one	BD	7	*Easier when at home*
	Medium to High	Julie	Injects when gets up (I2)	Rarely to stopped		In pocket (tablets) (I1), Kitchen cupboard (GLP-1)		SE, inconve-nience	None to OD	None to one	BD	6 to 5	*Not hard, easy*

	Medium to High	David	Takes with morning tea and meals	None to 2-3 times per week	Large box for daytime tablets, blister pack for night-time ones, daily	Coffee table by bed (night time tablets)	Pill boxes in pocket for morning & evening tablets, night-time tablets leave in hotel room	SE	N/A	N/A	TDS	*16 tablets per day*	*Stickler, routinist, it's a system, get used to it*
	Medium to High	James	Takes after checking email in morning, places by fork whilst meal getting ready	Once a week	Jars for morning & evening tablets, daily	Under-neath computer	In wallet, extra if staying out	SE	N/A	N/A	BD	*4 boxes and 4 boxes*	*Handy, pure routine, set pattern, manageable*

	High to Medium	Christo-pher	Takes with meals and coffee, takes all at once	1-2 times per week to BD	Plastic beaker-daily	Cupboard, coffee table for morning tablets, kitchen worktop evening tablets	Extra tablets, keeps in hand luggage. Needs to get organised (insulin)	Inconve-nience	None to OD	None to one	TDS	9	*organised*
	High Stable	Alison	Self- monitoring, takes all at once (I1, I2) Injects after swimming (I2)	OD to BD	pill box, 4 compart ments, daily, insulin in fridge, GLP-1 in case	Left hand side of sink	In handbag (insulin, tablets), All-inclusive holidays so can leave in hotel room		BD to BD (twice)	One to two	BD	*Blood pressure, cholesterol Thyroid, water tablets [&T2D tablets]*	*automatic ally*

	High Stable	Andrew	Takes with orange juice, SMBG	BD	In a box	Kitchen (morning and evening tablets), bedside table (bedtime tablets)		SE	N/A	N/A	TDS	8 to 9	*Automa-tic, all organised comes natural*
	High Stable	Elizabeth	SMBG, takes all at once	TDS	Computer drug tick off list in plastic box, insulin case, daily	Kitchen cupboard (tablets), Fridge/ spares upstairs (insulin)		SE, effecti-veness	BD	one	BD or TDS	14	*Mentally you get used to it, second nature*

NB: OD/BD/TDS/QDS refers to “once”/“twice”/ “three”/“four” times per day as a direction for prescriptions.

Although the pill boxes helped participants in taking their medicines, those participants who used these boxes to assist them to count their medicines on a daily basis instead of every week/month were more adherent. In addition, high adherents were more likely to take their tablets "*all at once*" instead of taking some before, during and after food. Moreover, those who placed their medicines in a location that was visual helped to improve their adherence, as the next quotes demonstrate:

The ones I take of a night time that's upstairs by the side of the bed. So before I get into bed, I take that tablet then. (Andrew, I2)

"*But I keep them both [insulin and Exenatide] by, on the left hand side of the sink really just by the unit….*
[Interviewer] Why there?
Because that's the first place I go to of a morning. I come out of the door and go straight to the - where if they were on the other side of the room or something like that, it's more convenient it's straight ahead, first point of call." (Alison, I2)

Hence, high adherent participants can be defined as those who used a combination of methods including triggers associated with time, location, and event, as well as repeating their routine on a daily basis and placing their medicines in front of them. In contrast, those with low adherence levels often made comments about having to get organised after changes in their routine, as a result of new medication changes, being busy or "*when I've been away, and your routine's disrupted, you know, and you're just a bit out of sync for your everyday things*." (Linda, I2).

Furthermore, participants were less likely to be adherent to their medicines if they took their medicine(s) (tablet and/or injections) more than once or twice a day. Both Vanessa and Kelly improved their adherence levels, at the time of the second interview, after having to take less injections throughout the day, which they found much more convenient.

6.3.6.2 Self-Regulation

Self-regulation strategies were a result of concerns and experiences of side effects of medicines and forgetfulness. Although some participants suggested that their "*body got used to*" their medicine because they found that the side effects settled relatively quickly within 24hrs or two weeks, others had to change treatment because they could not cope with them anymore. A few participants resorted to taking over the counter/prescription medicines (laxatives, anti-sickness and anti-diarrhoea tablets) to relieve the side effects of their new medicines, and found that they were then more able to cope with them. Whereas, other participants persevered with the side effects for months and years, and others adjusted their treatment to make it less interfering with their lifestyle. The quotes below describe the effect of side effects on participants' life and adherence (see Figure 6.7):

"…the effect of metformin can upset the bowel terribly. If I take anything more than a 500 dose at a time I can't cope with it. My body doesn't cope with that… [so when on holidays] it's that changeover day that's the difficult one, you've got to think to yourself hang on what am I taking here. I can't overdose because if I overdosed on metformin I'd be awful for a couple of days but I try and work out the time difference." (Angela, I1)

"…when I was on the metformin I was constantly going to the bathroom, as far as bowels being loose. I've put up with that for years, you know, so I used to, if I had to go somewhere early, first thing in the morning, I'd take my medicine after I'd been where I needed to go, because I knew with the metformin I'd be in trouble." (Irene, I1)

"*I wasn't well with them… I mean to begin with it was fine on that rate, I haven't took them for the last week because I was getting pains in my stomach and vomiting not long after them. So I have stopped, and I know I shouldn't have but I have stopped them for the last week and that, because they're big tablets I've got to take.*" (Kate, I2)

"[Teresa] I don't tend to eat out as much as we used to for that reason [diarrhoea], because I don't know, I don't know if it's going to be something that I'm eating that's going to cause it. But apart from that…

[Interviewer] So it has affected your social life?

[Teresa] Yeah, yeah. Especially when we're away, because as I said when we went away in May, we were staying with friends and it was awful. It was, because it was the time when it was really bad, and I didn't want to go out. No, no, I'll stay in, you go out, I'll stay in. But it's alright now that I do manage and it's a lot easier." (I2)

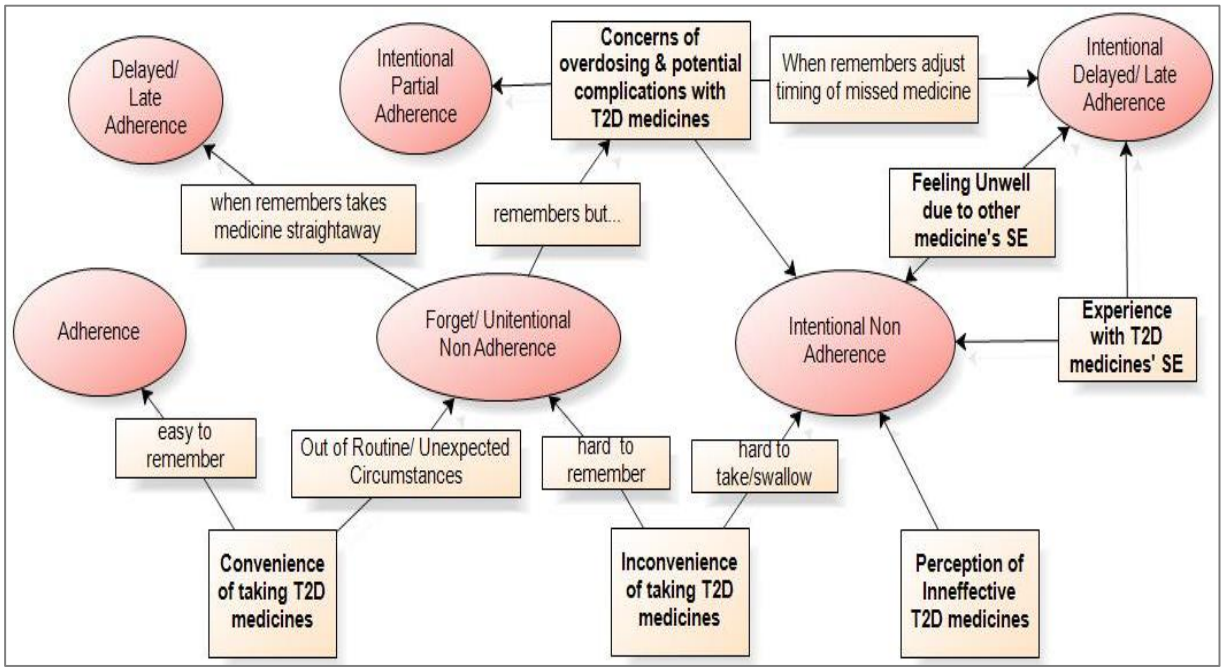

Figure 6.7: Patterns of Adherence

Participants reported they rarely missed their medicines, and therefore did not appear overly concerned about it. Also, few said they had no detrimental effects as a result of missing their medicines. Consequently, participants reported doing the following, which had an effect on how well they adhered to their medicines (Figure 6.7):

Angela and Gareth took their medicines later than instructed:

"*…when I'm cooking dinner and suddenly I'm sitting down and I think oh I haven't had my injection, that's the one which I have to have later then."* (Angela, I2)

"*And I come in the morning to get my next tablets out and I go oh bloody hell I forgot to take that one last night and the instructions are if you forget it, take it when you next find out. So I take it before I take my breakfast ones and that's okay with the doctor.*" (Gareth, I2)

Irene and Andrew did not want to take their medicine when they realised they had missed taking it at the right time:

"*I'd started doing the dinner, putting the dinner out, and I just sat down to eat. And I'd started to eat and I went I haven't done my injection. And [my husband] said well can't you do it now? I said no you're not supposed to. So I've left it, and that was the reason…I said I don't know what it'll do, they tell you to just leave it and just do the next one…*" (Irene, I2)

"*If I was out any length of time and I was getting back late, probably have a meal out and wouldn't take the tablets. But I'd just carry on as normal the next day. I wouldn't double the dose, just carry on with the dose. All right you've missed one part, forget it, carry on next, that's the way I do it.*" (Andrew I1)

More participants at the first interview reported forgetfulness compared to the second interview. Those participants who did not report forgetfulness at second interview had their levels of adherence increased over time from low to medium or medium to high (Table 6.2), with the exception of Elizabeth who was the only participant with stable high adherence levels.

6.3.6.3 Negotiation

Although not all participants provided examples where they had to negotiate changes to their treatment, negotiating skills were generally practiced when they wanted to avoid insulin treatment (see section 6.3.1.4), reduce the amount of medicines being taken, alleviate side effects from their medicines, reduce the risk of hypoglycaemia, or identify ways to manage them better (be more convenient or more effective) as the following quotes demonstrate:

"*I would like to discuss with the consultant about maybe just changing the oral medication a bit, and seeing if that helps the hypos.*" (Teresa, I2)

"*[the Diabetes Specialist Nurse -DSN] said obviously [liraglutide] can cause nausea so sometimes it's better taking it of a morning and then, because… you had to do it at the same time every day and that was what I was conscious of. So I thought I don't really get up at the same time every day, sometimes I get up very early and then sometimes I don't, but whereas I do tend to go to bed the same time of a night. And with me taking it in the day and starting feeling sick I thought well I need to change it. If I'm going to change it I need to change it right away. And I thought if I just do it of a night going to bed it might just be a bit easier with the side effects.*" (Karen, I2)

However, negotiating skills did not appear to influence adherence levels in these participants (Table 6.2)

6.3.6.4 Seeking information

Most participants read the leaflets that come with their medicines prior to taking their first dose. This was to become aware of the type of side effects associated with their medicine(s), any contraindications with other related health conditions and/or medicines they take, and what to do if they missed their medicine(s). Yet again, very few participants indicated they read the leaflet only after they experienced side effects, or forgot to take their medicine on time, as Elizabeth explained:
"*I don't actually read all the leaflets believe it or not, except when there's a problem, then I have a quick scan…*" (I1)

Participants suggested that when they encounter side effects with medicines or are made aware of the risk of complications, they tend to seek HPs' advice by contacting them on the phone. Yet, through the interviews, it was evident that they usually waited until their next appointment instead of contacting them right away.

"*I'm going to speak in detail to the specialist in September. I'm going to have a good chat with her over it. [The DSN] allayed my initial fears and put me a little bit more at*

rest. I mean I waited four or five weeks because I knew I had the appointment. It wasn't a knee-jerk reaction. I didn't just pick up the phone and say I want to come off this, I thought well what's another four or five weeks. I'm sure they must have been inundated with phone calls after that programme, which he said they were because there was that many people on the phone over it." (Oliver, I2)

Only those on insulin treatment seemed to contact their healthcare team when they encountered problems, particularly when it was related to adjustment of insulin dose as a result of hyper/hypoglycaemia, as Elizabeth suggests:

"*[The DSN] said we won't keep it for weeks on end, I want to see you here [in clinic] in two weeks and see how you're getting on, but I am at the end of the phone and you ring me anytime - which I do, because I don't pester her for no reason. She said if you want to know what to up [the dose of new insulin] to or lower it. She said you might find it's making you hyper because you're having too much*" (I1)

Internet and HPs themselves were the most common sources of information for participants. Of those who used the Internet, very few described using recognisable and reliable sources for information such as DUK, Patient Access and government websites related to diabetes treatment and driving licence.

6.3.7 Compromise and Perseverance

Participants conferred, through their beliefs, perceptions and experiences in taking their medicines, that generally there was no "*alternative*" treatment to diabetes other than taking the medicines they have been prescribed. Particularly with diabetes, they felt that there were few treatments available, as James indicated "*But you know, there's so few alternatives, it's either A or B isn't it with diabetes? We can give you another tablet, but once you've had so many tablets, there's nothing to do.*" (I2). This compromise about their diabetes treatment appeared to be strong among those participants who said they had no experience of side effects with their medicines.

In contrast, participants, mainly women, who had experienced side effects, indicated that they had (in the past) and would (in the future) "*put up with*" their medicines and "*persevere*" with their side effects to achieve diabetes control and/or weight loss.

"*Swings and roundabouts really, isn't it? I'm disappointed that I haven't [lost weight], but the fact that my blood sugars are better, that's got to be a benefit… You know, with all the complications that I could have with high blood sugars… it's got to be beneficial really, hasn't it?... I've got more energy, so you know, that's got to be worth something as well, hasn't it?... for all I was very unsure about going onto it originally, now I know even with the diarrhoea… It's a problem but I manage it, so I'd rather do that than come off it. Really. And if they said now to come off it, I'd be very reluctant to."* (Teresa, I2)

"*It would depend on the benefits I was getting from it. If I was getting good weight gain [means weight loss], then I know thrush can be treated and I know urine infections can be treated. If my bloods were abnormal, then I'd be more worried because I'd think my body's not happy with this really. But I wouldn't come off them straightaway, I would carry on, and I would imagine like thrush or UTIs would be treatable, I know they can be. If they progressively got worse and closer together, that's when I'd think maybe of saying well maybe I should come off it*." (Linda, I1)

Whereas a smaller number of participants, mainly men, suggested that "*no side effects the better*" so they would ask for a treatment change, if the side effects could not be tolerated, "*…because I can't see why your lifestyle should be changed. You know, why should you suffer if there's an alternative*?" (James, I2)

In addition, a few participants felt they had to persevere with the inconvenience of their medicines, specifically those taking insulin more than once per day, in order to get better diabetes control and improve/prevent deterioration of their kidney function.

Angela, who had missed her second insulin injection before dinner, when she realised that her blood glucose had improved with her new insulin regime, reported: "…*now I'm sort of quite elated that my readings are coming down and I'm not quite as thirsty as I was, I'll probably have more incentive of taking this injection and keeping it that way."* (I2)

It was apparent that participants' compromise and perseverance was a way of considering the risks and benefits of taking their medicines in order to achieve balance in their life. However, their acceptance about compromise and perseverance affected their adherence levels (Figure 6.7). Those participants who implied that they would not persevere with side effects were more likely to be medium to high adherents. Participants' adherence levels ranged from low to high if they persevered with their medicines' side effects for controlling their diabetes. However, those who persevered for the benefit of weight loss were more likely to be low to medium adherent.

6.3.8 Helpful and Unhelpful Support

According to participants there were mainly two key avenues of support for the management of diabetes. The most prominent support was that provided by HPs. However, equally, many participants valued the support from friends and family. A small number of participants, who had experience of injectable treatments, suggested that other people with T2D diabetes played an important part in giving them reassurance when they started those treatments. Most of the participants had a relative/ friend/ colleague who was on a similar injectable treatment. Furthermore, a very small number of participants found support in other organisations, such as DUK. Nevertheless, participants revealed experiences of both helpful and unhelpful support with regards to their diabetes management as seen in Figure 6.8.

The following sections will focus on participants' views of support they received from health care services, as this was the dominant issue discussed in both interviews. Participants' experiences of health care services varied, however all had accessed GP and PN support at some point since their diagnosis. Almost all of the participants in

this study had received support from a dedicated diabetes MDT in the community (i.e. a service located at a GP Practice/Health Centre) or at a SCDC. Nearly half of them had support from both their GP practice and their diabetes team, whilst the rest of the participants received care predominately by their diabetes team. Out of all participants, only Irene had experience of all three services.

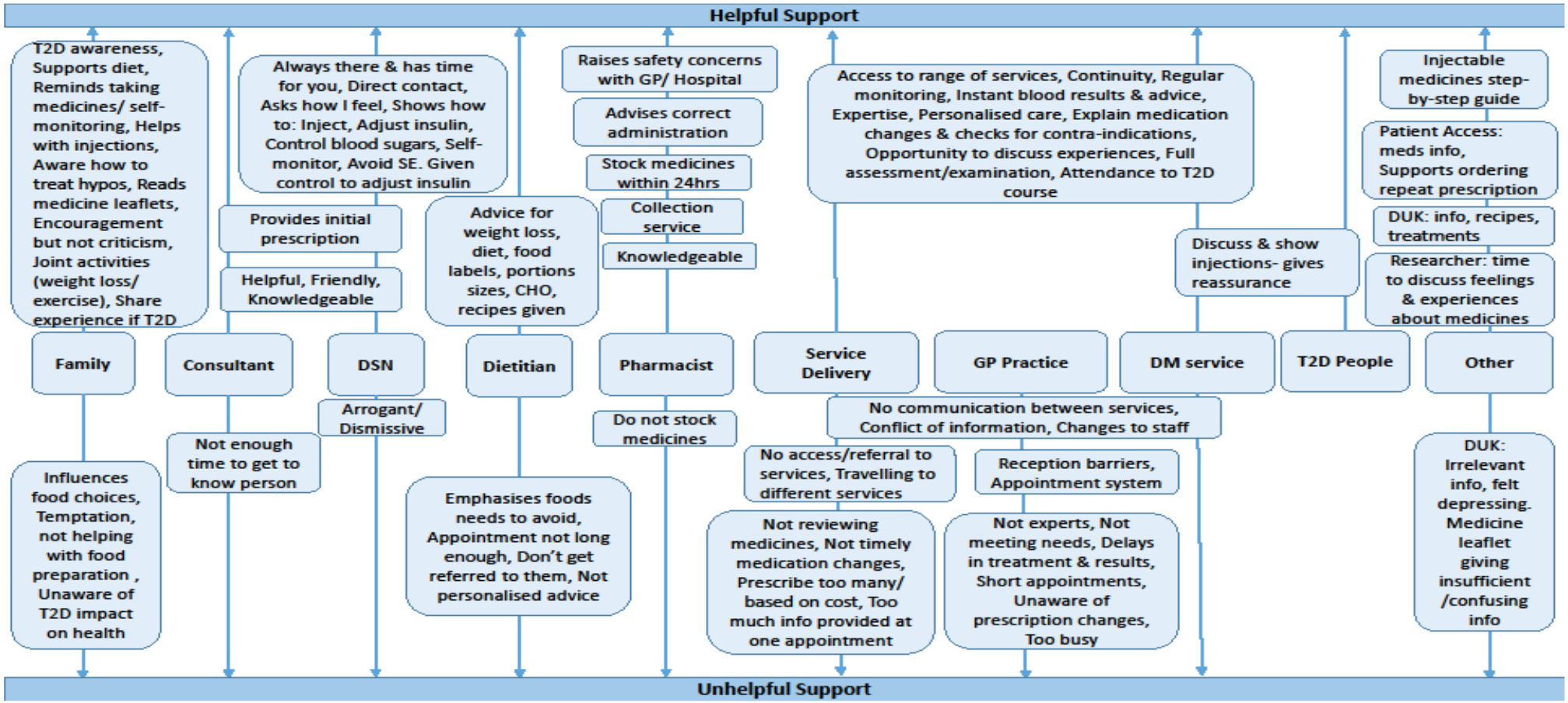

Figure 6.8: Examples of Helpful and Unhelpful Support (CHO= Carbohydrates)

6.3.8.1 Unhelpful Support

Participants often discussed their views about NHS care provision as a whole. They commented on the constant staff changes and NHS cutbacks, but equally how staff are "*inundated*", "*hard pushed*" and do not have the time to give to patients, as a result of the increased prevalence of diabetes. They understood that taking too many medicines and monitoring people with diabetes is "*costing millions*" for the NHS. Participants who experienced care provision from a diabetes team outside of their GP practice, suggested that GPs and practice nurses are lacking the knowledge and expertise in treating patients effectively. They are often unaware of available new diabetes treatments or if any changes were made to participants' treatment by their diabetes team. This resulted in being referred to various staff within the practice producing feelings like "*getting pushed from pillar to post*" (Keith, I2) and without any satisfactory outcome and delays in issuing repeat prescriptions.

Part of the problem was also staff attitude, mainly that of the receptionists, who were found to "*have too much to say*". For example, David gets annoyed "*when the receptionist sitting there says to you 'what do you want to see the doctor for?' ...why should I tell her what's wrong with me when she can't give me any medication, she can't diagnose what's wrong with me*." (I1). Whereas, Oliver said "*I'd have dispensed the prescription and then I get a phone call from the receptionist saying the doctor's not giving you that [new medicine]*" without giving any reason, despite the medicine having already been prescribed by the hospital doctor (I2). Such delays inevitably meant delays in managing their diabetes efficiently.

In their view, doctors "*watch money*" and were "*penny pinching*", so they "*outsourced*" diabetes services in different locations. Philip said that "*somewhere along the line there's two lots of people being wasted*." To explain this further, he said "*I don't know why my own nurse up there [GP practice], why should she test me up there when they've got one here [IMC diabetes team]? ...I could go to [local hospital diabetes centre] and get it all done. And the only reason we don't go up there is money. It's too expensive for me to go up there. Yeah. So why is it there?*" (I2)

Furthermore, doctors seemed to focus on prescribing "*cheaper*" medicines to save money for the NHS, "*albeit [these] might not be cheaper in the long run*" (Linda, I1), because they either take longer to become effective, or are ineffective from the outset. On the other hand, Patrick suggested that due to the problems with repeat prescriptions and lack of medication reviews, there was a lot of waste of prescribing drugs. He provided an example of what had happened when he ordered his repeat prescription after he had received a prescription for his new medicine linagliptin from the diabetes doctor,

"*So Friday I put the request in for my month's supply of tablets and I didn't tick the box for the sitagliptin [old medicine]. But when the doctor's done the prescription they'd put it on…. they haven't put the other one on [linagliptin], because they still hadn't the letter from here [diabetes team] to say they've changed it… So that'll go to the chemist now and the chemist will put it [sitagliptin] in the bag and I take it home, it's just going to be wasted, end up going in the bin. You know, if that's happening with everybody it can be very expensive*" (I1)

Overall, there appeared to be three key aspects which are relevant in contributing to delays in reviewing participants' diabetes and treatment(s), which situates under the umbrella of clinical inertia. These aspects include the NHS service organisation, the HPs and the patients themselves. Figure 6.9 shows how these aspects are interlinked.

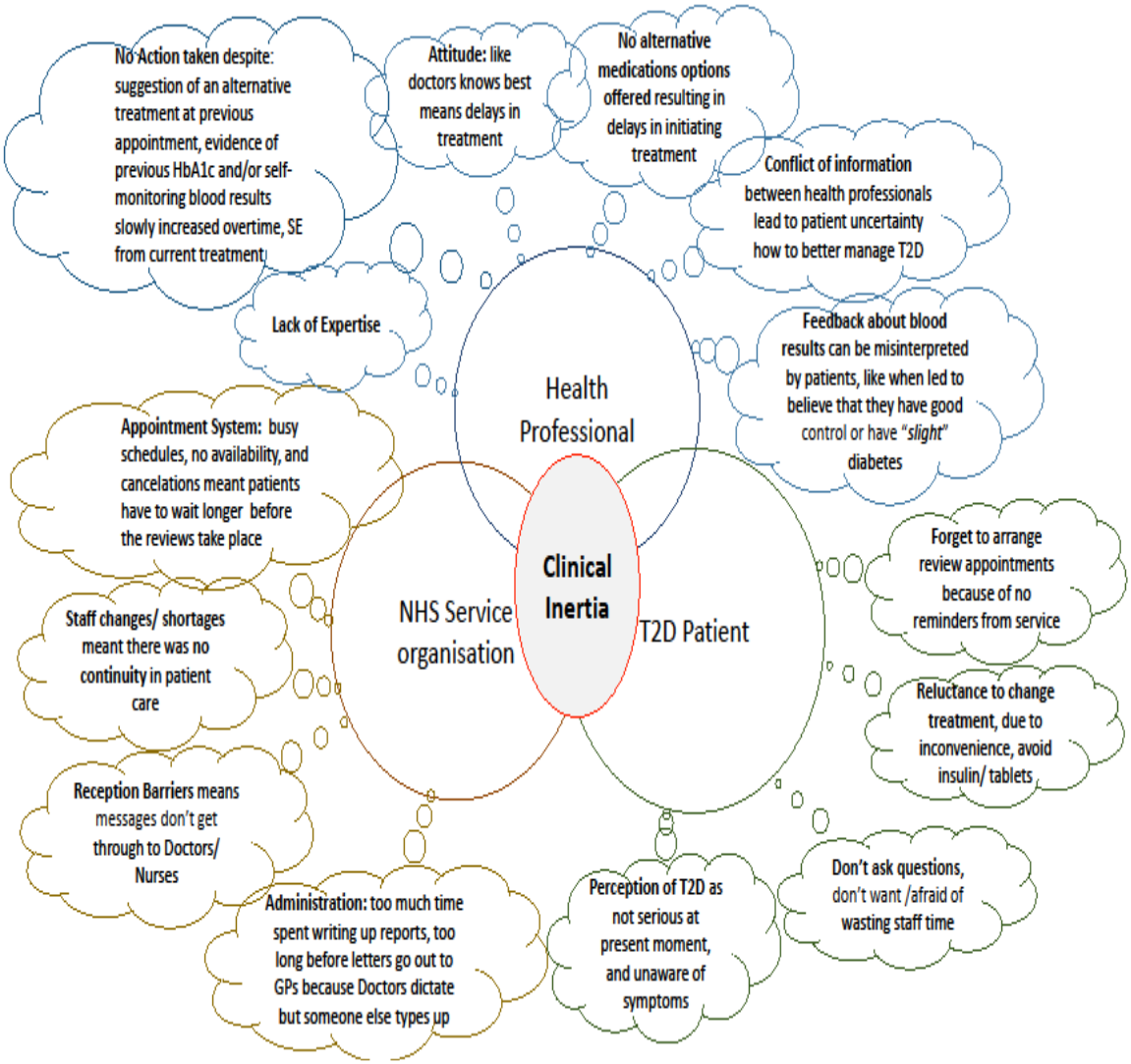

Figure 6.9: Interlinked reasons for clinical inertia

6.3.8.2 Helpful Support

It was clear from participant's discussions that there were certain vital features which determined satisfaction with the support they had received. Figure 6.10 shows the suggested model of care in T2D management. As expected, experience of helpful support formed suggestions which they deemed useful for future support for themselves and others who are prescribed the same type of new treatments they had received.

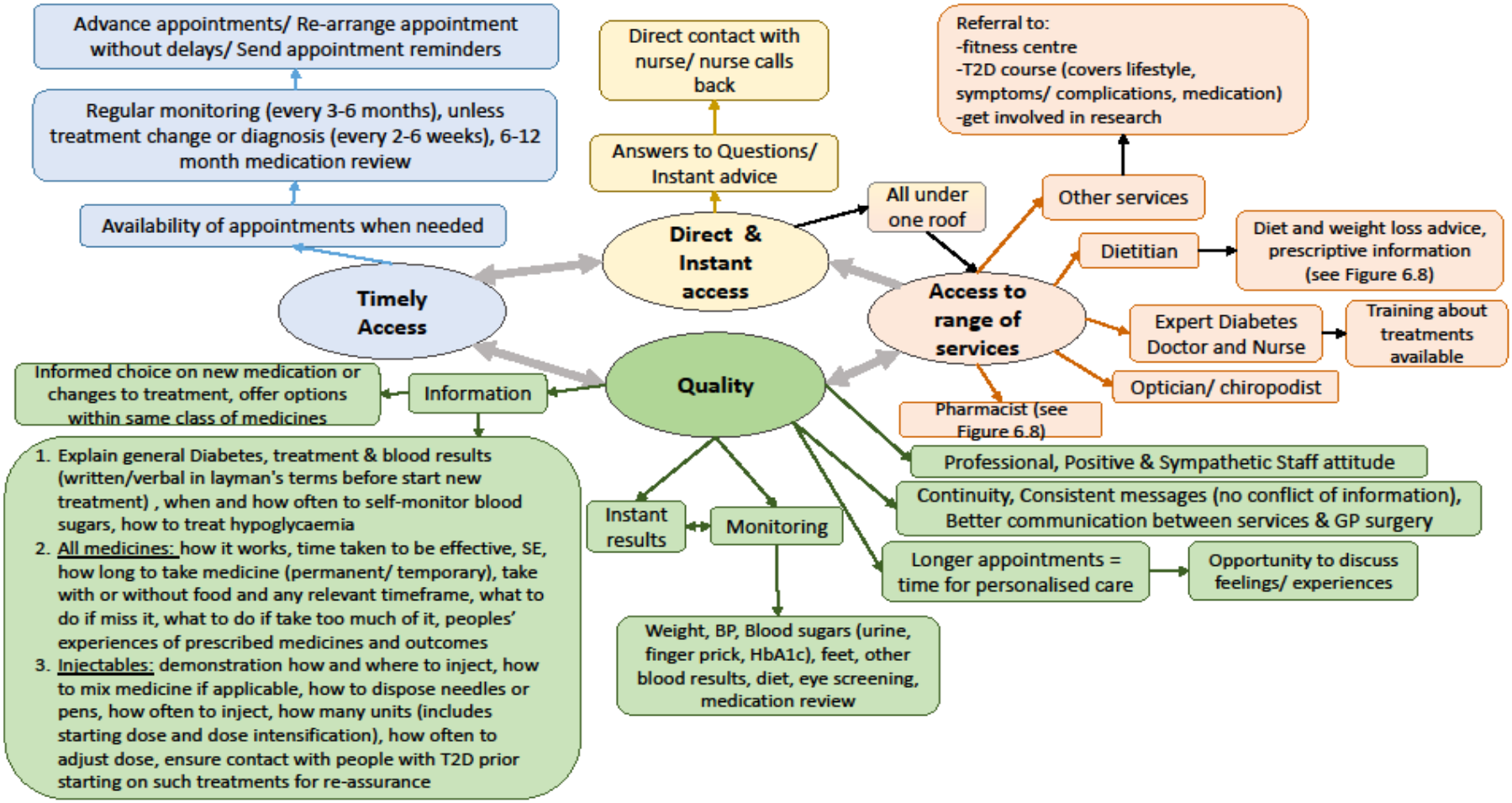

Figure 6.10: Model of care in T2D management

Participants wished for access to a range of services and HPs which had a focus and expertise in diabetes. Furthermore, referral to other services and access to research involvement was also thought to be helpful for participants. Accessing or being referred to these services was thought to be "*a good back up*" (I2), as Daniel and others reported, because, as Irene suggested, "*each one [of these professionals]… is for a different thing, so fills in the gaps if there's anything missing. Because from what I can see you all work together, so everybody knows what everybody's doing, which is a good thing*" (I2). So, the benefits of using such a service meant that the team would communicate with each other, as Irene implied above.

Also, the need for direct access was another key issue surrounding these services. Direct access represented services that were provided in one place/location. It is important to note that for most participants the exact location did not matter, for example whether close to home or at hospital, as long as they had access to these services. Opportunity to access the range of HPs gave confidence to participants about management of their diabetes, as Patrick indicated:

"*So… when they refer you to someone else, it's someone in the next room, so you can see them straightaway. …so instead of saying will you see somebody and then you've got to wait two months before you see them to get an appointment, with them everything's like compact. It seems to work well together.*" (I2).

In addition, Patrick said "*when you come to the Diabetes team they allow you a half hour appointment, so you're in with them for half an hour, they do your tests. Then you'll go in to see the [nurse], if you're seeing the dietician you're allowed a half hour appointment with her. Then you've got an appointment with the doctor. So you've got an hour and a half and all three are done, and it's explained to you. So by the time you get to the doctor you've had the chance to think about what the first one said, and if there's something you're not clear on, you can then ask the doctor. So you get all your information in one day.*" (I2)

Moreover, direct access was discussed in relation to day to day management of diabetes, and problems encountered with their medicines or with their blood glucose. Direct access, therefore, was also meant to be instant access to these services, in order to get instant advice and answers to their questions, as Julie's quote demonstrates:

"*But having a contact number and someone that you can call, that's the key isn't it? As long as you can speak to somebody it's not necessarily 'oh I'll have to come in and sit and see you and talk for an hour to you', if you've got a contact number and just say this is happening, you know, just someone to say oh yeah that is a side effect, oh yeah, it's fine, then it's putting your mind at rest, isn't it? That's all people want at the end of the day. They don't want to phone an answering machine, we are sure to phone back, and they don't want to hear that, you want a human voice, and preferably someone from the diabetic team who knows what they're talking about, yeah*." (I1)

This was in contrast with their experience with their GP practice, as participants describe:

"*Now you can't ring your GP practice up and say can I speak to the nurse; you've got to make an appointment to see the nurse. And you could be dead – which is true.*" (Alison, I1)

"*I know sometimes when I've been in, you know, the doctor said she doesn't deal with [diabetes] and she'd have to go away and then there'd be a good long wait before they came back, or I'd go home and get a telephone call a lot later*." (Linda, I1)

Direct access was therefore linked to timely access, which meant patients could access the services when needed. Delays in arranging review appointments were often disappointing and frustrating, as Robert explained:

"*So I went halfway through May to get the blood form and try and make an appointment, 'oh we haven't got any appointments until June for this'! So I don't think*

in a way they've helped, because I'm trying to not bother them and trying to organise it and do it at the three months stage, early enough to get the blood results back, allowing a week and then make the appointment, and they've said there are no appointments available until a month after that…. Then if you go and try and do it in a month in advance 'oh we're not doing appointments now'! So it's one of them sort of thing, why? …Because I've done the blood test… so it's over a month ago. I'm none the wiser [whether the medication is working or not]." (Robert, I2)

So timely access was considered when appointments were given *"…in advance. When you go to the clinic, your next appointment is given to you there and then. So it isn't as though as you are waiting for an appointment to come through the post*" (Alison, I1). Alternatively, a reminder system to patients to make their appointment was proposed as helpful, as Elizabeth mentioned about the diabetes team at her GP practice, because "*They write to me and say it's time for your review, so it's very well organised*" (I2). Also, appointments could be re-arranged with "*no ifs, no buts"* as David said "[*when*] *I thought my appointment was the 16th August and I come, [but] appointment on it was the 16th September. I said 'oh no', but I had to get a letter with the needles and what I carry for the going abroad in case they pull me. And they were fine, no trouble, they got me the [letter on that day].*" (I2).

Timely access was also when there was an appropriate timeframe between diabetes and medication reviews. Hence, yearly diabetes reviews were deemed too long and careless, as Andrew said: "*I only go once a year [at my GP practice]… this is stupid once in twelve months. It's like I could be dead within that twelve months, you know, you wouldn't know nothing about it! No difference just once a year… I don't think they're really bothered.*"(I2)

Regular monitoring was favoured because it meant that any changes regarding their diabetes symptoms/complications could be "*nipped in the bud*" (Kelly, I1). Oliver said "*I'd like to be every three months, you know, me personally, because again when I was first diagnosed I was going every three months and I knew for most of them three months I'd have to look after myself, my diet like... And then when I went to six*

months, to me it got progressively worse because I know no one's watching me like…" (I1). Whereas, Kate explained that "*So more I see people the more encouragement [I get]*" (I1). Hence, most participants suggested a timeframe between 3-6 months would be appropriate, unless there was a change in medication, and therefore, more frequent contact would be preferable, as James explained:

"*[the diabetes nurse] said well we'll try this new one [tablet]… and that's the first positive thing anyone's ever really done rather than just keep giving you tablets, …I'm back next week so she's monitored every six weeks which is not leaving it three months, six months. So it's every six weeks. So I feel as if someone is monitoring what I'm doing. So it's quite good.*" (I2)

The frequency of the appointments was related to the type of treatment initiated, so those on injectable treatments, particularly on insulin, expected to be reviewed much more frequently than those on tablets. Christopher mentioned that,

"*Originally I started coming, it might have been a fortnight then, but I phone up meanwhile to give my readings to whoever's on duty, and they'll tell me over the phone if I need to up [the insulin units]… So we have corresponded on the phone, and every month I actually come here to have a chat with the girls. So it's not just monthly, it's weekly on the phone or every two weeks, so yeah I've well looked after I think*." (I2)

However, participants felt that if they were confident their diabetes was in control and they had no problems with their medicines, they would be happy to be reviewed less often.

"*I come [to the diabetes service] on a regular basis or I see my doctor on a regular basis and I don't expect to be there every other day or every other week or every other month. As far as I'm aware every six months… I come here and get my eyes photographed to make sure they're okay, I get my feet and blood pressure and stuff*

checked, blood sugar levels…, and they tell me I'm okay and still alive and heart is still beating regularly so, can't be better with life." (Gareth, I2)

Most participants, in general, were disappointed that medication reviews were not performed yearly, as they hoped for, or not at all. Conversely, Elizabeth was the only participant who was pleased with her medication review because "*that does happen about every six months roughly*" and "*We've knocked out quite a lot of drugs with [my GP].*" (I1)

Another key issue about helpful support was the quality of the service they received. Quality included the type of monitoring taking place during their appointments (Figure 6.10). It appeared that the more aspects were examined, the service provision was of better quality. However, one significant aspect of monitoring was that they could receive instant results, as Linda indicated "*[the diabetes team] tell you the result of the blood that morning when you see the consultant or whoever you see. So you know the bloods there and then rather than waiting for them."* (I2).

Furthermore, quality was related to the time available given to patients whilst on their appointment. Longer appointment slots were favoured in contrast to short GP practice appointments where "*You went in, cursory talk, check whatever, and out*." (James, I2). Participants who experienced longer appointments perceived that staff had more time for them. They had the opportunity to discuss their experiences with their diabetes management and their medicines, and receive further information about their diabetes which they found educational and informative.

As suggested above, the format, type and amount of information participants received about their diabetes and their medication was, also, a characteristic of quality. Figure 6.10 shows all aspects of information participants found useful, as well as suggestions for future support. Informed choice about new treatments and/or medication changes was very important to them, since "*I know where I stand*" (Edward, I1) and "*[staff are] not going to leave you in limbo… they are going to make it better.*" (David, I2). Informed choice helped to gain trust in the staff and, as Adam

illustrates, *"…if you feel that they're confident it reflects on you as well… and I felt confident with the doctor because I felt he was just giving me a professional honest opinion*" (I2)

Alison said that her doctor "*put it to me that it was entirely up to me [to try the new medicine]… That it was my decision and that made a really big difference… And even at the end he said, you know, if you're not going to be happy, you don't have to do it. Which, you know, the ball was in my court then.*" (I1)

Christopher, too, felt the staff "*don't push*" (I2) about starting his insulin injection. However, after experiencing his insulin treatment, he was wondering whether there were easier insulin options from the one he was prescribed, because his friend "*…had a pen, and … it's just a click, like a fountain pen and that was his injection. I stick mine in and say count to 10, but his was literally seconds… [but mine] you've got to shake your pen, get the liquid all mixed up*" (I2)

In addition, having confidence in staff meant that participants valued when staff were happy with their progress/management of diabetes, and were able to cope better with their diabetes. Otherwise, as Gareth said, "*Well if they were unhappy there would be something pretty wrong wouldn't there…*" (I2)

Participants mentioned that being aware of potential side effects of their new medicine has helped in coping better with them, like Robert, who realised he was having a hypoglycaemic episode during work, because "*I was told I might have hypos [because of new medicine]… so it was like sort of 'oh' this must be what it was… So now… I'm more organised with work…*" (I2).

Yet, Oliver, echoing some participants' concerns, said that "*too much information is bad because if you're overloaded with it, you're not taking it in*." (I2). Christopher, also, said that when "[*the Specialist Diabetes Doctor] told me bits and bobs [about the insulin]… I didn't take it in that much because [I knew] I'm going to have another*

talk, I'm going to see the products and the diabetes team was going to go through it with me [again]..." (I1)

Moreover, participants revealed situations where they felt the lack of continuity had an impact on their diabetes management, "*because when you go to hospital and you see a consultant you might see him once and then you don't see him again. You see all different doctors after that. And they don't bother looking at your notes or asking you, talking to you, or nothing, so you, they don't know you and you don't know them. So when you go to see the same doctor they get to know you and you get to know them so it feels, it feels a lot more comfortable. You're at ease so you don't feel as stressed….when you're seeing different ones you're like, you're getting different things said to you, like one will say one thing and then you'll tell another one what they've said, and they'll say 'no, don't do that', or 'that's wrong'. Whereas, if you're to see the same one you're getting the same story all the time so, that's better."* (Vanessa, I2). Adam, like others, who had a similar experience of contradicting advice between diabetes nurses, was wondering whether "*I've had two years of being wrong… and [could] the diabetes attacked the nerve endings..."* (I1) resulting in permanent heart failure. Whilst Patrick, at both interviews, expressed that the different services he had accessed for his diabetes and his kidneys "*don't seem to be on the same wavelength*" (I2) with the Doctors at his GP practice. As he put it, "*Different doctors have different ways of doing things*." (I2) and "*the problem with dealing with too many people, if one doesn't agree, nothing happens.*" (I1)

Continuity from staff who were viewed as "*professional*", "*positive*", "*understanding*" and "*sympathetic*", helped participants to feel confident in managing their diabetes, as Karen and Angela describe:

"*knowing that they understand the feelings that you're going through and the symptoms that you have and, [that] it's a difficult stage in your life learning how to do injections and stuff, but they always make you feel like the support is there if needed.*" (Karen, I2)

"*Because when you come in and you are spoken to by the diabetic nurses or the doctors …you are an individual you are not a number and that's important. I've been very comfortable with every aspect of it. …I'm treated as me, not a diabetic. …I'm not number 43 on the list this week, I'm me, and that's what I've always felt…. Their whole attitude of speaking to me as me, and speaking to me as though I've got some intelligence and not speaking to me as though I'm dim. And they know that I can possibly manage whatever medication I'm taking… No, it's just personal, which is good, and that's all I can describe it as really. "* (Angela, I1)

It is no surprise, therefore, that those who had experienced care from a "*well organised*" service, specific to diabetes, with direct, timely and instant access to HPs, and of quality, appeared satisfied with their care. These participants felt they had been "*well looked after* "and received excellent support. Nevertheless, it is important to note that all participants elucidated that the management of T2D is "*down to individuals to say 'right I've got this [diabetes], I've got to fight it'… [and don't] abuse the diabetes by eating a box of chocolates or having ten pints of beer*", (James, I1). Individuals' "*mindset has got to be there*" (Julie, I2) and be prepared to make lifestyle changes, to "*take… notice*" (Gareth, I1) of their health, and *"…need to listen, to read and ask questions*" (Irene, I1), and "[*don't] muddle on and …think 'I'll wait until I see [staff] next time'*." (Alison, I1).

Individuals should "*just raise [your questions] and it will get sorted for you*" (Edward I2), "*and take somebody with you [at your appointment, as] two minds are better than one*" (Christopher, I1). Also, individuals should "*Let the partner know what [medicine's] for and how it will affect you…, you'll benefit from it in the long run*." (Keith, I1). "*People should take the opportunity to do [research] because I think it's really good.*" (Karen, I2). Individuals starting insulin injections were advised *"…if you know somebody that's on insulin have a little talk with them. And I think you will find out it's not as bad as you imagine*." (Christopher, I2) and "*be patient and don't think oh my god what's going to happen now… it will work out… Not going to happen overnight*." (Angela, I2).

6.4 Summary

The qualitative research aimed to answer two of the research questions as stated at the beginning of this chapter. Findings have shown, that regardless of the type of treatment that participants had received (lifestyle/medicine), they all explained that these treatments have not worked for them, and that staff (doctors/diabetes staff) were having to keep adjusting their treatment until they got the right one for them. Yet, the constant changes to their medicines had a negative impact on their emotional well-being and raised doubts towards the effectiveness of their medicines. Whether medicines were perceived as effective or ineffective, most participants implied that medicines were a temporary measure for controlling diabetes and/their body weight and, therefore expressed a perceived need to stop taking them.

Participants were aware of the potential complications of their diabetes despite most of them reporting that at the present moment their condition was not serious. In the hope of taking less, better, efficient and effective medicines both for their diabetes control and body weight, all participants accepted their new medicines considering the potential risks associated with taking such treatment along with the rest of their medicines. However, participants were in favour of medicines that can be taken at home, do not interfere with their work or when going out, and were easy to fit into their routine. In addition, preference was given to medicines which were taken only once a day, particularly taken at breakfast time or first thing in the morning, or flexible without being "*tied down*" to certain times, and not necessarily taken with food or having to adjust their eating patterns. Participants who were faced with the possibility of coming off some of their medicines therefore felt relieved and happy.

Nevertheless, participants engaged with a number of strategies to cope with the inconvenience, side effects and potential complications of their medicines, however even with the best attempts adherence to medicines was not optimal. Participants' adherence levels were more likely to be high when their medicines caused less side effects, were convenient and when they used a combination of methods as part of their daily routine.

Although, generally, participants expressed positive experience about their health care they received in relation to their diabetes, they raised issues which they considered unhelpful and detrimental to their health. Hence, when participants experienced a range of dedicated diabetes services, it gave them confidence that they received appropriate and professional advice. Despite acknowledging that they, too, have responsibility in managing their diabetes, they felt far more motivated to make changes when they were under the care of a diabetes team. Therefore, health care that provides timely treatment changes, timely repeat prescription changes, regular monitoring, instant advice, adequate time to discuss experiences and time to get adequate information would help to ensure diabetes treatment is effective (diet/meds) and get better control of diabetes faster. The sooner their diabetes is under control, the sooner they can lead a normal life.

The next chapter will combine the findings from quantitative and qualitative chapters. It will provide a discussion of the findings overall comparing and contrasting the two sets of findings, along with the findings of the systematic review.

CHAPTER SEVEN: DISCUSSION

7.1 Introduction

This chapter brings together all the results from the systematic review, and quantitative and qualitative chapters following mixed method analysis. It addresses the following questions:

1. How do the expectations, beliefs and attitudes of people with T2D towards different diabetes treatments that either promote weight loss, are weight neutral or result in weight gain, change over time?
2. What is the impact of this change on patients' adherence to their medicine(s)?
3. What type(s) of intervention(s) promoting treatment options, focusing on effects on body weight, are acceptable to patients in order to increase their understanding of their diabetes treatment and improve adherence?

The chapter presents the key issues emerging from the study. Two models were developed to explain the phenomenon of medicine taking behaviour in people with T2D. The first model represents the factors that influence perceptions and beliefs about diabetes and diabetes medicines and their impact on emotions, confidence in self-managing diabetes and adherence (Figure 7.1). The second model represents the spectrum of adherence for people taking T2D medicines (Figure 7.2). Underpinning theory and recommendations are presented in light of the findings. The strengths and limitations of the research study are covered here too. This chapter concludes with the implications for policy and practice, and directions for future research.

7.2 Key Findings

The findings of this study support some, but contradict other findings of previous studies looking at patients' perceptions, understanding and experiences of managing T2D. Furthermore, it offers unique insights by identifying factors associated with successful and unsuccessful use of T2D medicines, which may impact on adherence. Findings from the questionnaires, interviews and systematic review are supported by referring to key sections discussed in previous chapters; these are in parentheses.

7.2.1 Setting the context

The research study was taking place at a time of major reforms to the health and social care system, most significantly the transition of PCTs into numerous (diverse in size) clinical commissioning group [CCGs]. These are responsible for the commissioning of secondary and community care services based on the needs of the population they serve (Naylor et al., 2013), including that of T2D. At the time, there was some uncertainty of how these would operate and which services they would provide. In this study, there was evidence of an increase in uptake of services provided by multidisciplinary teams outside hospitals, which were situated within GP practices or health centres. However, the participants of this study appeared to be a good representation of patterns of care at the time. The most commonly prescribed new medication in this sample was GLP-1 agonist injections (36%), followed by insulin (24%) and DPP-4 inhibitors (19%), consistent with current prescription trends for diabetes during the recruitment period between 2012 and 2014 (HSCIC, 2014). Those participants in the weight reducing group were mostly women with higher BMI than the other two groups, probably reflecting guidelines that advise that GLP-1 agonist use should be mostly considered in more obese patients (NICE, 2009a). In addition, the weight reducing and weight neutral groups had significantly lower HbA1c levels than the weight increasing group, suggesting that different medicines are prescribed for different patient groups (Wei et al., 2017).

The median HbA1c of this group prior to initiation of their new medicine was 77mmol/mol signifying that there was already a delay in escalating glucose-lowering therapy (NICE, 2009a). According to the national diabetes audit (HSCIC, 2016) approximately 66% of T2D patients achieve an HbA1c below 58mmol/mol, however, this value could be overestimated, as there was a huge variation in the number of practices participating in the diabetes audit between 2012 and 2014 (70% in 2012-2013 and 57% in 2013-2014).

Furthermore, there is substantial evidence of clinical inertia when initiating oral glucose-lowering therapy, which in effect delays initiation to insulin therapy (Peyrot et al., 2010). In the UK, some people with diabetes remain on OGDs for a median time

of 7.7 years, despite having poor glycaemic control (Calvert et al., 2007; Khunti et al., 2013). Much of the discussion surrounding clinical inertia has focused on delays in insulin initiation and intensification by identifying a set of separate barriers related to patient, clinician or system levels (the latter mainly due to time constraints and insufficient guidance through clinical guidelines) (Khunti & Millar-Jones, 2017). However, evidence is lacking from patients' perspectives of delays in diabetes treatment(s). As seen in chapter 6 (6.3.6.1, Figure 6.9), one aspect that has not been considered is that of the NHS service organisation, in particular the lengthy administration systems, staff shortages/changes, reception barriers and appointment unavailability/cancelations. Most importantly, participants' interviews revealed how such barriers are interlinked with that of clinical and patient–level barriers. Therefore, considering the impact of chronic hyperglycaemia and the development of possibly irreversible complications in T2D (Inzucchi et al., 2012), tackling clinical inertia should be a key goal to help optimise treatment.

The key findings of this research are as follows, and are discussed in detail in subsequent sections:

1. Participants' views of their medicines and diabetes seriousness change over time (section 7.2.2).
2. Overall, participants were ambivalent about the effectiveness of the treatment for their diabetes and body weight (diet/medicines) (section 7.2.2).
3. The type of medicine initiated and subsequently experienced could influence the appraisal of such medicines in management of T2D (whether effective/ineffective) (section 7.2.3).
4. Most patients would accept new medicines if they portray a dual purpose, most importantly weight loss and/or reduction in number of medicines/doses (section 7.2.3/7.2.3.1).
5. Adherence to diabetes medicines is suboptimal and levels are influenced by perceptions of medicine's effectiveness, concerns and convenience, experience of side effects and everyday practices (self-efficacy levels) (sections 7.2.4-7.2.6).

6. Perceptions of blood glucose levels and lack/excessive self-monitoring could hinder appropriate management of diabetes and weight loss (section 7.2.7).
7. The level of support from health professionals, family and other people with T2D can have both a positive and negative impact on perceptions and adherence to their medicines and lifestyle (section 7.2.7).
8. Complex interventions focussing on individual and health service delivery, and utilising theory, could help improve T2D management and adherence (section 7.2.7-7.2.9, 7.3).

7.2.2: Perceptions and beliefs of diabetes and diabetes medicines

The systematic review and the qualitative part of this study showed that perceptions of seriousness of T2D change over time (Figure 7.1). The systematic review (2.4.2.1) and other previous research (Monsier-Pudar et al., 2009; Majit-Ariss et al., 2013) focused on the relation of this perception to the type of treatment patients received, for example insulin was considered as the "last resort". In addition, the quantitative part of the study showed that participants generally had strong perceptions about the necessity of their new diabetes medicine for the duration of the study (5.5.3.1), a finding similar to a cross-sectional study by Aikens and Piette (2009). However, the qualitative part of the study uncovered that despite the acknowledgement that T2D is a serious condition, for the majority of participants it was not perceived serious at the present moment (6.3.1.5). Seriousness was heightened by the presence of debilitating symptoms or complications, increase in number and/or changes to treatment as a result of consistent high HbA1c test results or unstable/high blood glucose, and type of support received by HPs in primary/secondary care services (Figures 6.2-6.3). In addition, seriousness was lessened by reprioritising other conditions due to a negative experience or other external factors, such as comparing themselves to important others. Most of these findings are comparable to other research (Lawton et al., 2005b; Morris et al., 2011).

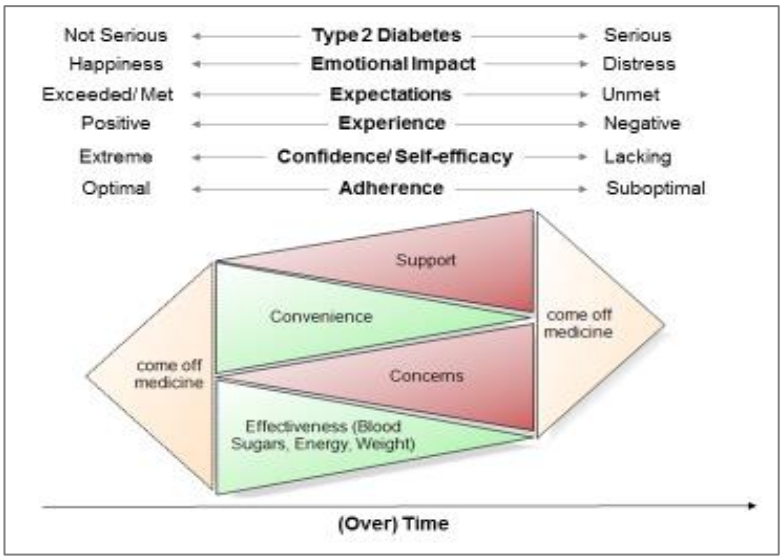

Figure 7.1: Conceptual Model on key factors influencing beliefs and adherence to medicines over time

Although in this study beliefs relating to the necessity, concerns, benefits, harm and overuse of medicines remained generally stable over time, there were variations within the whole group and weight-effect groups. For instance, participants felt strongly that their present health was dependent on their new medicine, however, this was not the case for their future health. Furthermore, there appeared to be an increase in uncertainty that these medicines would protect them from becoming worse or that they would be very ill without them. Surprisingly, only 19% of the weight increasing group had stronger beliefs about the necessity of their new treatment at follow-up, although the majority in this group were prescribed insulin treatment, the agent considered the most effective for lowering blood glucose levels (1.6.9, Table 1.1). Recent qualitative research showed, too, that majority of patients did not expect they would need additional medications for diabetes in the future (Fairchild et al., 2017)

Ambivalence about the necessity of diabetes medicines was found in interviewees since most of them reported ambivalence in their medicines' effectiveness, coupled with the experience of constant changes to their treatments since their diagnosis. Hence, ambivalence was related to the duration of taking their diabetes medicines (Figure 7.1). As found in interviews (6.3.3.2-6.3.3.3) and the systematic review

(2.4.1.4, 2.4.1.7), reasons for ambivalence included participants' high expectations of their medicines in relation to either blood glucose or body weight, particularly when they anticipated that the treatment would provide instant results. These expectations are common amongst patients on medicines for long-term conditions (Dohnhammar et al., 2016). Those interviewees who initiated insulin and were insulin-naïve found that at three months their medicine did not have the instant effect they expected. Other research supports that those who initiate basal insulin rarely achieve glycaemic targets (HbA1c <7%, 53mmol/mol) in the first three months, or even within 2 years of initiation (Mauricio et al., 2017). Whilst, some patients believed they should come off their ineffective medicines, other patients suggested stopping their medicines (completely/intermittently) if they achieved blood glucose target and/or weight loss (6.3.3.3), or perceived them as instant relief of diabetes-related symptoms (2.4.1.11). Fairchild et al. (2017) also found that only one-fifth of patients expected to take their diabetes medications for life.

Ambivalence about effectiveness was also linked to the frequent concerns over taking medicines expressed by participants in interviews and the systematic review (6.3.3.4, 2.4.1.6). These concerns were for both individual medicines and the number of medicines as a whole for diabetes and other conditions. Concerns were related to side effects, long-term complications/contraindications of taking their medicines, type of form (tablet/injection) and convenience, as well as the perceptions of others about the type and number of medicines they take. Furthermore, participants' past experiences of side effects, inconvenience and perceptions of injectable treatment made them wary of new medicines. Expectations of medicines are also thought to be influenced overtime by personal continuous evaluation of these through experience and societal negative values upon medicines (Dohnhammar et al., 2016). However, analysis from the questionnaires showed that, participants concerns over the potential adverse effects of their medicines significantly lessened over time, particularly for the weight reducing group (5.5.3). Yet, over a third of the weight increasing group (36%) appeared to have stronger concerns about their new medicine. Although overall medication burden did not increase over time, diabetes medication burden increased for both weight neutral and weight increasing groups

(Table 5.4). However, the weight increasing group was prescribed significantly more medicines than the weight neutral group.

Increased concerns in the weight increasing group could be associated with insulin's perceived seriousness, as discussed above, or other negative attributes (Brod et al., 2009c). Most interviewees presenting with either less or stronger concerns at the end of the study were on injectable treatments (insulin and GLP-1 agonists). The difference between them was that those presenting stronger concerns discussed insulin's ineffectiveness and inconvenience, with two participants reporting stigma about injecting in public. Aspects of effectiveness, side effects and convenience of new treatments are discussed in detail in section 7.2.3.

At the end of the study, the weight neutral and the weight increasing groups had stronger beliefs that medicines are overused by doctors. Whereas, at three months, the weight neutral group believed that doctors place too much trust on medicines, the weight increasing group believed that doctors will prescribe fewer medicines if they had more time with patients. Nevertheless, almost 40% of patients in each of these groups were uncertain about these aspects. Both the systematic review and the interviews showed that participants display trust in doctors to prescribe appropriate medicines (6.3.3.1, 2.4.2.3), despite their general concerns and associated negative stigma about taking medicines (6.3.3.4, 6.3.3.6, 2.4.1.2, 2.4.1.6). Participants in interviews accepted that starting a new medicine is a case of "*trial and error*" (6.3.3.5), acknowledging the risks and benefits of taking their medicines. Yet, there appears to be a complex interplay when it comes to preferences for medicines, particularly over efficacy and convenience and less so over safety (Laba et al., 2015, Pound et al., 2005).

7.2.3: Expectations and experiences of new diabetes medicines

Although there was no statistically significant difference between whether overall expectations decreased, remained unchanged or were exceeded, it was apparent that there were certain aspects about participants' new medicines that were impacted by their experience in taking them. Overall, most participants had their

expectations exceeded or met by experience, whilst a third felt their expectations of their new medicine(s) were unmet, with 39% of weight neutral group changing in this direction (5.5.1). Despite individual variations in satisfaction levels, participants, in general, were significantly satisfied with their new medicine(s), and the impact of these on managing their weight and daily life, with no change in psychological health at three months (5.5.4-5.5.5). However, it was the weight reducing group which had significant improvement in satisfaction levels in all aspects of their medicine (burden, efficacy, symptoms, impact on weight and daily life) over time. Other studies also found that patients treated with GLP analogues over 6 months had greater overall treatment satisfaction and well-being scores (Bode et al., 2010) compared to insulin treated patients (Grant et al., 2011) and those taking oral medications (Davies et al., 2011; Davies & Speight, 2012).

7.2.3.1 Effectiveness

Participants had higher expectations of their new medicine in relation to controlling their blood glucose and making them feel better. However, after three months they felt their new medicine was not controlling their blood glucose as they thought it would, and it did not make them feel any better (5.5.1), perhaps anticipating instant results, as discussed earlier (7.2.1). Nonetheless, all weight-effect groups showed significant improvement with their diabetes medicine efficacy in relation to the drugs ability in helping prevent them feeling tired and lacking energy and, keeping blood glucose stable, with the weight reducing and weight increasing groups being significantly more satisfied with their medications' impact on their physical and emotional well-being (5.5.4.2). This was evidenced by the improvement in HbA1c levels at three months with median reductions of 8-13mmol/mol since initiation of their new treatment.

Although, HbA1c levels were decreased at 3 months for all three weight-effect groups and some participants were able to reduce HbA1c levels to target (range 35-123mmol/mol), median HbA1c levels of 66mmol/mol are still considered high based on current guidelines (NICE, 2015a). As seen in chapter 6 (6.3.3.2-6.3.3.3), participants main focus on drug treatment is the effect on their blood glucose

(evident through SMBG or HbA1c tests) and physical effects (energy levels and body weight). Furthermore, participants' expectations of the dual purpose of their new medicine (blood glucose control and weight loss/less medication burden) could set the bar high, resulting in the ambivalence about the effectiveness of this and/or other treatments for their T2D (6.3.1.4). It appears that patients generally overestimate the benefits of their medicines (Dohnhammar et al., 2016). In addition, as seen in chapters 2 (2.4.1.9) and 6 (6.3.3.3, 6.3.5), both positive and negative experiences of diabetes medicines resulted in participants being more reluctant to treatment changes or keen to stop them, or even prioritise certain diabetes-related treatments over others.

7.2.3.2 Side effects and hypoglycaemia

Experience of side effects from diabetes medicines varied between, and within, individuals and their satisfaction levels, thus, varied over time. Medicines in tablet form or non-insulin injections were mostly associated with gastrointestinal effects, while insulin was associated with risk of hypoglycaemia (2.4.1.7, 6.3.4.2). Although there were no significant changes to satisfaction levels with regards to participants' experiences of side effects with their diabetes medicines over time, more people in the weight reducing group (37%) were satisfied in this aspect, whilst more people in the weight increasing (26%) and weight neutral (32%) groups were less satisfied (5.5.4.3).

As explained previously, past negative experiences of side effects made participants worry and wary about starting new medicines. During interviews, participants who initiated a new medicine with weight-reducing effect, discussed their awareness of the potential side effects of these medicines, mainly affecting the gastrointestinal tract. Yet, after the experience of taking them, they indicated that these effects were short lived, or were able to cope with them by taking prescribed/over the counter medicines (6.3.6.2). On the other hand, interviewees from the weight neutral and weight increasing groups did not particularly describe awareness of any side effects with their new medicines. Therefore, this explained the reason of no improvement in satisfaction levels about the information they received from health professionals

compared to the weight reducing group which was significantly satisfied in all aspects of their medicine (action and usage and potential problems with medicine) (5.5.2). Although the weight neutral and weight increasing groups had mixed views at three months, with a substantial proportion of patients whose satisfaction levels decreased (33% and 31% respectively), this was in relation to the action and usage of their medicine. This suggested that even after taking their medicine for three months they were still unsure how it worked, what it did and how long they needed to be on it.

Concerns of (risk of) hypoglycaemia with the new medicine were significantly reduced for the weight neutral and the weight increasing groups at follow-up, and to a lesser extent for the weight reducing group. It is known that some treatments such as insulin and sulphonylureas have higher risk of hypoglycaemia compared to biguanides, DPP-4 inhibitors and GLP-1 agonists (Table 1.1.). Yet, fear of hypoglycaemia is a general phenomenon for people with T2D regardless of what type of treatment they take. Evidence shows that those who are prescribed medicines with low risk of hypoglycaemia still display worry about low blood glucose (Lund & Knop, 2012). Additionally, some interviewees in this study expressed worry of hypoglycaemia as a result of polypharmacy, particularly if part of their treatment displayed such risk. Although, it is unknown whether level of risk of hypoglycaemia with the new treatment was discussed during participants' clinical consultation, the qualitative interviews revealed that participants became more confident about treating hypoglycaemia by ensuring sugary snacks and drinks were available should they feel their blood glucose is coming down (6.3.1.2, Figure 6.2).

7.2.3.3 Body weight

As expected, the weight reducing and the weight neutral groups were significantly more satisfied with the impact of their new medicine on their weight at three months. The weight reducing group also indicated that they were not bothered by or did not experience any weight gain (61% of the group) (5.5.5.2). This is expected with the type of treatment they received, as GLP-1 agonist injections, SGLT-2 inhibitors and orlistat are drugs that promote weight loss.

Although it appears that participants in this study had significantly better weight related quality of life, inevitably, in line with the type of treatment, it was the weight reducing group which had the most significant improvement in their quality of life, whereas quality of life decreased over time in 28% of the weight increasing group (5.5.8). Although the data collected in this study are only short term (3 months), the weight reducing group had the greatest amount of weight loss during the period of the study as a result of taking their new medicine compared to the weight increasing group who gained weight (median values -2.5kg Vs +1kg respectively) (Table 5.4).

There is evidence that weight related quality of life improves following GLP-1 analogue treatment (Davies & Speight, 2012) and greater satisfaction could reflect greater weight loss and HbA1c reduction, consistent with previous studies (Davies et al., 2011). Yet, the weight reducing group's quality of life was still lower than the weight neutral and weight increasing groups at both baseline and follow-up, suggesting that this group of people are still concerned with their weight. In addition, quite a substantial proportion of patients (quarter to half) in all groups appeared to be not satisfied with how well their new medicine was helping them to lose weight, or bothered by weight loss plateaus. The DAWN study (Peyrot et al., 2009) identified that weight worry was common amongst T2D patients. Most interviewees in this study were worried about their weight but found themselves unable to lose it or prevent further weight gain, because of their previous unsuccessful attempts with lifestyle changes and/or weight loss treatments (6.3.2.1). Still, individuals' perceptions of the effect of their medicines on their body weight varied (6.3.2.2). As a consequence, perceptions of causes of diabetes, type and effectiveness of treatment initiated had an impact on the priorities for weight management. This meant that some patients would prioritise medicines for diabetes over body weight or vice versa (6.3.2.3). Those who prioritised their efforts to decrease their body weight suggested that their diabetes might even disappear, contrary to the findings of the systematic review, which showed that people varied in their perceptions of lifestyle measures resulting in weight loss as an effective way of managing their diabetes (2.3.3.3).

7.2.3.4: Burden and Convenience

As described in interviews and the systematic review, different experiences with medicines shape what is perceived as inconvenient (2.4.1.6, 2.4.1.7, 6.3.4.1). In general, having to take medicines more than once a day, which encompasses various different doses through the day, having to take medicine with meals or food or make dietary adjustments, or having to take medicines outside of home was considered a "*nuisance*". Although there was general improvement in satisfaction levels about how burdensome the new medicine was, again, the weight reducing group was significantly satisfied at follow-up, with the highest proportion (39%) amongst the weight–effect groups. Conversely, satisfaction levels decreased for 25% of the weight increasing group, the highest proportion between all groups (5.5.4).

Nevertheless, participants' who initiated injectable treatment (weight reducing and weight increasing groups) were more positive about the delivery system at follow-up (5.5.1.2). Whilst those who initiated GLP-1 agonists indicated that their new medicine was convenient to take, easy to use away from home and not physically painful, those initiated insulin found it easy to get the dose (or amount) and were more satisfied that it did not interfere with planning meals. There is evidence that insulin-naïve patients (and to that effect injectable-naïve patients) are generally concerned over technical aspects of injections including mastering the skill of giving oneself an injection and preparing the correct dose of this type of treatment (2.4.1.3, 2.4.1.6, 6.3.3.6). However, when they become experienced in taking insulin, injection-related concerns become less of a worry (Brod et al., 2009c; Casciano et al., 2011; Holmes-Truscott et al., 2017), a finding that resembles interviewees' experiences on all injectable treatments (6.3.3.6).

Furthermore, an advantage of most common GLP-1 agonists and basal insulins (prefilled pens) currently prescribed on the NHS is that they are taken once a day, and generally T2D patients seem to be more satisfied with this treatment compared to oral medications (Bradley & Gilbride, 2008; Davies et al., 2011). During interviews, most participants prescribed GLP-1 agonists or insulin expressed preference and receptiveness towards injectable treatments compared to tablets, due to the

perceived efficiency of injectable treatments, and due to the minimal associated side effects with insulin (6.3.3.6). The difference in the interviewees with injectable treatment was that those on GLP-1 agonists were on a standard dose which did not require to change over time and were less likely to be asked by HPs to SMBG excessively as those (starting) on insulin. Also, those on GLP-1 agonists, particularly those on once daily or once weekly dose, found it much more convenient to take it because it did not affect their food intake, could be taken at their home any time of the day, could be kept outside of the fridge, and it did not affect their driving licence and car/holiday insurance (6.3.4.1).

On the other hand, 75% of the weight neutral group, at three months, indicated their new medicine did not interfere with their daily life, and 53% stated it never interfered with following their recommended diet (5.5.4.2). Most patients in this group were on DPP-4 inhibitors or on metformin extended release, which both are in tablet form taken once a day and are well-tolerated drugs (Richter et al., 2008; Chacra, 2014). Furthermore, some participants in the interviews indicated that they did not have to take their new medicine with foods or at a specific meal time, particularly those on DPP-4 inhibitors. However, participants prescribed metformin as part of their diabetes regime, raised concerns over the size of this tablet, which made it difficult to swallow. Additionally, those taking metformin more than once a day, found it challenging to take this medicine with food, often resulting in eating more food, or avoiding eating altogether (6.3.4.1). Thus, participants' engagement with their medicines (tablets/injections) suggests that there is a varying degree of resistance and receptiveness to medicines, consistent with other research (Pound et al., 2005; Jenkins et al., 2010).

7.2.4: Adherence

There was no significant change in the medication adherence levels following initiation of the new treatment (5.5.6). Despite a slight increase in adherence levels at three months, only a third of the group (30%) was classified as high adherent with the majority (70%) classified as low to medium adherent (Morisky et al., 2008). This is a lower percentage of adherence level than other studies which show adherence

levels ranging between 38.5 and 93.1% (Krass et al., 2015). However studies appear to use different methods to measure medication adherence (Krass et al., 2015). Only two studies in the systematic review by Krass et al. (2015) had used the latest version of MMAS (i.e. MMAS-8) and these reported adherence levels of 38.5% and 44.1%. It has been argued that there are important factors to consider when interpreting the literature on medication adherence. These include whether patients are experienced in using medicines or they take medicines for the first time, the way the adherence rates are reported (mean or categorical percentages), the different methods of assessment (various self-report and quantitative measures) (Blackburn et al., 2013) and whether self-management has been taken into account (de Vries et al., 2014).

Adherence levels remained stable for approximately 50% of the individuals in this study, although the change in individuals' levels of adherence varied over time. Of the three weight-effect groups, the weight neutral group had the highest proportion of patients classified as high adherent (36%) than the other two groups (26%) at three months, and the weight increasing group had a higher proportion of patients who became low adherents (34%) compared to baseline (28%). Lloyd et al. (2014) demonstrated a similar pattern of adherence and non-adherence in a 2-year follow-up study in T2D patients. Blackburn et al. (2013) describes three patterns of medication use in the first year in patients with T2D (primary non-adherence, non-persistence and poor execution), which require different support strategies to encourage patients to enhance adherence. Hence identifying these can ensure appropriate preparation of patients at initiation of any new diabetes treatment. A meta-analysis found that the proportion of patients who were considered adherent with the OGDs was 67.9%, with persistence rates ranging from 41-81.1% and with approximately one third of patients discontinuing their medicines at follow-up (Iglay et al., 2015).

In this study, just over 7% indicated they had discontinued the medication at follow-up, although another 16% were missing data. Reasons for discontinuation were not recorded, however interviews revealed that reasons for changes to diabetes medicines were to protect/preserve kidney function or due to experiencing

intolerable side effects (6.3.1.3-6.3.1.4). Although there was no evidence of primary non-adherence, interviews and the systematic review showed that most participants were poor executers and very few demonstrated non-persistence. While this study only measured adherence levels over the first three months of initiating new diabetes treatments, patterns of non-persistence and poor execution in the first three months can account to up to 50% of non-adherence cases in the first year (Blackburn et al., 2013), whereas premature discontinuation and non-persistence becomes more evident after six months of therapy (Yeaw et al., 2009).

The results of this study suggest that the type of medication does not influence the levels of medication adherence (5.5.6, 5.6.1). This is in contrast with the findings from other studies. The INITIATOR study (Wei et al., 2017) showed that there are different persistence levels at 12 months between patients initiating insulin glargine (64%) versus those initiating liraglutide (49%). While the SHIELD study (Grandy et al., 2013) showed patients prescribed medicines promoting weight loss and who actually lost weight during the duration of the study (>1yr) had significantly higher medication adherence levels than patients who gained weight and were prescribed medicines associated with weight gain (insulin, sulphonylureas, thiazolidinedione therapy). On the other hand, both the systematic review and the interviews uncovered the spectrum of adherence patterns in patients with T2D (Figure 7.2). Adherence, therefore, was influenced by convenience, effectiveness, concerns and experience of side effects, as well as confidence levels in establishing routine medication practices and other self-regulation strategies, which were specific to individual circumstances (Figure 7.1).

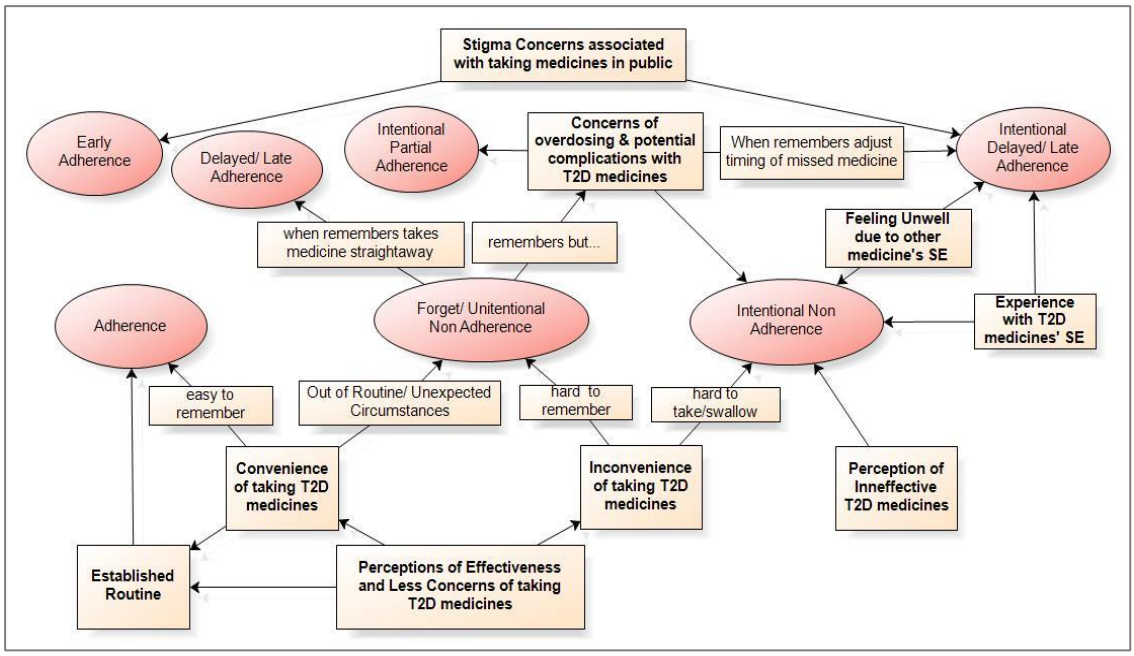

Figure 7.2: Adherence Spectrum

7.2.5 Self-efficacy (Routine practices and Self-regulation)

Most participants' self-efficacy in taking medicines correctly improved overtime, although this significantly improved in the weight reducing group compared to the other two groups (5.5.7). This improvement was specifically in relation to self-efficacy under conditions of uncertainty. Conditions of uncertainty include situations such that when individuals are not sure how to take their medicine, they don't know what time of the day to take it, when refill medicines look different, when they are feeling unwell and when the medicines cause side effects. The weight reducing group also showed significant improvement in their confidence levels in taking their medicine correctly under difficult circumstances, such as when they take several different medicines each day, when they take several medicines more than once a day, when they are away from home and when their normal routine gets messed up. Whereas, confidence levels in this area decreased over time for most people within the weight neutral and weight increasing groups.

When interviewees with high and low baseline self-efficacy levels (6.3.6.1) were compared, it became clear that those with more established routines were more confident in taking their medicines correctly, including what to do when they forget

to take their medicines or how to prevent side effects or hypoglycaemia. Whereas, those with low self-efficacy did not have an established routine, especially when they went out of their home. So when they forgot to take their medicine (and subsequently remembered), they were uncertain whether to take it or omit it. Alternatively, those whose confidence levels under difficult circumstances improved over time, were more likely to report less (or no) side effects or fear of hypoglycaemia, and more convenient medicines, i.e. easy to fit within their current routine.

During interviews, it was apparent that a variety of different strategies were used by participants to help them remember to take their medicines. Remembering to take medication is a prospective memory task relying upon cognitive processes for completing an action in the future (Stawarz et al., 2014). As seen in table 6.2, participants described that their medication routine was an automatic habit associated with specific time, location or event. Yet, habitual memory tasks, over time, can introduce errors of repetition or omission (i.e. take more/ less medicines than required) particularly when routine is disturbed (Zogg et al., 2012; Staward et al., 2014). External cues (such as use of pill boxes and family reminders) along with conjunction reminders (a cue paired with an event like SMBG) are more effective than internal reminders (based on thoughts/hunger) (Staward et al., 2014). Findings from the interviews (6.3.6.1) and the systematic review (2.4.1.11), support that the more external cues and conjunction reminders are adopted, the likelihood of medication adherence increases. As described earlier, the majority of the participants in this study were (low to) medium adherent, partly because combination reminders were often adopted only to specific medicines, and partly because participants associated taking their various medicines with complex tasks.

As mentioned earlier, SMBG as a self-regulation strategy when used appropriately (i.e. conjunction reminder), helped improved adherence in these patients. Evidence suggests that SMBG helps improve glycaemic control (measured by HbA1c) in non-insulin treated T2D, particularly if this was used to adjust therapeutic regimens (Poolsup et al., 2008). Despite SMBG being acknowledged as important in

determining control and seriousness of diabetes (2.4.1.10, 6.3.1.2, 6.3.1.5), interviewees in this study largely used self-monitoring to identify the instant level of blood glucose based on their food consumption or presence of symptoms, making it a less useful measure for improving glycaemic control (Evans et al., 2013).

In addition, misperceptions of self-monitored blood glucose resulted in mismanagement of diabetes control (6.3.1.2). For example, those who excessively monitored their readings became obsessed with the types and amount of foods they were eating and, those who rarely self-monitored, fear of hypoglycaemia resulted in them eating more sugary foods and drinks, therefore consuming more calories than necessary. Consequently hindering appropriate management of diabetes and weight loss in the long term. Peel et al. (2007), too, found self-monitoring was not particularly used to guide ongoing change to T2D patients' lifestyles. Similar to this study, over time, Peel et al. (2007) found patients suggested that HPs do not provide guidance on how often to self-monitor, and they are not interested in their readings, as these may not be as important as the results of the HbA1c test.

Participants conferred, through their beliefs, perceptions and experiences in taking their medicines, that generally there was no "*alternative*" treatment to diabetes other than taking their prescribed medicines. Many studies (Lawton et al., 2006b; Monsier-Pudar et al., 2009), including this and the systematic review, showed that patients find it difficult to modify their dietary habits and engage in regular physical activity and, therefore, rate medication (specifically insulin) as more important than these lifestyle measures and report higher medication adherence (Broadbent et al., 2011). However, lack of appropriate guidance to self-monitoring and lifestyle interventions could further impact weight management, an integral outcome of T2D management (Aicher et al., 2010).

Self-regulation strategies, such as avoiding social events, changing eating habits, adjusting the timing of their medicines or taking other additional medicines, were a result of concerns and experiences of side-effects of medicines and forgetfulness. It is not uncommon that patients taking medicines for long–term conditions to self-

regulate and modify their regime (Pound et al., 2005, Mohammed et al., 2016). Other self-regulation strategies, for instance, seeking out information about their medicines and negotiating their treatment with health professionals were, also, reported in chapter 2 and other research (Bajcar, 2006; Rashid et al., 2014, Mohammed et al., 2016). Identifying which of these strategies have an impact on medication taking behaviour could prevent potentially inappropriate therapy outcomes.

7.2.6 Impact of medicines' concerns and self-efficacy on adherence

Multivariate analyses showed that medication adherence following initiation of a new diabetes treatment was significantly influenced by age, initial adherence levels, confidence levels (self-efficacy) in taking medicines correctly and a change in beliefs over concerns of potential adverse effects of the new medicine (Table 5.9). Multivariate analysis also showed that certain modifiable and unmodifiable factors can influence a change in adherence levels (either a decrease or increase) following initiation of a new diabetes treatment (Table 5.13). Unmodifiable factors included socioeconomic and marital status, whereas modifiable factors included initial medication adherence and HbA1c levels, beliefs that medicines are overused by doctors, and changes to self-efficacy levels.

Systematic reviews have shown that demographic, socioeconomic and cultural factors influence adherence to OGDs in various ethnic groups (Peeters et al., 2011), and factors such as age, being female, travelling, type of delivery system related to insulin injections, and cost of medication are associated with nonadherence to insulin therapy (Davies et al., 2013). Although the current study did not explore all of these factors, gender was associated with medication adherence in the weight reducing group (Table 5.15). It was predicted that females are more likely to decrease their adherence levels following initiation of a new diabetes treatment. Moreover, an increase in low adherence levels was observed in participants within the weight increasing group, which mostly consisted of patients prescribed insulin (Figure 5.59). It is believed factors such as smoking, drinking, and living alone, are associated with greater difference in insulin dose timing which results in high frequency of hypoglycaemic episodes and being overweight (Nishimura et al., 2017).

The multinomial regression analysis showed that those individuals who are widowed (as opposed to be married) were more likely to increase their adherence levels following an initiation to a new medicine (5.6.1.2). Furthermore, interviews showed that some patients found the support of family conflicted with their efforts in managing their diabetes (Figure 6.8), whereas those who are widowed had perhaps greater support around them particularly from their health care team. Whilst family support for people with diabetes is widely acknowledged, families need psychosocial and education resources to better support their relatives with diabetes (Kovacs-Burns et al., 2013). On the other hand, interviewees who live in the most deprived areas were generally low to medium adherents, contrasting with other research (Lloyd et al., 2014) but there were interviewees who live in such areas whose adherence levels increased during the study. Reasons for enhanced adherence were related to modifiable factors such as belief that medicines are effective, convenient, have less side effects and increased support from health care team, rather than place of residence.

The degree of difference between beliefs over necessity and concerns of medicines is thought to predict medication adherence (Clifford et al., 2008). Approximately half of the participants were ambivalent towards their new diabetes medicines both at baseline and follow-up, based on the necessity-concern framework (i.e. they had strong beliefs of both necessity and concerns towards their medicines) (Horne at al., 1999; Aikens et al., 2005) and were classified as medium adherent (Morisky et al., 2008). Meta-analyses (Horne et al., 2013; Foot et al., 2016) found that high adherence was associated with strong perceptions of necessity of treatment and fewer concerns about the treatment, although there were few longitudinal studies in these reviews with varied measures of adherence. On the other hand, the current study found that only beliefs about concerns of treatment predicted non-adherence. Other studies also identified concerns over adverse effects of medicines to be associated with non-adherence (Mann et al., 2009; de Vries et al., 2014; Holmes et al, 2014), and the key motivation for not taking medicines (Pound et al., 2005).

Additionally, gender perspectives may have an influence on whether patients persevere with the side effects of their medicines (6.3.7). Nevertheless, interviewees' compromise and perseverance was a way of considering the risks and benefits of taking their medicines in order to achieve balance in their life. However, their acceptance about compromise and perseverance affected their adherence levels (Table 6.2). Those who indicated they would not persevere with side effects were more likely to be medium to high adherents, those persevering for the benefit of their diabetes control were low to high adherents, whereas those persevering for the benefit of weight loss were more likely to be low to medium adherent.

Although strong beliefs that medicines are overused by doctors can influence a change in adherence levels (both increase and decrease), medication burden did not predict non-adherence, a finding supported by (Grant et al., 2003) and in contrast with other research (Lloyd et al., 2014). An increase in diabetes medication burden overtime appeared to decrease the odds of becoming highly adherent in the WN group (Table 5.16). Essentially, as seen in interviews, beliefs about overuse can be overridden by the experience of support patients receive and other modifiable factors such as self-efficacy. On the other hand, high HbA1c levels prior to initiation of a new treatment predicts a decrease in adherence levels over time.

Self-efficacy has been identified as the most significant predictor of medication adherence in chronic disease (Holmes et al., 2014) over time (Schoenthaler et al., 2016). A comparison of interviewees who were low-to-high adherents and had various levels of self-efficacy, showed that high adherents used a combination of methods including triggers associated with time, location, and event, as well as repeating their routine on a daily basis, placing their medicines in front of them and taking them "*all at once*" (6.3.4.1). In line with Campbell et al.'s (2003) review, less guilt as a result of not taking medicines on time was only apparent to those who appeared confident and fully aware of the reasons for adhering or not to their medicines. Hence, despite most participants being classified as (low-to) medium adherent, interviewees reported they rarely missed their medicines, and therefore did not appear overly concerned about it, resulting in the spectrum of adherence

seen in figure 7.2. On the other hand, for those patients who reported less forgetfulness over time, adherence levels increased. However, adherence levels in those participants who negotiated or sought further information/advice about their medicines were not affected. A meta-analysis by Gherman et al. (2011), identified that individuals with diabetes who are more adherent are more confident that they can perform behaviours such as taking medication and intent to engage in such behaviours compared to individuals who are less adherent, as they are more likely to perceive barriers with adherence and feel less confident in dealing with these barriers and worry about medication side effects. In addition, Lloyd et al. (2014) found that prior adherence status was the most important factor in predicting adherence at various points during a 2-year follow-up study.

This study predicted that older individuals with T2D, who are highly adherent and extremely confident in taking their medicines correctly under conditions of uncertainty and under difficult circumstances, are up to seven times more likely to be highly adherent at three months after initiation of a new diabetes treatment, than younger, less adherent and less confident individuals. In addition, during the period of taking the new treatment, if individuals have fewer concerns about the potential adverse effects of their new medicine, and there is no decrease in confidence levels in taking their medicines, they are still three to four times more likely to be highly adherent at three months after starting the treatment, compared to those individuals who have high concerns about their medicines and lose confidence in how to take them correctly. On the other hand, individuals whose confidence levels in taking their new medicine correctly decreases over time, then they are twice as likely to have their adherence levels decrease. There was a noticeable trend that adherence levels were less likely to decrease for participants who were prescribed a new treatment when their HbA1c levels were below 75mmol/mol (median HbA1c level for those who improved adherence over time). This trend could also be related to delays in treatment as discussed earlier (7.2.1). Hence, increased clinical inertia could potentially be associated with poor adherence.

7.2.7: Expectations of Care: Helpful and Unhelpful Support

This study found that similar avenues of support were used by participants as in other studies (Lawton et al., 2005c, Stuckey et al., 2014), such as family, friends, Diabetes UK and other people with T2D. However, interviewees placed higher value on the support they received from health professionals in managing their diabetes, which, in return, gave them confidence to self-manage their condition. Although, in this study, the role of health care support in medication adherence was not investigated, research has shown that having better provider-patient communication, social support mainly by the health care team, and high self-efficacy is associated directly with performing diabetes self-care behaviours including medication taking, and indirectly to improvements in glycaemic control (Gao et al., 2013).

Like Lawton et al. (2005c), this study found that people with T2D generally want to be seen by diabetes experts and appreciate instant access and timely feedback and information on their treatment(s). Findings from the questionnaire showed that all participants were significantly more satisfied at three months with the information they received about their new medicine from HPs, particularly about potential problems relating to side effects (for example feeling drowsy, affecting sex life, alcohol intake). However, as noted above (7.2.3.2), the weight reducing group had the greatest improvement while participants from the other two groups remained uncertain about their medicines.

While the interviewees in this study expressed a preference to be seen at a specialist diabetes service, whether community or hospital, they found having access to their GP practice and to a range of other services as a good back up for their T2D management (6.3.7.2). A good quality service was described as providing regular, full examination of diabetes related aspects and sufficient time during a visit to discuss experiences and concerns (Figure 6.10). However, GPs and practice nurses were viewed by patients as lacking knowledge and expertise in diabetes, despite that many of them leading diabetes care within the practice. This corroborates findings of DAWN2, a multinational large scale study into perceptions of diabetes care, where

HPs themselves felt insufficiently equipped to provide diabetes self-management education, including emotional and psychological support (Byrne et al., 2017).

Furthermore, during interviews, participants were either underusing dietetic services or undervaluing their support in relation to dietary management and weight loss. On the contrary, people who attended group sessions run by dietitians and other health professionals valued this support with regard to the information provided about diabetes, diet, physical activity, SMBG, and medication-related issues. Although, this kind of support was only provided when they were diagnosed, formal diabetes education is imperative both at the outset and at regular follow-up intervals (Sherr & Lipman, 2015). Interviewees seemed to appreciate receiving tailored information about their diabetes during appointments, and suggested this should happen more often, highlighting the fact that HPs need to reinforce the importance of lifestyle behaviours at each clinical visit (Reusch & Manson, 2017) and encourage informed treatment choice. Participants' desire for continuity of care was also paramount in maintaining effective and appropriate care and fostering good relationships between patients and professionals. Education, informed choice and continuity are aspects in line with the National Service Framework Standards for Diabetes (DOH, 2001a), recommendations from NICE for the management of T2D (2009a, 2015a), as well as guidance on improving the experience of care for people using NHS services, and their medicines (NICE, 2012, 2009b, 2015b).

Evidence from interviews suggest that there is a close link between the level of support from health professionals and self-management of T2D (Figure 7.1). Participants were empowered to make lifestyle changes when they had excellent support (as defined by Figure 6.10) and perceived their diabetes treatment was effective, convenient and had less side effects. In addition, the systematic review showed that HPs could inhibit/impact patients' views about diabetes and medicines and subsequent strategies at various points during their illness journey (Figure 2.4). In addition, a recent review (Frost et al., 2014) identified that for effective self-management strategies, T2D people need to take ownership of their disease, fostered by timely and tailored information and support over time. This is important

when considering that adherence levels, found in this and other studies (Lloyd et al., 2014), change over time from high to low and vice versa, and that any changes to treatments or treatment intensification may be ineffective if patients are already low adherent. Support needs to provide the foundation to explore patients' perceptions and experiences of managing their diabetes and to guide the development of a flexible regimen that can facilitate both quality of life and medical outcomes (Frost et al., 2014).

This study aimed to identify suitable intervention(s) for T2D patients which would enable them to (self) manage weight loss goals and medication adherence. However, there was considerable discussion during interviews about health care support for these patients, which guided the development of the model of care in Figure 6.10. Thus, as expected, experience of helpful support formed suggestions which interviewees deemed useful for future support for themselves and others who are prescribed the same type of new treatments they had received. Details of these suggestions and aspects of information participants found useful can be seen in Figures 6.8 and 6.10. Although there is a debate whether to take patients' preferences for granted and change delivery of care based on these preferences (Lawton et al., 2013), it has been argued that preferences could change over time in light of patients' direct experiences of care. The interviewees in this study, however, had varied experience of health care settings, from either primary or secondary care or both, with different prescribed treatments for T2D. In addition, irrespective of care received, suggestions outlined in Figures 6.8 and 6.10 were echoed by all participants. These suggestions are not uncommon amongst patients (2.4.1.5, 2.4.2.5), as evidenced in research and guidance literature (Peyrot et al., 2006; NICE, 2009a,b; 2015a,b; McMullen et al., 2015; Mohammed et al., 2016; Fairchild et al., 2017) and endorsed by UK policy (DOH, 2004a,b, 2005b, 2006).

7.2.8 Emotional impact of taking diabetes (and other) medicines

It is no surprise that participants' beliefs, perceptions and experience of taking medicines for diabetes, body weight and other conditions had an impact on their emotional well-being (Figure 7.1). Furthermore, most participants were worried

about their body weight and linked this to either diabetes itself, specific diabetes medicines, or the amount of medicines they take. Hence, the majority of participants revealed they do not like taking medicines and would prefer to take less or none, resonating preferences of other people with long-term conditions (Pound et al., 2005). This contradicts the progressive nature of T2D from lifestyle management to that of lifestyle combined with pharmacotherapy in order to achieve glycaemic control. This suggests that regardless of the duration of their condition (median=7yrs) and the recognition of self-responsibility of managing their condition, there are still unresolved issues when treatment changes occur, involving the acceptance/denial of their diabetes. Perception of personal failure when starting/increasing medicines was evident in both the systematic review and the interviews, although none of the interviewees implied there was a sense of "punishment" as a result of initiating insulin. Communicating the progressive nature of the disease process is important for minimising ill-perceptions of lifestyle failure or self-blame (Reusch & Manson, 2017).

The emotional impact of medicines on patients with T2D is not new. Similarly to the systematic review, interviewees portrayed representations of grief (Brown, 1985) from shock to adjustment, not only to their diagnosis but also to taking medicines for diabetes. Taking medicines for diabetes had a greater impact than the actual act of swallowing or injecting them. Some interviewees described a sense of restriction in the types of foods, their eating patterns and social activities regardless of the form of their medicine, and discrimination related to driving licence and holiday insurance. Negative impact and feelings of discrimination have also been reported elsewhere (Stuckey et al., 2014; Dohnhammar et al., 2016; Holmes-Truscott et al., 2016). As mentioned earlier (7.2.3.1, 7.2.3.4), interviewees displayed receptiveness and resistance to their medicines, reflecting other qualitative research on T2D patients on insulin (Holmes-Truscott et al., 2016). Stigma about taking medicines in public was not only related to insulin injections (Polonsky & Jackson, 2004), but also to tablets. Although tablets were less visible to others, and participants confined taking them whilst at home. Societal stigma was not however the dominant factor, but instead the inconvenience of medicines in fitting them to their current routines.

Understanding the personal meaning of medicines for patients with long-term conditions, whether it is a source to aid control or impose restriction, could help in understanding and addressing the management of prescribed medicines (Dohnhammar et al., 2016).

This study also adds that as progression to different treatments impacted their emotions and how they coped, so too the increased number of medicines over time (6.3.7), which included frequency of doses/injections. The level of successful management of T2D was affected by the level of self-efficacy and strategies employed on a day to day basis. Whilst the experience of successful and unsuccessful practices and perceptions of successful and unsuccessful medicines reinforced or undermined patients' beliefs about their diabetes treatment, it also led to a re-evaluation of self, and the key goal for all was to regain control of their life (Figure 2.4).

7.2.9 Potential Future Intervention(s)

This study aimed to identify suitable intervention(s) for T2D patients which would enabled them to (self) manage weight loss goals and medication adherence. This research question was mainly addressed through the qualitative interviews. However, as mentioned previously (7.2.7), participants considerably discussed areas to improve the support from their health care team when they were asked how they can be supported when starting and experiencing a new diabetes medication. Nevertheless, throughout the interviews a number of aspects have been identified that could be used in the future (7.2.5, 7.2.6, 7.2.8), either in practice or research, and as a result, a range of visual models (Figures 6.2-6.4, 6.6, 6.7/7.2, 6.8-6.10, 7.1) were developed to support patients and health professionals. In summary, evidence from this study has highlighted the need for developing interventions that are focusing on health care support, communication/education about the disease, self-efficacy strategies, and psychological help. Future research should focus on identifying the complexity of potential interventions, as well as their development, execution and implementation (Moore et al., 2015).

7.3 Theory review

Emotional impact, and perceived self-efficacy, beliefs about and experiences of taking medicines for T2D and interactions with health professionals were key drivers influencing medicine taking behaviour. Theory-based interventions have failed to provide substantial evidence in medication adherence and clinical outcomes to adult patients prescribed polypharmacy, mainly because they have not been optimally used (Patton et al., 2017). Additionally, the systematic review in chapter 2, as others (Holmes et al., 2014), demonstrated that no single theory can be used to fully illuminate medicine taking behaviour. Likewise, this study demonstrates that more than one theory is needed to explain medication taking practices for people with T2D. An in-depth analysis of these theories is beyond the scope of this thesis, but brief explanations of these can be found in section 2.3.4. Medication taking related theories include, in no particular order:

(i) Theories such as social cognitive theory (Bandura, 1977) and the model of illness representations (Leventhal et al., 1980 cited in Bower et al., 2012) describing perceived self-efficacy and coping efficacy as a key construct that influences one's behaviour including medicine taking. Furthermore, others aspects covered by the models include emotional (grief reaction) and other cognitive factors (illness and medication related beliefs, and expectations) which are involved in changing the self-view and self-practices. Although, the environment (physical and social including health care support) play an important part in changing individuals' behaviour, it is unclear how other external factors such as health related policies and politics directly impact on behaviour. Perhaps the influence of these external factors is an indirect one. This study did not explore the role of multi-morbidity on illness representations, however, like Bower et als' study (2012), there is evidence of causal relationships between diabetes and obesity and other cardiovascular related conditions, priority among conditions resulting in both synergies and antagonisms, medication burden, and coherence.

(ii) Although the Necessity-Concerns framework (Horne et al., 1998, 1999) proposes that perceived need for diabetes medicines and ongoing concerns about

medicines influences patient medication adherence, in this study, concerns about side effects and convenience of taking them had the most impact on adherence. Nevertheless, patients related the necessity of their medicines if they believed they were effective; i.e. reducing blood glucose levels and body weight and increasing energy levels. Additionally, necessity and effectiveness corresponded to some diabetes medicines rather than the whole diabetes medication regime.

(iii) It is believed that patients and health professionals portray different explanatory model of illness (Kleinman et al., 1978). The systematic review and this study did not explore health professionals' views about T2D. However, patients' accounts suggested that there is a discrepancy in views around: severity, treatment recommendations by HPs and difficulties encountered, passive/active patient role and adherence/non-adherence, which can potentially impact medicine taking behaviour.

(iv) Starting a new medicine for T2D and ongoing additional medication therapy, and not just at the onset of their chronic illness, indicates a biographical disruption (Bury, 1982). Psychological medicine resistance and receptiveness was found in this study prior to initiation of the new treatment. There was no resistance to the new treatment, as all participants accepted it, however, interviewees discussed other treatments that they had refused prior to the new prescription or in the past, which included insulin, other injectable treatments and tablets. Therefore psychological resistance to medicines appears to be a phenomenon that occurs as a result of peoples' individual experiences and beliefs about their condition and their medicines, and interactions with their wider environment. May et al. (2009) advocates that medicine taking behaviour is structurally induced by the health care system and the way patients utilise health care services. They suggested the burdens of treatments are very different from the burdens of illness, referring to the concept of minimally disruptive medicine (2009), and the newly proposed Burden of Treatment theory (2014). Both of which focus on the relationship of people with chronic conditions, their social networks and the healthcare services. The final model in the systematic

review (Figure 2.4) clearly demonstrates how patients evaluate their self and reconstruct their biography and it is supported by the findings in this study.

7. 4 Strengths and Limitations

The strengths of this study lie in the mixed methodology approach and study design, which not only assessed quantitatively the views of T2D patients about their medicines, but explored qualitatively the meaning they attach to their medicines and their daily practices which affected or promoted adherence over time. It may be that individuals recruited to the study, at both the questionnaire and interview parts, were better at self-managing their diabetes. However, this potential bias would have underestimated non-adherence. Still, the non-adherence levels reported in this study were equal or even higher than seen in other studies (Krass et al., 2015) for T2D population, supporting the generalizability of the findings. Also, as seen by the findings of the interviews, participants' adherence levels ranged from low to high. Moreover, participants were frank about their management of diabetes and provided many insights into their everyday practices with lifestyle measures as well as medication. The rapport established between the researcher and the interviewees, over the period of this research study, enabled the patients to provide such detail strengthening the findings (Legard et al., 2003).

Furthermore, the mixed methods analysis legitimised/validated the findings of the study (Onwuegbuzie et al., 2011) together with the findings of the systematic review in chapter 2, enabling an evidenced-based explanation of the phenomenon of medicine taking behaviour in people with T2D. The mixed method approach is consistent with the initial stages of process evaluation for developing complex interventions that can have impact on a number of levels from individual, to health service delivery and policy by targeting individual, interpersonal and organisational components to produce change (Moore et al., 2015).

In addition, the study involved a large sample contributing to a prospective longitudinal study which is currently lacking in the literature (Horne et al., 2013; Foot

et al., 2016). By employing a multi-sited recruitment strategy across Merseyside, participants recruited had both diverse socio-economic background and experiences of diabetes services and treatments. While 65% of the participants recruited were from primary care, this corresponds to current services provided for T2D in England, since there has been a focus on GP practices to deliver care locally (DOH, 2004b; NHS England, 2014). Although recruitment rate varied for each primary care trust, this may reflect on the services provided in different areas. For example, Sefton and Knowsley PCTs have dedicated multidisciplinary teams in some areas running frequent community clinics and therefore a greater chance of recruiting participants at the point of prescription, compared to the other PCTs where GPs with a specialist interest in diabetes or nurse prescribers recruited participants on an ad-hoc basis. A small percentage of participants were recruited from community pharmacies (9%) suggesting the study was able to identify patients where there may not be a dedicated service for diabetes patients.

Other methods of participant recruitment were considered, including sampling from the local diabetes register. However, recruiting participants following a clinical encounter or collection of a new prescription from a community pharmacy was best suited in this study, in order to capture patients at the point of change in their medication regime, and therefore this approach was less likely to suffer from a selection bias. The sample was representative of those who are changing treatments. The median baseline of HbA1c of the research participants was 77mmol/mol, and therefore within current practices in UK, where treatment changes occur when mean HbA1c range between 72-84mmol/mol (Khunti et al., 2013; Wilding et al., 2017).

Although establishing recruitment sites was a challenge despite the training and support provided by the research team and the Primary Care Research Network [PCRN], the study had an acceptable, good response from patients for both questionnaires and interviews (Sitzia & Wood, 1998; Bowling, 2009), as most individuals approached consented to the study. Despite the length of the questionnaires, almost 66% of consented participants returned both questionnaires, indicating that medication therapy and its effects on weight, adherence and other

psychological factors is of interest to people with T2D. Significantly more individuals (45.7%) who did not return the second questionnaire were those in full-time employment, suggesting the length of the questionnaire might have impacted on their time and willingness to complete it. Reasons for participants withdrawing from interviews following consent (n=28) were not collected at the time, but 24 of these participants completed both study questionnaires. Furthermore, individuals with significantly poor kidney function (Median eGFR=78) returned the second questionnaire, indicating they may have had additional concerns when taking diabetes medicines, as identified during the interviews.

While the study aimed to include patients from a range of ethnic groups, only 1% of the sample were from BME groups and all of the interviewees were Caucasian, consistent with the regional demographic data (Rasdale, 2013). Therefore, it is not possible to generalise the findings beyond this group. Nevertheless, the systematic review, which included at least 42% participants from BME groups, showed that these patients have similar concerns about their diabetes medicines and patterns of adherence. Another potential limitation of this study is the recruitment of participants from the UK, particularly to the North West region. However as noted above, findings are corroborated with other studies (see 2.5.2). Hence, inference validity has been demonstrated by supporting findings from this study with findings from other research (Lewis & Ritchie, 2003).

Although the study did not reach the original proposed sample size for the questionnaire part of the study (i.e. n=300), the quantitative data collected were sufficient to run all statistical analysis as planned. Many of the clinical data collected at 3-month follow-up (i.e. cholesterol, blood pressure, renal function) were not available to use for statistical analysis, as 36-70% of them were missing. However, this reflects real world clinical care for T2D patients, as these clinical values are often repeated at 6-month or yearly intervals (rather than at 3-months). Furthermore, important clinical data such as HbA1c and BMI were recorded as close as possible to three months, ranging from 2-4 months. Therefore, these data were recorded either slightly before or after administration of the second questionnaire. This was to

minimise missing data (~25%) to enable meaningful statistical analysis. However, this approach could have under/overestimated the impact of such clinical data on participants' views on their medicines.

Although there is no gold standard for assessing minimal important change in individuals (Wyrwich et al., 1999; Rejas et al., 2008), using the SEM allowed exploration of how participants' medication views changed over time irrespective of the type of drug prescribed. Moreover, the quantitative part of the study systematically measured low to high adherence levels in these patients prescribed different new diabetes treatment at the point of prescription and three months later. This established which factors predicted high adherence levels after initiation of new treatment and what aspects can influence a change in adherence over time. Although there are many "rules of thumb" for calculating appropriate sample sizes for regression analysis (Green, 1991; Wilson VanVoorhis & Morgan, 2007) based on the number of predictors, the multivariate regression analysis perhaps was lacking sufficient numbers, particularly when the whole group was split into the three weight-effect groups. An original analysis of the whole group irrespective when participants had completed their first questionnaire (n=213), showed that the exact same predictors influenced adherence (Psarou et al., 2016). On the other hand, each weight-effect group had a small sample size with limited observations across the different adherence levels, for example 26% of the WR group (n=68) was high adherent at follow-up (section 5.5.6.3). Therefore, more cases are needed in order to perform multivariate regression analysis in the individual weight–effect groups and further research should address that.

Further limitations could include the lack of use of confidence intervals and a heavy reliance on p-values for the majority of analyses. Nevertheless, median values and interquartile range provided in the result sections as most of the data were ordinal (Field, 2009). These are the preferred measurements when reporting the results of nonparametric tests (Field. 2009). In addition, to overcome the likelihood of increasing Type I errors (the belief that there is a genuine effect in the sample population when there is not one), the Bonferroni correction test was used when

multiple testing between pair groups. However, this is a conservative test, which in effect could increase type 2 errors, i.e. when there is a genuine effect in the sample population but it has been rejected due to decreasing the probability value to below 0.05 (Field. 2009).

Several approaches were used throughout the study to ensure methodological rigour for the interviews. Such approaches included: piloting the interview schedule, sampling purposively to reach adequate representation, researcher's experience in conducting research interviews, cross-checking transcripts and original recordings for typographical errors or unclear sections, using the framework approach to data analysis which is both systematic and comprehensive, the supervisors and/or the research steering group reviewing themes generated and confirming the interpretation of findings to ensure that the implications of the study are relevant to clinical practice (Lewis & Ritchie, 2003; see section 4.3.1). Data saturation was reached after interviewing 24 participants, a sample which was considered both sufficient and representative of the questionnaire sample. The triangulation of the mixed method data in this study further confirms data saturation and limits selection bias (Oppong, 2013; Fusch & Ness, 2015).

Furthermore, reflexivity is a tool for bringing transparency to the research process and its outcomes (Etherington, 2007) by recognising and acknowledging the pre-understandings that the researcher and the participants bring to the study, and the impact of these in generating the data. Ways to exercise reflexivity during the process of analysis have been proposed (Warin, 2011). Yet, Finlay (2002) argues that researchers who adopt a reflexive approach risk concentrating on excessive self-analysis at the expense of focusing on the research participants and developing understanding.

Nevertheless, being self-aware throughout the research process helped eliminate any influences in the design, analysis and representation of the data. For example, during the design and piloting of the interview guide, input from both supervisors and the research steering group which consisted of HPs and lay representatives with

T2D, ensured that the researcher's prior professional background did not affect the development of the tool (see 4.3.1). Furthermore, to minimise potential influence on participants' responses during interviews, they were informed that the researcher was independent to their health care team, and the treatment and services they received would not be affected by taking part in the study, but it was their views and experiences of the treatment they had received that was sought. Yet, one out of the two participants who had a health professional background, was less forthcoming on their understanding about diabetes, perhaps because they considered the researcher to be a HP too. In addition, a few participants discussed the positive impact the research involvement and researcher's personality had on them, which might have inhibited a true appraisal of the health care service. Nonetheless, most participants discussed both positive and negative aspects on the support they had received for their diabetes. Initial nervousness during the conduct of the first few interviews could potentially impact on the outcome of the interview and some aspects not being followed up. However as the interviews progressed, familiarisation with the interview guide helped to eliminate such impact, and all participants were given the opportunity to discuss anything that was not covered during the interview. Researcher's concerns about misunderstandings related to the use of dialect or colloquial speech by participants during interviews was overcome by questioning them about the meaning of such words or phrases and the use of a professional transcription service.

7.5 Implications for policy and practice

Given the strengths and limitations of the study, this mixed methods study provides new insights into the reasons for poor adherence. Specific (practical) issues have been identified through the models developed which may help in the development of more patient-centred interventions by changing practice and informing policy.

Health professionals can change consultations so that patients feel understood and, in return, they understand their diabetes and their medications. Informing patients of the variety of medication treatments available for T2D as well as the inevitable

progression from tablets to injectable medicines could make patients aware and give them time for grieving, so when eventually a prescription is required, these medicines are more easily accepted. In addition, weight management is an important aspect of diabetes, however amongst patients, there are mixed perceptions of the effects of the different medicines on their body weight. Considering that most patients with T2D are worried about their weight but only a few patients associated weight management with their diabetes management, HPs need to ensure that they communicate better the impact of certain treatments on body weight, the role of maintaining a healthy body weight, and offer patients guidance on dietary and other lifestyle changes that can minimise impact. Nevertheless, recent changes to diabetes treatment guidelines (Inzucchi et al., 2015; Handelsman et al., 2015) which opt out of phase-level treatment and offering insulin or other injectable treatments at various stages of the disease, may be another approach to overcoming barriers with managing T2D, although these changes are not supported by current NICE guidelines (2015a). The merits of using GLP-1 analogues and SGLT2 inhibitors earlier in the management of T2D has been discussed elsewhere (Wilding et al., 2016; Chatterjee et al., 2016), yet this study demonstrated these treatments are preferable and contribute to significantly more positive patient reported outcomes than other treatments, particularly in relation to weight loss.

In addition, focusing on areas of concerns about medicines prior, and during treatment is a priority for helping patients to minimise these concerns and accept medicines in a way that promotes better adherence. Short term positive impact on medication adherence following initiation of chronic disease medication (at 3-6months) through a tailored intervention based on discussion about medication and disease beliefs with a pharmacist has shown potential (Nguyen et al., 2016). It is understood that patients may struggle with complex drug regimens, therefore their perspective and experience on medicine-taking must be taken into account when prescribing new treatments. Prescribers should bear in mind that patients seem to prefer medicines taken at home, that do not interfere with work or lifestyle, and are easy to fit into routine, particularly if taken only once a day, at breakfast or first thing in the morning, or are flexible without being "*tied down*" to certain times like having

to take with food or adjust eating patterns. Additionally, if they have less side effects/complications, they are then viewed more favourably by patients and this could enhance adherence. Moreover, interventions could be designed to promote treatment adherence by taking into account emotional and cognitive factors, as well as determining preferences to treatment and building confidence in daily practices and social and family support mechanisms. Emotional distress, social support and self-efficacy are strongly associated with diabetes self-care behaviours (Walker et al., 2015; Gonzalez et al., 2015; Sleath et al., 2016) and habit formation has shown to predict medication adherence (Phillips et al., 2016). Findings from this study support that daily practices and routines should be built with multiple external cues and conjunction reminders.

Most patients appear to trust their doctors and accept that doctors make decisions about their medicines. Patients prefer expert professionals in diabetes, particularly at diagnosis and at every medication change or initiation. If patients receive services at both primary and secondary care, then continuity of care is paramount not only between services but also between HPs. Furthermore, services should aim to provide timely treatment changes, timely repeat prescription changes, regular monitoring, instant advice, adequate time to discuss experiences and time to get adequate information to ensure diabetes treatment is effective (diet/meds). Patients, therefore, can become confident about the care they receive and motivated to make changes to better control their diabetes and body weight. Yet the current constraints and the increased demands on the health care budget in providing such an intensive support through the NHS can be challenging. The role of the community pharmacist in the management of people with T2D has been investigated (Twigg et al., 2015; Nguyen et al., 2016), as well as recent advances to eHealth via text, voice or video (Nelson et al., 2016; Odnoletkova et al., 2016; Peimani et al., 2016; Thakkar et al., 2016; Car et al., 2017). Whilst these show promise in improving medication adherence and/or glycaemic control for a short period, the long term impact and the cost-effectiveness of such interventions need to be further explored.

Pound et al. (2005) argue that policy needs to change with less emphasis on modifying patients' behaviour but on determining what sort of treatments patient prefer and developing and evaluating the safety, efficacy and cost-effectiveness of those preferred treatments. Recent guidelines (NICE, 2015b) have been developed about medicine optimisation which considers both patients' perspectives, and efficacy and safety of medicines. However, more needs to be done to ensure sufficient evidence from patient research and public and patient engagement is utilised when developing guidelines (Heaton et al., 2017) and commissioning self-management support services (Reidy et al., 2016). This is to implement services that effectively address peoples' needs, enhance the management of their condition, and improve quality of care and medical outcomes. Such services should further address the problem of clinical inertia as reported here and elsewhere (Khunti & Millar-Jones, 2017).

7.6 Future Research

- A potential limitation is that the study only focused on patients' views and accounts of managing their diabetes; hence, future work could focus on the perspectives of health professionals involved in their care, as well as those of family and friends in order to identify ways that could better support patients in managing their diabetes and adhering to their medicines.
- Although this study provides some of the first longitudinal results for T2D patients in respect to medication adherence, the follow-up of three months is relatively short, particularly for those on insulin treatment. Therefore future research should be extended in order to provide more useful and relevant information on the relationship between patients' beliefs about medicines, confidence in self-managing diabetes and the impact on medication adherence. Of particular importance would be identifying the views of people who refuse or do not initiate treatment, or those in full-time employment and their support mechanisms, and how these may influence adherence.
- Statistical and qualitative analysis was focused by grouping people into weight-effect groups, however, not all drugs are the same in spite of their effect on body weight. Therefore, future studies should focus on individual

drugs or on drugs with other similar attributes, such as the risk of hypoglycaemia, or compare drugs in tablet or injectable form.

- Although, interview findings suggest that support from health care services can improve confidence in self-managing T2D and therefore adherence, it is not clear whether this kind of support predicts adherence levels over time. Future longitudinal studies should investigate how service delivery/models of care can impact on adherence and glycaemic control.
- This study provides the basis for the development of a complex intervention which focuses on both changes to health care delivery and individual's medicine taking practices. However, future interventions should demonstrate clearly how related theories, identified here, have been applied and contributed to intervention outcomes.

7.7 Conclusion

Mixed method studies are used in much policy research and the combination of quantitative and qualitative longitudinal data is potentially very powerful in providing links between causation, processes and outcomes (Corden & Millar, 2007). This study builds on previous cross-sectional and qualitative work around the role of beliefs about medicines and self-efficacy in medication adherence. It is the only prospective study to date which examined these factors (amongst others) on a large scale using multiple health-care sites as well as analysing complex mixed method data. The study population is similar to other T2D populations in relation to prescribed medication trends, health service provision and sub-optimal medication adherence levels supporting the generalisability of the findings. This study contributes to new knowledge by highlighting how the needs and desired outcomes of T2D patients change over time after an initiation/change to a new medication.

The study showed that patients' short-term priorities and needs focused on medical treatment that is effective, and regular support from expert health professionals to manage unanticipated effects of their new treatment. Whereas, in the longer term, their priorities and needs focused on sufficient support to prevent further complications and a return to meaningful, functional life and normalisation.

Furthermore this study revealed that beliefs about medicines (Concerns, Overuse, Harm and Benefits), and self-efficacy in taking medicines correctly appear to have the greatest impact on medication adherence following initiation of new treatment for T2D, instead of the medicines' effect on body weight. These are modifiable factors and patients could benefit from NHS services that provide support in increasing confidence levels in taking medicines as well as exploring beliefs about medicines particularly in relation to concerns, and overuse, in order to help patients overcome these concerns.

Regardless of the type of treatment (lifestyle/medicine), over time, participants raised doubts about their effectiveness for T2D management, reinforced by the constant changes to treatments by HPs. This has had a negative impact on their emotional well-being and implied that medicines were a temporary measure for controlling their diabetes and/or body weight and therefore expressed a perceived need to stop taking them.

Most of the participants reported that at the present moment their T2D was not serious. However, they accepted their new medicines despite the risks associated with them, in hope of taking less, better, efficient and effective medicines both for their diabetes control and body weight. It is imperative that health professionals understand patients' experiences with their diabetes medications in order to provide responsive health care services within the NHS to meet patients' needs, improve quality of life and minimise costs. This study developed a range of visual models that could be used in both future research and practice to explore further patients' views and medication adherence.

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APPENDICES

Appendix 2.1 Systematic Review Search Terms

Systematic Review Search Terms

Stages of literature search with common key words- combination of keywords, phrases and subject heading terms

Literature Search Stage A

Search 1	AND Search 2
Diabetes Mellitus Type 2 (keyword, Medline MeSH- therapy, ethnology, nursing, psychology) OR Type 2 Diabetes OR Non*insulin dependent diabetes (keyword, EMBASE MeSH- therapy, disease management) OR Diabet* patient* (keyword, EMBASE MeSH)	medic*taking OR Medication Therapy OR Medication Therapy Management (Medline and EMBASE MeSH) OR Medication treatment* OR Antidiabetic agent* (keyword, EMBASE MeSH- therapy, Adverse drug reaction) OR Antidiabetic drug* OR Hypoglyc*emic drug* OR Hypoglyc*emic agent* (keyword, MesH- therapeutic use, Therapy, adverse effects) OR Glucose lowering drug* OR Glucose lowering agent* OR Anti*obesity agent* (keyword, Medline MeSH- therapeutic use, adverse effects, EMBASE MeSH- adverse drug reaction) OR Anti*obesity drug* OR Weight loss drug* OR Weight loss agent* OR Anti*glyc*emic drug* OR Anti*glyc*emic agent* OR Insulin (Medline MeSH- therapeutic use, therapy, adverse effects, EMBASE MeSH- Adverse drug reaction) OR Insulin therapy

Literature Search Stage B

Search 3	OR Search 4
Adhere* OR Compliance OR Patient* compliance (keyword, Medline and EMBASE MeSH) OR Concordance OR Treatment compliance OR Medication compliance (keyword, EMBASE MeSH) OR Treatment adherence OR Medication adherence (keyword, Medline MeSH) OR Non*adherence	Belief* OR Health belief* (keyword, EMBASE MeSH) OR Attitude* OR Health attitude* OR View* OR Perspective* OR Expectation* OR Experience* OR Perception* OR Behavio*r* OR Health behavio*r* (keyword, Medline & EMBASE MeSH) OR preference* OR Patient* preference* (keyword, EMBASE MeSH, Medline MeSH-psychology, ethnology, stats & numerical data) Opinion* OR attitude to health (keyword, Medline MeSH)

Literature Search Stage C

Search 5
Weight gain OR Weight loss OR Weight management OR Body weight changes (keyword, Medline MeSH) OR Weight change (EMBASE MeSH)

Literature Search Stage D: Stage A AND Stage B (use this if no results found in search E)
Literature Search Stage E: Stage C AND Stage D

Appendix 2.2 Adapted CASP Tool

Adapted CASP tool from (CASP) Qualitative Research Checklist (v 31.05.13)

Paper ID:

Authors name:

Year of Publication:

Geographical Location of Study:

Does the paper report on findings from qualitative research and did that work involve both qualitative methods of data collection and data analysis?

Yes No

If the answer to above questions is "no", exclude paper and provide the reason for exclusion.

Reason(s) for exclusion:
If the answer to above questions is "yes" continue with the following screening questions

1. Was there a clear statement of the aims of the research? Yes Can't tell No

HINT: Consider
• What was the goal of the research?
• Why it was thought important?
• Its relevance

2. Is a qualitative methodology appropriate? Yes Can't tell No

HINT: Consider
• If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants
• Is qualitative research the right methodology for addressing the research goal?

3. Was the research design appropriate to address the aims of the research?
Yes Can't tell No

HINT: Consider
• If the researcher has justified the research design (e.g. have they discussed how they decided which method to use)?

4. Is there a theoretical perspective identified? Yes Can't tell No
How would you categorise the theoretical perspective:

- Phenomenology
- Grounded Theory
- Ethnography
- Action research
- Other
- Not Classifiable

5. Was the recruitment strategy appropriate to the aims of the research?
Yes Can't tell No

HINT: Consider
• If the researcher has explained how the participants were selected
• If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study
• If there are any discussions around recruitment (e.g. why some people chose not to take part)

6. Was the data collected in a way that addressed the research issue?
Yes Can't tell No

HINT: Consider
• If the setting for data collection was justified
• If it is clear how data were collected (e.g. focus group, semi-structured interview etc.)
• If the researcher has justified the methods chosen
• If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews were conducted, or did they use a topic guide)?
• If methods were modified during the study. If so, has the researcher explained how and why?
• If the form of data is clear (e.g. tape recordings, video material, notes etc)
• If the researcher has discussed saturation of data

7. Has the relationship between researcher and participants been adequately considered?
Yes Can't tell No

HINT: Consider
• If the researcher critically examined their own role, potential bias and influence during
(a) Formulation of the research questions
(b) Data collection, including sample recruitment and choice of location
• How the researcher responded to events during the study and whether they considered the implications of any changes in the research design

8. Have ethical issues been taken into consideration? Yes Can't tell No

HINT: Consider
• If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained
• If the researcher has discussed issues raised by the study (e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study)
• If approval has been sought from the ethics committee

9. Was the data analysis sufficiently rigorous? Yes Can't tell No

HINT: Consider
• If there is an in-depth description of the analysis process
• If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data?
• Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process
Are quotes numbered / identified?
• If sufficient data are presented to support the findings
• To what extent contradictory data are taken into account

Are you confident that all the data were taken into account?
• Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation

10. Is there a clear statement of findings? Yes Can't tell No

HINT: Consider
• If the findings are explicit
• If there is adequate discussion of the evidence both for and against the researchers arguments

• If the researcher has discussed the credibility of their findings (e.g. triangulation, respondent validation, more than one analyst to ensure reliability)
• If the findings are discussed in relation to the original research question
Do the researchers indicate how they developed their conceptual interpretations of what the data contain?

11. How valuable is the research?

HINT: Consider
• If the researcher discusses the contribution the study makes to existing knowledge or understanding e.g. do they consider the findings in relation to current practice or policy?, or relevant research-based literature?

Is there descriptive, conceptual, or theoretical congruence between this and other work?
• If they identify new areas where research is necessary
• If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

What is the overall assessment of study?

(max score = 11, each main questions is scored one point)

Appendix 2.3 Translational Synthesis: key components of perceptions of T2D and T2D medicine taking, including illustrative quotes (1st and 2nd order constructs) from primary studies

Themes (3rd order constructs)	**Participants Quotes (1st order constructs)**	**Authors Interpretations (2nd order constructs)**
Emotions- Negative Feelings	*"I was devastated [about being prescribed glipizide]. I wasn't happy at all. But it was explained to me that diabetes always progresses, no matter how careful you are."*[1] "*Well me Grandmother used to have diabetes … and I remember this dirty great syringe, like an icing sugar thing*."[3]	Initial Reaction[1] Shock[3] Fear of injections[3], Needle Anxiety Denial[14]
My Diabetes is serious	*'...from my experience of diabetes, it's just an inevitable part of it that you're going to end up being on insulin anyway...I was expecting it .... it was suggested a few times that I took insulin as my tablets were going up'*[9]	Acceptance[14], Beliefs about Necessity of Insulin[9], Priority[16], Commitment to taking OGDs[2B], Perceptions of OGDs[1]
My Diabetes is not serious	'*My health will remain good, by the Grace of God, so long as I keep praying*.'[5]	Contextual Knowing[2A], Priority[16], Disease severity, insulin leading to premature death and social stigma[5]
Expectations of Treatment (medicines)	"*Keep me alive*"[2C], "*When I was put on metformin it was almost sold as a good one that would help lose weight as well…."*[2C]	Expectations and Concerns[2B]
Expectations of Care	*'The right hand doesn't seem to know what the left hand does. He looks at his screen and reckons he hasn't heard from the hospital yet, but that's always the excuse.*'[4], "*You need to be educated to do it correctly [referring to educators]. It can really help."*[6], "*That's for cholesterol . . . eh, I get (inaudible 00:25:10) . . . I have no idea what that's for . . . 'cos I go to my doctor; they don't tell me what the tablets are for . . .* "[16]	Education and Information needs[2B], Information and Support[4], Doctor-Patient Consultation[6], The message[6], experiences of health care interactions[10], Barriers to knowledge acquisition[11]

Negative Perceptions and Experiences with Medicines	"*It's a foreign substance, and you're shoving it in your body*"[3], "*I can't do anything and I can't go abroad. I can't do anything 'cause I've got to take this insulin, and it devastated me.", 'really bad stomach cramps'*[2B]	Negative experiences[2B], Friend or Foe[3], Fear of causing harm[3], Insulin as a restriction[3], Knowledge adnunderstanding[6], mistrust in the value of treatment[12], beliefs about over prescribing & resistance to additional medicines[15], Loss of control[5], treatment convenience[8]
Positive Perceptions and Experiences with Medicines	"*Feels like I am normal now, I've got strength. I am a normal man*"[3], '*I was always waking in the morning with it [blood sugar levels] very high […]. So, they put me on this one which keeps it steady at night*.'[7B], *"[the GP] 'tested it, and it's come down to seven point something and he's really pleased'"*[2A]	Synergies and antagonism in the management of multimorbidity[16], Regaining Health[3], Quality of Life[6], Receptiveness towards instensification[7B], Importance of medicines[15], Person and context[13]
Self-Regulation	"*And now in the morning I take three pills, sometimes two, meaning I check it [blood glucose] and according to that I do or don't take all the pills*."[1]	Topping-up[7B], Strategies to control diabetes[12]
Medicine Taking Behaviour - Adherence and Unintentional non-adherence with Guilt - Unintentional non-adherence without guilt - Intentional non-adherence with guilt - Intentional non-adherence without guilt	"*Sometimes you do say that to yourself, you know, you say to yourself, 'Oh I feel fine and I'll take one today, I won't take two.'*[1], "*I did start to take glucosamine, but I take my tablets that I have for my blood pressure, my diabetes and my cholesterol and then the aspirin, I forget about the others. I think to myself, I'm knocking about, feeling alright, why bother?*"[16], "*It's just slipped into my lifestyle in that come four o'clock in the afternoon I take my pill'*[2B], *"I'm very bad for the one during the day, I forget that*''[2A], "*With this injection, aspart, you can do it 20 minutes before hand and then it begins to get into the bloodstream or you can do it after your meal but I*	Forgetfulness[2B], Managing two types of insulin[7B], The importance of medicines[15], Strategies to promote adherence[2B]

	usually do it before because you have a meal out and then you don't want to dash home."[7B]	
Strategies to overcome negative aspects of insulin	"*I wouldn't go out to lunch with them (friends) and in the end I had to tell them why. I said, 'I can't. I have got to have insulin. And I am not going to go into a toilet*"[7B], *'If I go out with anybody I always go and do it (inject) in the toilet. I won't ever do it outside.'*[7B]	Difficulties with injecting in public[7B], Managing two types of insulin[7B] Information and support[4]
Lifestyle Behaviour	"*Yeah but sometimes I taste a little thing what I know I don't supposed to really eat … You can eat everything but small amount of it.*"[6], *"…we changed our diet overnight, for the whole of the family. The sugars went out and the fat went out and healthy food just came in immediately and that helps."* [15]	Down to me[2C], Activities of daily living[4] Attitude to self-mangement[11], Integrating the diabetic regimen[10]

NB: 1st order constructs represent the views and understandings of primary research participants and 2nd order constructs represent the interpretations offered by primary authors. Please note that some 2nd order constructs are not directly derived by 1st order constructs. Please note not all 1st and 2nd order constructs are represented in this table.

Appendix 3.1 Research Flyer

UNIVERSITY OF LIVERPOOL

Aintree University Hospital NHS
NHS Foundation Trust
Where quality matters

You Can Take Part in Type 2 Diabetes Research if You Start a New Diabetes Medicine

This is a research study to find out the views of people with Type 2 Diabetes about their medicines.

WHO CAN TAKE PART: People with Type 2 Diabetes who are starting on a new diabetes medication, ages 18 plus.

WHAT DO I NEED TO DO: Complete a questionnaire, **before** you start taking your new medication and complete a second questionnaire in 3 months time.

You may also be given the option to participate in an interview.

If you do decide to take part, you may withdraw at any time without giving a reason.

WHAT ARE THE BENEFITS OR RISKS: There are no risks in participating in this study. The information we get from this study aims to help improve the treatment and health care services for people with Type 2 Diabetes.

You can request more information about this study from your Doctor, Nurse, Pharmacist or directly from the research team, if your practice or pharmacy are not aware of the study.

The research is led by Professor John Wilding, Department of Obesity and Endocrinology at University of Liverpool, and conducted by lead researcher Mrs Katie Psarou.

For further information please contact Katie on :

Mobile: 07501095512 Email: Katie.Psarou@nhs.net

Funded By

DIABETES UK
CARE. CONNECT. CAMPAIGN.

Appendix 3.2 Potential Participant Research Invitation Letter

Katie Psarou
Research Fellow
Department of Obesity and Endocrinology
Clinical Sciences Centre
Aintree University Hospital
Longmoor Lane
Liverpool
L9 7AL

Tel: 0151 5295940
email: a.psarou@liv.ac.uk

Dear Patient

Research study about patients' expectations and views on medicines for Type 2 Diabetes

We are writing to ask if you would like to take part in a research study. The study is funded by Diabetes UK and is being managed by Department of Obesity and Endocrinology, based at Clinical Sciences Centre, Aintree University Hospital.

The aim of the study is to explore:

- Patients' expectations and views of taking new diabetes (and/or weight loss) medication. and
- The effects of these expectations on their body weight, diabetes control and management.

We want to improve our understanding of patients' experiences. This will help us to improve services and future treatment of people who develop Type 2 Diabetes.

Information about the study is given on the attached sheet. If you would like to take part, please complete and return the attached consent form and questionnaire in the prepaid reply envelope.

Interviews will also take place as part of this research project, if you wish to take part in this further study, please complete your telephone number together with suitable times to contact on the consent form. A member of the research team will then get in touch with you to discuss this part of the project. If you are happy to do so, we will arrange an interview at a time and date to suit you.

We hope you will consider helping us with this important confidential study, but your participation is entirely voluntary.

Yours sincerely,

Mrs Katie Psarou
Research Fellow
University of Liverpool

Professor John Wilding
University of Liverpool

Professor Helen Cooper
University of Chester

Date: 02/02/2012, Version: 6.0

Appendix 3.3 Study Consent Form

UNIVERSITY OF LIVERPOOL

Aintree University Hospital NHS
NHS Foundation Trust
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DiABETES UK
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CONSENT FORM (Version 3 – 02/02/2012)

Title of Research Project: What do patients with Type 2 Diabetes think about their medicines?

Researcher(s): Mrs Aikaterini Psarou, Professor John Wilding, Professor Helen Cooper

Centre ID Number: ☐☐☐ Participant ID Number: ☐☐☐☐☐

Please Initial Box

1. I confirm that I have read and have understood the information sheet dated 31st January 2012 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from this study, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. I understand that my personal data will be processed and stored securely in compliance with the 1998 Data Protection Act. ☐

4. I agree to take part in face to face interviews. I understand that my GP will be informed, as I may need to delay starting my new medicine for up to one week. *(Optional)*. ☐ *(optional)*

5. I agree that my data gathered in this study may be stored *(after it has been anonymised)* in a specialist data centre and may be used for future research examining similar scientific questions. I understand that any such studies will undergo formal ethical approval procedures prior to using any of my data. ☐

6. I agree to take part in this study ☐

_____ / / _____

Participant Name *(Print in Capitals)* Date Signature

_____

Participants telephone number and best times to contact you

_____ / / _____

Name of Researcher (Print) Date Signature

Please use the prepaid envelope to return consent form and questionnaire to researcher. The contact details of researcher (Principal Investigator) are at the back of the questionnaire.

When completed, 1 copy for participant; 1 copy for researcher 1

Appendix 3.4 Participant Information Sheet

UNIVERSITY OF LIVERPOOL

Aintree University Hospital NHS
NHS Foundation Trust
Where quality matters

Funded By
DiABETES UK
CARE. CONNECT. CAMPAIGN.

Participant Information Sheet

What do patients with Type 2 Diabetes think about their medicines?

You are being invited to take part in a research study at University of Liverpool. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully. Feel free to ask us or your Doctor if there is anything that is not clear or if you would like more information. We would like to stress that you do not have to accept this invitation and should only agree to take part if you want to.

What is the purpose of the study?
Obesity has become a common condition and a major public health concern in this country. As you probably know, Type 2 Diabetes is often closely linked with being overweight and obese. Also, an increase in body weight above a healthy weight can further increase the risk of health complications for those who have diabetes. Therefore, weight management in diabetes is important to delay the progression of this condition and keep it under control.

Medicines for Type 2 Diabetes can have effects on body weight causing either weight gain or weight loss. Therefore some patients may be reluctant to take medicines, mainly due to fear of weight gain. We know little about how expectations, beliefs and attitudes of patients with Type 2 Diabetes towards their medicine (s) change over time. This is important to know as the number of medicines prescribed to them often increases over time.

Overall the purpose of the study is to understand:

- What people think about their diabetes and weight loss medicines?
- Their reasons for taking or not taking these medicines?

And to identify:

- Effective ways of focusing on body weight to support patients to manage their condition and treatments(s); to enable them to take their prescribed medicine as advised
- In the future, knowledge from this research could be used to examine similar scientific questions that may improve health care services for Type 2 Diabetes patients,

  and

- To inform the training of those directly involved in the delivery of diabetes care
- Results from this research study will also be published

Why have I been chosen to take part?
Your family doctor, pharmacist, and/ or hospital health care team have identified you because you have Type 2 Diabetes and you have recently had a change to your diabetes treatment. That means you have been prescribed a new medicine to manage your diabetes and/or your body weight. We are recruiting participants from a variety of health care services, including some GP practices and community pharmacies in the Merseyside area, and the Diabetes Centre at Aintree University Hospital. The research study will recruit approximately 300 patients over a period of one year.

Do I have to take part?

Participation is voluntary. It is up to you to decide whether to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time, without giving a reason. Results up to the period of withdrawal may be used, if you are happy for this to be done. Regardless of whether you take part, your healthcare service will not be affected in any way.

What will happen if I take part?

Questionnaires:
We will ask you to fill in a questionnaire **before you begin to take your new medicine** and return it to us in the prepaid envelope provided. **It is important that you fill in the questionnaire before you start your new medicine, as we want to identify your expectations of it before you take it.**

After 3 months taking the new medicine, we will send you a second questionnaire to fill in. Again you will need to return this to us in the prepaid envelope. You do not have to change your medicine regime in any way. Each questionnaire should take about 35 minutes to fill in and less than one hour of your time.

Medical Records:

We will also access your medical records to look at recent blood results; related to your diabetes control, and your body weight. We will collect these values to do some further analysis in relation to your answers to the questionnaires. We will only access your medical records twice; once at the beginning of the research and then 3 months later. Any information that leaves your GP practice and/or the hospital will have your name and address removed. You are free to stop this access at any point without giving a reason.

Interviews:
In addition, we will ask you to consider taking part in face to face interviews to further explore the findings from the questionnaires. This is optional. You can if you want to consent to the questionnaires but not the interviews. If you agree to take part, we will ask you to sign another consent form before the interview starts. The study will involve two interviews. The first one will occur shortly after you fill in the first questionnaire and **before you start your new medicine**. You may have to delay starting your new medicine for up to one week. We will ask your GP to check if this is safe. You will need to be available for the first interview within the first week of agreeing to take part in the study. The second interview will take place 3 months after starting your new medicine, shortly after you fill in the second questionnaire. Each interview will last around 45 minutes, and no more than 2 hours of your time.

The interviews are important method for this study to explore the findings of the questionnaire in more detail. They would take place at a convenient time and date for you. Under special circumstances (unable to get to interviews due to disability or childcare), we can arrange the interview to take place in your own home or at your GP practice. With your permission the interview would be recorded. This is more accurate and quicker than trying to write things down during the interview. The recording will then be transcribed (written out) in a way that carefully removes any of your personal details (called anonymous transcription). The interview transcript will be anonymous from this point on. The digital record of the interview will be destroyed once it has been transcribed. A copy of the transcript can be sent to you to keep, if you wish.

Any information given by you will be treated in the strictest confidence and will be used only for the purpose of the study. Your personal details are removed at the analysis of all questionnaires, medical record data and, if applicable to you, interviews. This means that you cannot be identified from the study or any later publications.

Expenses and / or payments
Your participation in this study is voluntary. You will not have to pay any expenses for the survey part (questionnaires) of this study as a prepaid envelope will be given to you. If you take part in the

interviews, we will pay you back any travel expenses for travelling to and from the Clinical Science Centre at University Hospital Aintree, where the interviews will be carried out.

Are there any risks in taking part?
There are no risks foreseen in taking part in this study. Your treatment will not be affected whether you choose to take part or not. The study may address some sensitive areas around your diabetes management and/or your body weight. Should you feel distressed at any point during the study or as a result of the questionnaires or interviews, you are encouraged to contact the researcher and access your "health care team" directly. Your "health care team" will remain your GP practice or your diabetes hospital team.

Are there any benefits in taking part?
We cannot promise the study will help you, but the information we get from this study will help improve the treatment and health care services of overweight and obese people with Type 2 Diabetes.

What if I am unhappy or if there is a problem?
If you have a concern about any aspect of the study, please feel free to let us know by contacting the researcher, Katie Psarou, in the first instance (contact details below). Katie will do her best to answer your questions. Should you wish to take any concerns further which you feel you cannot come to us with, then you should contact the Research Governance Officer at University of Liverpool on 0151 794 8290 (ethics@liv.ac.uk). When contacting the Research Governance Officer, please give details of the name or description of the study (so that it can be identified), the researcher(s) involved, and the details of the complaint you wish to make. Regardless of this, the normal National Health Service complaints systems will still be available to you.

Will my participation be kept confidential?
All information collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the GP practice/hospital will have your name and address removed so that you cannot be identified. Questionnaires will be stored in a locked filing cabinet at the Clinical Sciences Centre, University Hospital Aintree and the original digital records of interviews will be destroyed after anonymised transcription. Only the research team and academic supervisors will have access to the anonymised data. These will be stored for 7 years to be used for the analysis of this project and future research.

What will happen to the results of the study?
Overall, the findings will be used to put together a PhD thesis. The findings will also be published to scientific journals and used to produce a report that will be made available to local health services and Diabetes UK. Seminars and other events will be organised to distribute the results in conferences and diabetes local support groups. On request, at the end of the study, a newsletter will be made available. Anonymity and confidentiality will still be in place in all cases.

Who is organising and funding the research?
The research is being led by Professor John Wilding, Department of Obesity and Endocrinology at the University of Liverpool, which is based at the Clinical Sciences Centre, University Hospital Aintree and funded by Diabetes UK.

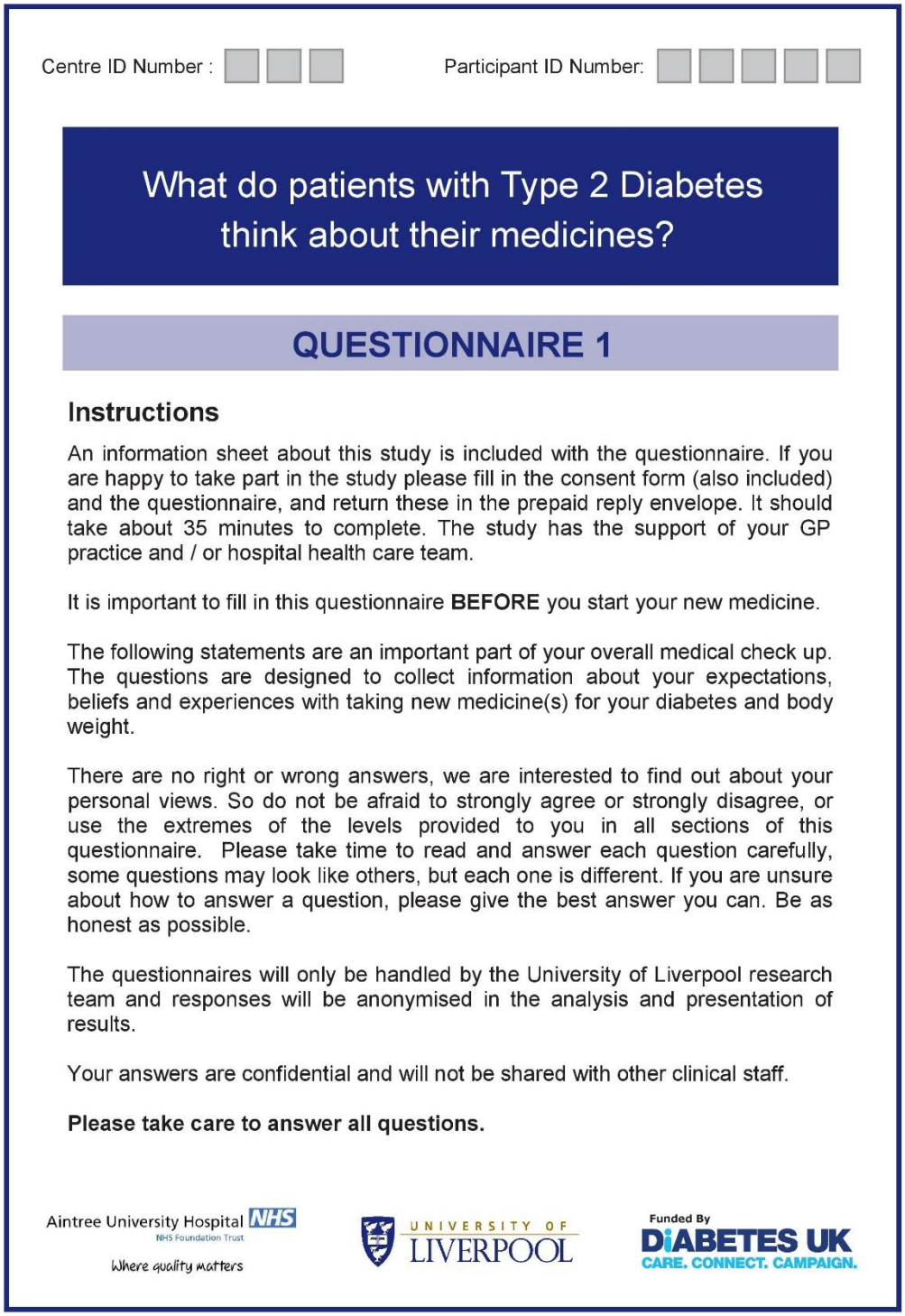
Who has reviewed the study?
All research in the NHS is looked at by separate group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by Berkshire Research and Ethics Committee.

Thank you for reading this.

For further information contact:
Katie Psarou, Research Fellow, Office Telephone: 0151 5295940, Email: a.psarou@liv.ac.uk

Appendix 3.5 – Questionnaire 1 and 2

Questionnaire 2 is exactly the same except there is no section A (Background Information). Sections in questionnaire 2 are labelled from A through to H.



Centre ID Number : ☐☐☐ Participant ID Number: ☐☐☐☐☐

What do patients with Type 2 Diabetes think about their medicines?

QUESTIONNAIRE 1

Instructions

An information sheet about this study is included with the questionnaire. If you are happy to take part in the study please fill in the consent form (also included) and the questionnaire, and return these in the prepaid reply envelope. It should take about 35 minutes to complete. The study has the support of your GP practice and / or hospital health care team.

It is important to fill in this questionnaire **BEFORE** you start your new medicine.

The following statements are an important part of your overall medical check up. The questions are designed to collect information about your expectations, beliefs and experiences with taking new medicine(s) for your diabetes and body weight.

There are no right or wrong answers, we are interested to find out about your personal views. So do not be afraid to strongly agree or strongly disagree, or use the extremes of the levels provided to you in all sections of this questionnaire. Please take time to read and answer each question carefully, some questions may look like others, but each one is different. If you are unsure about how to answer a question, please give the best answer you can. Be as honest as possible.

The questionnaires will only be handled by the University of Liverpool research team and responses will be anonymised in the analysis and presentation of results.

Your answers are confidential and will not be shared with other clinical staff.

Please take care to answer all questions.

Aintree University Hospital NHS NHS Foundation Trust Where quality matters

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Section A: Background Information

Firstly we would like to know a little more about you. This information is helpful for statistical purposes. Remember that your responses become anonymous in the analysis. Please answer the following questions by completing or ticking the box as appropriate to you.

Please complete date and time questionnaire completed:

Date ☐☐ Month ☐☐ Year ☐☐☐☐

Time ☐☐ : ☐☐ am / pm (please circle)

Question A1

Are you Male ☐ or Female ☐

Question A2

What is your date of birth?

Date ☐☐ Month ☐☐ Year ☐☐☐☐

Question A3

When were you diagnosed with Diabetes? (please insert month and year)

Month ☐☐ Year ☐☐☐☐

Question A4

Are you currently ?

- ☐ Single
- ☐ Married/ Partnered/ Living with someone
- ☐ Divorced/Separated
- ☐ Widowed

Question A5

To which of these ethnic groups do you consider you belong? (*optional*)

- ☐ White British / other White Background
- ☐ Black or Black British (e.g. African/ Caribbean)
- ☐ Asian or Asian British (e.g. Indian, Pakistani, Bangladeshi)
- ☐ Mixed / Multiple ethnic groups background
- ☐ Other: _____ (Please state)

Question A6

What is the highest level of educational qualification you have completed?

- ☐ University Degree or Higher
- ☐ 'A' level or equivalent
- ☐ GCSE or equivalent
- ☐ Diploma
- ☐ Vocational (NVQ, HNC, HND)
- ☐ No formal qualifications

Question A7

Are you currently?

- ☐ Working full-time
- ☐ Unemployed
- ☐ Other:_____ (Please state)
- ☐ Working Part-time
- ☐ Retired

Section B: Expectations about New Medicine(s)

Even though you may never have taken this new medicine, you probably have some expectations about this therapy. Below are statements about taking your new medicine and medicine delivery system (for example, oral pills or solution, vial and syringe, insulin pen).

Each numbered statement finishes the sentence "I expect that...".

Please circle the number below the word or phrase that best indicates your level of agreement with each statement. It is important that you respond to every statement.

	I expect that taking this new medicine for my diabetes (or my weight) will:	**Strongly disagree**	**Disagree**	**Slightly disagree**	**Neither agree nor disagree**	**Slightly agree**	**Agree**	**Strongly agree**
B1	make it easier to control my blood sugars	1	2	3	4	5	6	7
B2	restrict my life (for example, make it harder to travel or eat out)	1	2	3	4	5	6	7
B3	cause me to have severe episodes of low blood sugar	1	2	3	4	5	6	7
B4	make me feel better	1	2	3	4	5	6	7
B5	cause me to gain an undesirable amount of weight	1	2	3	4	5	6	7

 EITQ version 2.0 modified 2012

	I expect that my new delivery system (oral / injectable) will:	Strongly disagree	Disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Agree	Strongly agree
B6	be physically painful or difficult to swallow	1	2	3	4	5	6	7
B7	be easy for me to use away from home or as prescribed	1	2	3	4	5	6	7
B8	not be noticed by others when I use or take it	1	2	3	4	5	6	7

		Strongly disagree	Disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Agree	Strongly agree
B9	I expect that it will be easy to get the medicine dose/ amount I need with my new medicine delivery system (oral / injectable)	1	2	3	4	5	6	7
B10	I expect that my new medicine delivery system will be convenient	1	2	3	4	5	6	7

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5

Section C: Satisfaction with information about your New Medicine(s)

In this section, we would like to ask you about the **information you have received about your new diabetes (and/or weight loss) medicines**. Please rate the information you have received about each of the following aspects of your medicine by ticking the appropriate box.

	Have you received enough information about:	Too much	About right	Too little	None Received	None Needed
C1	What your medicine is called?	☐	☐	☐	☐	☐
C2	What your medicine is for?	☐	☐	☐	☐	☐
C3	What it does?	☐	☐	☐	☐	☐
C4	How it works?	☐	☐	☐	☐	☐
C5	How long it will take to act?	☐	☐	☐	☐	☐
C6	How you can tell if it is working?	☐	☐	☐	☐	☐
C7	How long you will need to be on your medicine?	☐	☐	☐	☐	☐
C8	How to use your medicine?	☐	☐	☐	☐	☐
C9	How to get a further supply?	☐	☐	☐	☐	☐
C10	Whether the medicine has any unwanted side effects?	☐	☐	☐	☐	☐
C11	What are the risks of you getting side effects?	☐	☐	☐	☐	☐

SIMS modified 2012

		Too much	About right	Too little	None Received	None Needed
C12	What you should do if you experience unwanted side effects?	☐	☐	☐	☐	☐
C13	Whether you can drink alcohol whilst taking this medicine?	☐	☐	☐	☐	☐
C14	Whether the medicine interferes with other medicines?	☐	☐	☐	☐	☐
C15	Whether the medicine will make you feel drowsy?	☐	☐	☐	☐	☐
C16	Whether the medicine will affect your weight?	☐	☐	☐	☐	☐
C17	Whether the medicine will affect your sex life?	☐	☐	☐	☐	☐
C18	What you should do if you forget to take a dose?	☐	☐	☐	☐	☐

Other information please specify below

Section D: Your views about your Medicine(s) prescribed for Diabetes/ Weight Loss

In this section, we would like to ask you about your personal views about the medicine(s) prescribed for you for your diabetes (including weight loss medicines). These are statements other people have made about their medicines.
Please show how much you agree or disagree with them by ticking the appropriate box.
There are no right or wrong answers. We are interested in your personal views.

		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
D1	My health, at present, depends on these medicines	☐	☐	☐	☐	☐
D2	Having to take these medicines worries me	☐	☐	☐	☐	☐
D3	My life would be impossible without these medicines	☐	☐	☐	☐	☐
D4	I sometimes worry about the long-term effects of these medicines	☐	☐	☐	☐	☐
D5	Without these medicines I would be very ill	☐	☐	☐	☐	☐
D6	These medicines are a mystery to me	☐	☐	☐	☐	☐
D7	My health in the future will depend on these medicines	☐	☐	☐	☐	☐
D8	These medicines disrupt my life	☐	☐	☐	☐	☐
D9	I sometimes worry about becoming too dependent on these medicines	☐	☐	☐	☐	☐
D10	These medicines protect me from becoming worse	☐	☐	☐	☐	☐
D11	These medicines give me unpleasant side effects	☐	☐	☐	☐	☐
D12	I worry that taking these medicines will cause me to gain weight	☐	☐	☐	☐	☐

Section E: Your views about Medicines in General

In this section, we would like to ask you about your personal views about medicines in general. These are statements other people have made about medicines in general.

Please show how much you agree or disagree with them by ticking the appropriate box.
There are no right or wrong answers. We are interested in your personal views.

		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
E1	Doctors use too many medicines	☐	☐	☐	☐	☐
E2	People who take medicines should stop their treatment for a while every now and again	☐	☐	☐	☐	☐
E3	Most medicines are addictive	☐	☐	☐	☐	☐
E4	Natural remedies are safer than medicines	☐	☐	☐	☐	☐
E5	Medicines do more harm than good	☐	☐	☐	☐	☐
E6	Doctors place too much trust on medicines	☐	☐	☐	☐	☐
E7	If doctors had more time with patients they would prescribe fewer medicines	☐	☐	☐	☐	☐
E8	Without medicines doctors will be less able to cure people	☐	☐	☐	☐	☐
E9	Medicines help many people to live longer	☐	☐	☐	☐	☐
E10	In most cases the benefits of medicines outweigh the risks	☐	☐	☐	☐	☐
E11	Medicines help many people to live better lives	☐	☐	☐	☐	☐

BMQg-11

Section F: Satisfaction with Diabetes/ Weight Loss Medicine(s)

Your diabetes treatment is a combination of diet, exercise and medicines. **The following questions are concerned only with the MEDICINES (pills, and/or injections) that you take for your diabetes.**

If you take medicines for other conditions, please try to think only about the medicines you take for diabetes (including weight loss medicines) when answering the questions. If you take more than one medicine for your diabetes, please consider all of your diabetes medicines when answering these questions.

Please tick the box that most closely represents how you have felt about your diabetes medicines over the PAST 2 WEEKS. Please tick only one box for each question.

If you have never taken a medicine for diabetes and weight loss please tick this box ☐

Please continue with section H (page 17)

Over the **PAST 2 WEEKS**, how **BOTHERED** have you been by:

		Not at all bothered	Slightly bothered	Somewhat bothered	Very Bothered	Extremely bothered
F1	The amount of home monitoring (blood sugar testing) required as part of using your medicine(s)?	☐	☐	☐	☐	☐
F2	The number of times you need to take your medicine(s) every day?	☐	☐	☐	☐	☐
F3	The need to adjust the dosing (amount) of your medicine(s)?	☐	☐	☐	☐	☐
F4	How your medicine(s) interferes with your daily life?	☐	☐	☐	☐	☐

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Over the **PAST 2 WEEKS**, have you been **BOTHERED** by any of the following due to your diabetes (or weight loss) medicine(s)?

		Not at all Bothered	Slightly Bothered	Somewhat Bothered	Very Bothered	Extremely Bothered	Did not have this side-effect
F5	Unwanted weight gain?	☐	☐	☐	☐	☐	☐
F6	Pain or discomfort?	☐	☐	☐	☐	☐	☐
F7	Flatulence and bloating?	☐	☐	☐	☐	☐	☐
F8	Diarrhoea?	☐	☐	☐	☐	☐	☐
F9	Symptoms of low blood sugar (such as trembling, sweating, dizziness or blurred vision)?	☐	☐	☐	☐	☐	☐

Over the **PAST 2 WEEKS**, how **DISSATISFIED** or **SATISFIED** have you been with your diabetes (or weight loss) medicine(s) ability to:

		Extremely Dissatisfied	Very Dissatisfied	Slightly Dissatisfied	Neither dissatisfied or satisfied	Slightly Satisfied	Very Satisfied	Extremely Satisfied
F10	Keep your blood sugar levels stable (avoid highs and lows)?	☐	☐	☐	☐	☐	☐	☐
F11	Help you from feeling tired and lacking energy?	☐	☐	☐	☐	☐	☐	☐

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11

Overall, over the **PAST 2 WEEKS**, how **DISSATISFIED** or **SATISFIED** have you been with:

		Extremely Dissatisfied	Very Dissatisfied	Slightly Dissatisfied	Neither dissatis-fied or satisfied	Slightly Satisfied	Very Satisfied	Extremely Satisfied
F12	The ease and convenience of your diabetes (or weight loss) medicine(s)?	☐	☐	☐	☐	☐	☐	☐
F13	The impact of your diabetes (or weight loss) medicine(s) on your physical well-being?	☐	☐	☐	☐	☐	☐	☐
F14	The impact of your diabetes (or weight loss) medicine(s) on your emotional well-being?	☐	☐	☐	☐	☐	☐	☐

Thinking about your diabetes (or weight loss) medicine(s) over the **PAST 2 WEEKS**:

		Not at all	Slightly	Somewhat	Very	Extremely
F15	How difficult has it been for you to plan daily activities around your medicine(s)?	☐	☐	☐	☐	☐
F16	How much of a burden has it been to take your medicine(s) as prescribed?	☐	☐	☐	☐	☐
F17	How embarrassed or awkward have your felt because of taking your medicine(s)?	☐	☐	☐	☐	☐
F18	How worried have you been that your medicine(s) is not helping you to slow down or prevent long-term complications?	☐	☐	☐	☐	☐

DiabMedSat Modified 2012

12

Over the **PAST 2 WEEKS**, how often has taking your diabetes (or weight loss) medicine(s) as prescribed **INTERFERED WITH** your ability to…

		Never	Rarely	Sometimes	Often	All the time
F19	be flexible with planning meals (when you eat and what you are able to eat)?	☐	☐	☐	☐	☐
F20	do your recommended physical activity or exercise?	☐	☐	☐	☐	☐
F21	follow your recommended diet?	☐	☐	☐	☐	☐

F22

Overall, thinking about each of the aspects of your diabetes (or weight loss) medicine(s) mentioned above, how **DISSATISFIED** or **SATISFIED** have you been with your current diabetes medicine(s)?

Extremely dissatisfied	Very dissatisfied	Slightly dissatisfied	Neither dissatisfied or satisfied	Slightly satisfied	Very satisfied	Extremely satisfied
☐	☐	☐	☐	☐	☐	☐

F23

Overall, based on your current experiences with your diabetes (or weight loss) medicine(s), how **INTERESTED** would you be to change the type of medicine(s) you take or the way you take it, if it was possible?

Not at all interested	Slightly interested	Somewhat interested	Very interested	Extremely interested
☐	☐	☐	☐	☐

DiabMedSat Modified 2012

13

For the following questions, please circle the response that most closely represents how you have felt about your diabetes/ weight loss medicine(s) over the **PAST TWO WEEKS**.
Please circle only one number for each question.
Remember there are no right or wrong answers to these questions.

	How satisfied or dissatisfied are you with:	**Not at all satisfied**	**A little satisfied**	**Somewhat satisfied**	**Very satisfied**	**Extremely satisfied**
F24	How well your medicine helps you lose weight	1	2	3	4	5
	How much of a problem or not a problem is it for you to:	**Never/ Almost never a problem**	**Rarely a problem**	**Sometimes a problem**	**Often a problem**	**Almost Always/ Always a problem**
F25	Be as active as you would like (because of your medicine)	1	2	3	4	5
	How satisfied or dissatisfied are you with your medicine's ability to:	**Not at all satisfied**	**A little satisfied**	**Somewhat satisfied**	**Very satisfied**	**Extremely satisfied**
F26	Control your appetite	1	2	3	4	5
	How bothered or not bothered are you by:	**Not at all bothered**	**A little bothered**	**Somewhat bothered**	**Very bothered**	**Extremely bothered**
F27	Weight loss plateaus (periods of no weight loss)	1	2	3	4	5
F28	Being tired or drowsy during the day because of your medicine	1	2	3	4	5

TRIM-Weight

14

	Because of your diabetes / weight loss medicine, how often do you feel:	Never/ Almost never	Rarely	Sometimes	Often	Almost Always/ Always
F29	You have problems with mental functioning (for example concentrating, focusing, being distracted)	1	2	3	4	5
F30	Depressed	1	2	3	4	5
F31	Frustrated	1	2	3	4	5
F32	Embarrassed	1	2	3	4	5
F33	Stressed	1	2	3	4	5
	How often does your medicine interfere or not interfere with your:	**Never/ Almost never interferes**	**Rarely interferes**	**Sometimes interferes**	**Often interferes**	**Almost always/ Always interferes**
F34	Social activities (meeting with friends, going out)	1	2	3	4	5
F35	Being as productive as you would like (either at home or at work)	1	2	3	4	5
F36	Relationships with friends, family or at work	1	2	3	4	5

TRIM-Weight

15

Section G: Medicine(s) Regime

The following questions are specifically about the medicine regime as prescribed from your doctor. You indicated that you are taking medicine(s) for your diabetes and / or body weight.
Individuals have identified several issues regarding their medicine-taking behaviour and we are interested in your experiences. There is no right or wrong answer. Please answer each question based on your personal experience with your diabetes/ weight loss medicine.

	(Please circle the correct number)	No=1	Yes=0
G1	Do you sometimes forget to take your diabetes / weight loss medicine(s)?	1	0
G2	People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your diabetes / weight loss medicine(s)?	1	0
G3	Have you ever cut back or stopped taking your diabetes / weight loss medicine(s) without telling your doctor, because you felt worse when you took it?	1	0
G4	When you travel or leave home, do you sometimes forget to bring along your diabetes / weight loss medicine(s)?	1	0
G5	Do you sometimes skip your diabetes / weight loss medicine(s) when you go on holiday?	1	0
G6	Do you sometimes skip your diabetes / weight loss medicines(s) if you are gaining weight?	1	0
G7	Did you take your diabetes / weight loss medicine(s) yesterday?	1	0
G8	When you feel like your diabetes / weight loss is under control, do you sometimes stop taking your medicine(s)?	1	0
G9	Taking medicine(s) everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your diabetes / weight loss treatment plan?	1	0

G10

How often do you have difficulty remembering to take all your medicines?

Never/ Rarely	Once in a while	Sometimes	Usually	All the time
☐	☐	☐	☐	☐

16

Section H: Confidence about taking your new Medicine(s)

The following statements are regarding your confidence about taking your new medicine as prescribed by your doctor. Please tick the box that best indicates your level of agreement with each statement. It is important that you respond to every statement. There is no right or wrong answer. We are interested in your personal views.

How confident are you that you could take your new medicine(s) correctly....?

		Not at all confident	A little confident	Somewhat confident	Very confident	Extremely confident
H1	...when you take several different medicines each day	☐	☐	☐	☐	☐
H2	... when you take medicines more than once a day	☐	☐	☐	☐	☐
H3	... when you are away from home	☐	☐	☐	☐	☐
H4	...when you have a busy day planned	☐	☐	☐	☐	☐
H5	...When they cause some side effects	☐	☐	☐	☐	☐
H6	... when no-one reminds you to take your medicine	☐	☐	☐	☐	☐
H7	...when the schedule to take the medicine is not convenient	☐	☐	☐	☐	☐
H8	...when your normal routine gets messed up	☐	☐	☐	☐	☐
H9	...When you are not sure how to take the medicine	☐	☐	☐	☐	☐
H10	...when you are not sure what time of the day to take your medicine	☐	☐	☐	☐	☐
H11	...when you are feeling unwell (you know like having a cold or the flu)	☐	☐	☐	☐	☐
H12	...when you get a refill of your old medicine and some of the pills look different than usual	☐	☐	☐	☐	☐
H13	...when a doctor changes your medicines	☐	☐	☐	☐	☐

Section I: Your feelings about your weight

The following statements are about your quality of life in relation to being overweight and trying to lose weight. For each of the following statements, please tick the box that best describes your answer **at this time**.

		Not at all	Hardly	Somewhat	Moderately	A good deal	A great deal	A very great deal
I1	Because of my weight, I try to wear clothes that hide my shape	☐	☐	☐	☐	☐	☐	☐
I2	I feel frustrated that I have less energy because of my weight	☐	☐	☐	☐	☐	☐	☐
I3	I feel guilty when I eat because of my weight	☐	☐	☐	☐	☐	☐	☐
I4	I am bothered by what other people say about my weight	☐	☐	☐	☐	☐	☐	☐
I5	Because of my weight, I try to avoid having photograph taken	☐	☐	☐	☐	☐	☐	☐
I6	Because of my weight, I have to pay close attention to personal hygiene	☐	☐	☐	☐	☐	☐	☐
I7	My weight prevents me from doing what I want to do	☐	☐	☐	☐	☐	☐	☐
I8	I worry about physical stress that my weight puts on my body	☐	☐	☐	☐	☐	☐	☐
I9	I feel frustrated that I am not able to eat what others do because of my weight	☐	☐	☐	☐	☐	☐	☐
I10	I feel depressed because of my weight	☐	☐	☐	☐	☐	☐	☐

OWLQOL

18

		Not at all	Hardly	Somewhat	Moderately	A good deal	A great deal	A very great deal
I11	I feel ugly because of my weight	☐	☐	☐	☐	☐	☐	☐
I12	I worry about the future because of my weight	☐	☐	☐	☐	☐	☐	☐
I13	I envy people who are thin	☐	☐	☐	☐	☐	☐	☐
I14	I feel that people stare at me because of my weight	☐	☐	☐	☐	☐	☐	☐
I15	I have difficulty accepting my body because of my weight	☐	☐	☐	☐	☐	☐	☐
I16	I am afraid that I will gain back any weight that I lose	☐	☐	☐	☐	☐	☐	☐
I17	I get discouraged when I try to lose weight	☐	☐	☐	☐	☐	☐	☐

OWLQOL

Please state when you intend to take the first dose of your new medication:

Date ☐☐ Month ☐☐ Year ☐☐☐☐

Time ☐☐ : ☐☐ am / pm (please circle)

Please go back to the questions you just answered to make sure you did not miss any items.

Thank you for your participation!

19

A stamped envelope has been provided for you to return this questionnaire to:

Katie Psarou
Department of Obesity and Endocrinology
Clinical Sciences Centre
Aintree University Hospital
Longmoor lane
Liverpool
L9 7AL

20

Appendix 3.6 Interview Consent From

Aintree University Hospital NHS
NHS Foundation Trust
Where quality matters

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CONSENT FORM – INTERVIEWS (Version 3 – 02/02/2012)

Title of Research Project: What do patients with Type 2 Diabetes think about their medicines?

Researcher(s): Mrs Aikaterini Psarou, Professor John Wilding, Professor Helen Cooper

Centre ID Number: ☐☐☐ Participant ID Number: ☐☐☐☐☐

Please Initial Box

1. I confirm that I have read and have understood the information sheet dated 31st January 2012 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I agree to the interview consultation being audio recorded. ☐
4. I agree to the use of anonymised quotes in publications. ☐
5. I agree that my data gathered in this study may be stored *(after it has been anonymised)* in a specialist data centre and may be used for future research examining similar scientific questions. I understand that any such studies will undergo formal ethical approval procedures prior to using any of my data. ☐
6. I agree to take part in the first and second interview for the above study ☐

	/ /	
Participant Name *(Print in Capitals)*	Date	Signature
Name of Researcher (Print)	/ / Date	Signature

The contact details of researcher (Principal Investigator) are:
Katie Psarou,
Tel: 0151-5295940, Email: a.psarou@liv.ac.uk
Department of Obesity and Endocrinology
Clinical Sciences Centre
Aintree University Hospital
Longmoor Lane
Liverpool
L9 7AL

When completed, 1 copy for participant; 1 copy for researcher

1

Appendix 4.1 Clinical Data Form

Type 2 Diabetes Medicines Study

Clinical Data Form

Centre ID Number: ☐☐☐ **Participant ID Number:** ☐☐☐☐☐

Date Form Completed: _____

Clinical Data/ Information	Value	Date Data Recorded*
Weight (kg)		
BMI (kg/m^2)		
HbA1c (mmol/mol)		
Systolic Blood Pressure (mm/Hg)		
Diastolic Blood Pressure (mm/Hg)		
Total Cholesterol (mmol/l)		
LDL Cholesterol (mmol/l)		
HDL Cholesterol (mmol/l)		
Triglycerides (mmol/l)		
Serum Creatinine (umol/l)		
eGFR (ml/min)		
New Diabetes Medicine Prescribed *(Brand and Generic Name including dose)*		
Medical History *(list all current medical conditions)*		
Current Repeat Prescriptions *(list all drugs taken, and doses where possible)*		
Diabetes Complications *(tick all that apply; if none please state "none")*	PVD ☐ MI/Angina ☐ Neuropathy ☐ Retinopathy ☐ Nephropathy ☐ ACR/Microalbuminuria ☐ Stroke/TIA ☐ Other (please state) ☐	

***Needs to be within 3 months of recruitment date as per consent form OR date of follow-up letter**

Appendix 4.2 Interview Guide 1 and 2

Patients' expectations and views of new diabetes (or weight loss) medicines

Interview Guide- Interview 1

Purpose of the Interview

To explore participants' expectations and perceptions of diabetes/weight loss medication in relation to their:

1. past experiences of taking medicines in general, diabetes/weight loss medicines and effects on their blood glucose and body weight
2. past experiences of diabetes services re: medication prescription and guidance received (including Lifestyle changes- i.e. diet, physical activity and behaviour)
3. past experiences of barriers and facilitators for managing (accepting) new diabetes/ weight loss medicines [based on previous experience, beliefs about medicines and interaction with HPs]

Introduction

- Introduce self and research study. I understand that you have read the information sheet. Have you got any questions/concerns?
- The interview will take approximately 40mins to 1hr
- No names will be identified
- Establish that there are no right or wrong answers and that it is interesting to find out about everyone's views about their medicines. Your views are important. The information you are providing me with today will not go back to your doctor / nurse/ pharmacist.
    - Sign interview consent form
    - Set up audio equipment
    - Icebreaker: Tell me a little about your diagnosis of Diabetes. How long have you had it? when did you start taking medicines for Diabetes?

AIM 1: *To explore participants' lived expectations and perceptions of diabetes/weight loss medication*

We want to find out your personal experiences about taking medications in general and then specifically for diabetes (or weight loss medication). Please feel free to say anything you want.

1. **In general, what it is like having to take medicines [diabetes medications/ weight loss medications]?**

   PROMPTS

   - What are the benefits of taking medicines for you?
   - What are the disadvantages of taking medicines for you?
     - If mentions side effects, ask what kind of side effects and what happens when they experience them

Interview Guide Date: 12/12/12, version 2

- Have you had to think about changing your lifestyle as a result of taking your diabetes/ weight loss medicines? In what way?
- Have you had to think about what to eat or when to eat as a result of taking your medicines?

2. **What are your overall feelings/expectations about this new medicine you have been prescribed?**
   PROMPTS
   - What do you see are the benefits of taking this new medicine?
   - Is there anything that troubles you about taking this medicine?
   - Do you think anything will change for the better?
   - Do you think anything will change for the worse?
   - How do you think this new medicine may affect:
     - your diabetes, overall health
     - your weight,
     - your daily life,
     - your relationships with family or work mates,
     - your relationship with health care professionals
   - What are your next steps for ensuring you take this medicine as advised?
   - In the long run, what do you think this medicine will do for your diabetes and your body weight?

AIM 2: ***To explore participants' past experiences of taking diabetes / weight loss medication and effects on their blood glucose and body weight***

3. **What have you learnt from past experiences in taking diabetes (or weight loss) medicines?**

4. **In what way has your experience with other diabetes (or weight loss) medicines has affected how you feel about this medicine?**
   PROMPTS
   - Many people worry about side effects when taking medicines, are there any particular side effects that you worry about, and if so, what are these?
   - Have you got any worries about your weight when you take medicines?
   - How do you feel about taking this medicine when you take other medicines as well? What helps you?
   - How might your previous experience with medicines help you to manage taking the new medicine as advised?

AIM 3: ***To explore participants' perspectives of diabetes services in relation to medication prescription and guidance received (including Lifestyle changes- i.e.***

diet, physical activity and behaviour)

Now I would like to take you back to your appointment with your GP/ Consultant/ Nurse when it was decided that you will need to take this new medicine for your diabetes/ body weight. [This is the time you were first prescribed the medication]

5. **Can you describe to me what happened during your appointment with your doctor/ nurse?**
   PROMPTS
   - How did it come about that you need to take a new medicine?
   - What were your first thoughts?
   - What information were you given?

I would like to get an idea of your views on the support you have had so far from your practice (or diabetes service) in relation to this new medicine.

6. **What kind of support at this stage will help you manage taking this new medication (as advised)?**
7. **How might the support to you (in starting taking this medicine) be improved?**
8. **What kind of support do you think other people who are about to start this medicine will need?**
   PROMPTS
   - Support:
     - GP/PN/Consultant/ DSN/Pharmacist
     - Verbal or written information given (different leaflets)
     - Face to face contact
     - Family/ friends support
     - Other- to be described

AIM 4: ***To explore barriers and facilitators for managing (accepting) new diabetes/ weight loss medicines [based on previous experience, beliefs about medicines and interaction with HPs]***

9. **Overall, what could prevent you from taking your medicine (as prescribed)?**
   (And what makes it easy for you to take your medicine?)
   PROMPTS
   - Have you ever missed a dose of your medicines? If so what was the reason(s)?
   - You mentioned before about...[*participant's responses from questions 1,2,and 3*] could that prevent you from taking medicines?
     - Could be any of the following:

- Time, Multiple meds, Regime, Side effects → ? weight gain/ loss,
- Lifestyle, Work, Family, Living on your own, Driving
- Content of meals, Planning meals

- Are there any ways that help you or work for you to take your medicines as advised?

Close Interview

10. Is there anything else you would like to say about your medicines that perhaps we haven't covered today?

Thank you for your time

Patients' views and experiences of new diabetes (or weight loss) medicines

Interview Guide- Interview 2

Purpose of the Interview

To explore participants' lived experiences and perceptions of new diabetes/weight loss medication in relation to:

1. their experiences in taking this medication and effects on blood glucose and body weight
2. diabetes services re: medication prescribing and guidance received in the last three months (incl. Lifestyle changes- i.e. diet, physical activity and behaviour)
3. barriers and facilitators for managing (accepting) new diabetes/ weight loss medicines [based on previous/current experience, beliefs about medicines and interaction with HPs]

Introduction

- Remind re: confidentiality and timing of interview. The interview will take approximately 40mins to 1hr and no names will be identified.
- Have you got any questions/concerns before we start?
- Establish that there are no right or wrong answers and that it is interesting to find out about everyone's views and experiences about their medicines. Your views are important.
- The information you are providing me with today will not go back to your Doctor / nurse.
  - Set up audio equipment
  - Icebreaker: So how have you been since last time we met?

AIM 1: *To explore participants' lived experiences and perceptions of taking new diabetes/weight loss medication including effects on blood glucose and body weight*

We want to find out about your personal experiences of taking this new medication for your Diabetes (or body weight). Please feel free to say anything you want.

1. **What is it like having to take this new medicine [for your diabetes/ body weight]?**

   PROMPTS

   - What are the benefits of taking this medicine for you?
   - What are the disadvantages of taking this medicine for you?
   - Have you had to think about changing your lifestyle as a result of taking this new diabetes/ weight loss medicine? In what way?
   - Have you had to think about what to eat or when to eat as a result of taking your medicines?
   - How did you overcome the side effects (if any)? Where there any strategies that worked for you? (what have you tried?)

Now, I would like to know your views on this medicine and if it has affected your life in any way.

2. **What did you find?**

   PROMPTS

   - What have you learnt from your experience in taking the new medicine?
   - How did you feel now about the effects on your diabetes and/ or body weight?
   - In the long run, what do you think will be the effects on your diabetes and /or your body weight?

AIM 2: ***To explore participants' perspectives of diabetes services in relation to medication prescribing and guidance received in the last three months (including Lifestyle changes- i.e. diet, physical activity and behaviour)***

Now we would like to get an idea about your views on the support you have received whilst taking this diabetes/ weight loss medication and if this could be improved in any way.

3. **Overall, how do you feel about the support you have received from your practice or diabetes service [doctor/ nurse] since you were prescribed this new medicine?**
4. **Could the support to you (in taking the medication) be improved?**
5. **Is there anything you would like to see happening for other people taking this medication?**

   PROMPTS

   - What do you think about the support you have received?
   - Support:

- GP/PN/Consultant/ DSN/Pharmacist
- Verbal or written information given (different leaflets)
- Face to face contact
- Family/ friends support
- Other- to be described

AIM 3: *To explore barriers and facilitators for managing (accepting) new diabetes/ weight loss medicines [based on previous experience, beliefs about medicines and interaction with HPs]*

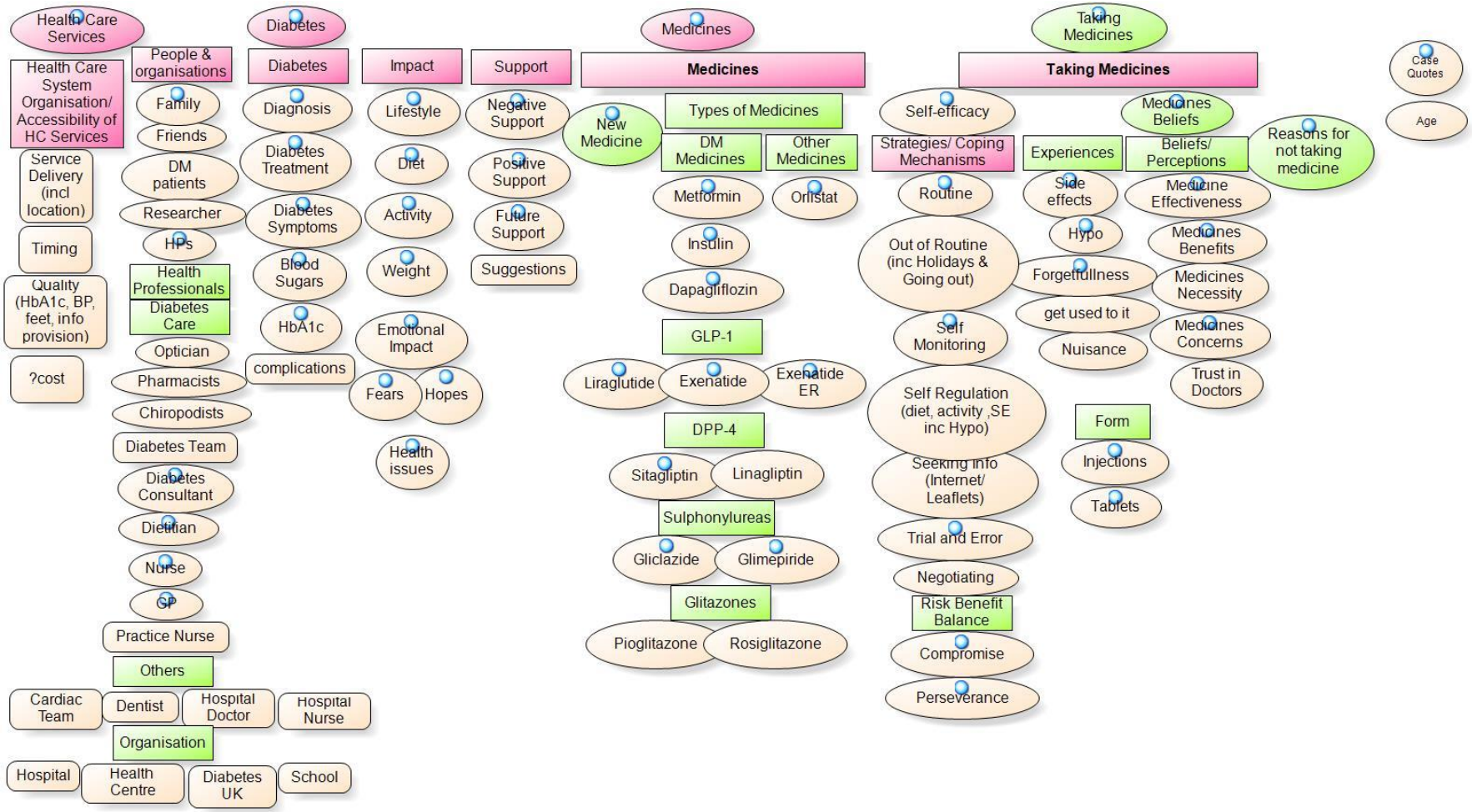
6. **Overall, what could prevent you from taking your medicine (as prescribed)?**
   (And what makes it easy for you to take your medicine?)
   PROMPTS
   - Have you ever missed a dose of this new medicine? If so, what was the reason(s)?
   - You mentioned before about...[*participant's responses from questions 1,2,and 3*] could that prevent you from taking medicines?
     - Could be any of the following:
     - Time, Multiple meds, Regime, Side effects → ? weight gain/ loss,
     - Lifestyle, Work, Family, Living on your own, Driving
     - Content of meals, Planning meals
   - Are there any ways that help you or work for you to take your new medicine as advised?

Close Interview

7. **Is there anything else you would like to say about your medicines that perhaps we haven't covered today?**

Thank you for your time

Appendix 4.3: Thematic Framework - Node Hierarchy



Appendix 5.1: Internal reliability of adapted questionnaire scales

Scale Name	**Questionnaire 1**	**Questionnaire 2**	**Original Scale** (sections 4.2.1.1-4.2.1.7
EITQ	0.71		0.80
PITQ		0.72	0.72
BMQ	Concerns=0.73 Necessity=0.83 Harm=0.65 Overuse=0.79 Benefit=0.75	Concerns=0.79 Necessity=0.87 Harm=0.66 Overuse=0.75 Benefit=0.84	Concerns=0.80 Necessity=0.74 Harm=0.62-0.70 Overuse=0.65-0.72 Benefit=0.62-0.66
MMAS-8	0.60	0.65	0.83 (for hypertensive patients)
MMAS-8, plus 2 Weight related questions	0.64	0.68	
SIMS	SIMS=0.90 SIMS-AU=0.86 SIMS-PPM=0.89	SIMS=0.92 SIMS-AU=0.83 SIMS-PPM=0.90	SIMS: 0.81 (insulin treated), 0.88 (OGDs) Subscales:0.61 -0.79
DiabMedSat	DiabMedSat=0.88 Burden=0.84 Symptom=0.80 Efficacy=0.78	DiabMedSat=0.89 Burden=0.84 Symptom=0.76 Efficacy=0.87	DiabMedSat=0.90 Burden=0.87 Symptoms=0.89 Efficacy=0.87
TRIM-Weight	TRIM-Wt-DL=0.59 TRIM-Wt-WM=0.60 TRIM-Wt-PH=0.91	TRIM-Wt-DL=0.62 TRIM-Wt-WM=0.67 TRIM-Wt-PH=0.91	TRIM-Wt-DL=0.91 TRIM-Wt-WM=0.70 TRIM-Wt-PH=0.87
SEAMS	SEAMS=0.96 UDC=0.95 UCU=0.92	SEAMS=0.97 UDC=0.96 UCU=0.92	SEAMS=0.86 UDC=0.86 UCU=0.79
OWLQOL	0.98	0.98	0.93-0.96

Baseline Cronbach's alpha calculated based on 248 participants and at follow-up on 213 participants.

Appendix 5.2: Demographic characteristics of whole group, participants returned questionnaire 1 and participants returned both questionnaires.

	(%) or Median (IQR)		
	Whole Group n (%)	Returned Q1 Only n(%)	Returned Q1 & Q2 n(%)
N	248	35	213
Centre Site n (%):			
GP Practice	137(55.2)	17(48.6)	120(56.3)
SCDC	83(33.5)	12(34.3)	71(33.3)
CP	28(11.3)	6 17.1)	22(10.3)
Mean Age (yrs)	59 (51,68) [Range 24-86]	55 (51,64) [Range 31-73]	60 (51,69) [Range 24-86]
Gender n(%)			
Men	132(53.2)	19(54.3)	113(53)
Women	116(46.8)	16(45.7)	100(47)
Ethnicity n(%):			
Caucasian	246(99.2)	35(100)	211(99)
Asian	1(0.4)	0(0)	1(0.5)
Mixed	1(0.4)	0(0)	1(0.5)
Marital Status:			
Alone/Single	36(14.5)	10(28.6)	26(12.2)
Married/ with partner	173(69.8)	20(57.1)	153(71.8)
Divorced/Separated	20(8.1)	3(8.6)	17(8.0)
Widowed	19(7.7)	2(5.7)	17(8.0)
Education :			
University /Higher Degree	21(8.5)	2(5.7)	19(8.9)
A level	28(11.3)	6(17.1)	22(10.3)
GCSE	49(19.8)	7(20.0)	42(19.7)
Diploma	10(4.0)	0(0)	10(4.7)
Vocational	35(14.1)	7(20.0)	28(13.1)
No Formal Qualifications	102(41.1)	13(37.1)	89(41.8)
Missing	3(1.2)	0(0)	3(1.4)
Employment Status:			
Full time	59(23.8)	**16(45.7)***	**43(20.2)***
Part-time	21(8.5)	3(8.6)	18(8.5)
Unemployed	32(12.9)	7(20.0)	25(11.7)
Retired	107(43.1)	**8(22.9)***	**99(46.5)***
Other [most on benefits]	27(10.9)	1(2.9)	26(12.2)
Missing	2(0.8)	0(0)	2(0.9)
IMD:			
20% most deprived	153(61.7)	24(68.6)	129(60.6)
21% to 40%	35(14.1)	4(11.4)	31(14.6)
41% to 60%	31(12.5)	3(8.6)	28(13.1)
61% to 80%	18(7.3)	3(8.6)	15(7.0)
20% least deprived	11(4.4)	1(2.9)	10(4.7)
Missing	0(0)	0(0)	0(0)

IQR reported as (Q1,Q3), *Fisher's Exact test = 15.317, p=0.003

Appendix 5.3: Clinical characteristics of whole group, participants returned questionnaire 1 and participants returned both questionnaires.

	(%) or Median (IQR= 25th,75th) Or Mean(±SD)		
	Whole Group n (%)	Returned Q1 Only n(%)	Returned Q1 & Q2 n(%)
N	248	35	213
Years Diagnosed with T2D Missing	7 (3,13) [Range 0-59yrs] 7(2.8)	8 (4,13) [Range 0-24yrs] 4(11.4)	7 (3,13) [Range 0-59yrs] 3(1.4)
Number of Diabetes Complications- Baseline:			
None	121(48.8)	23(65.7)	98(46.0)
One	67(27)	5(14.3)	62(29.1)
Two	35(14.1)	4(11.4)	31(14.6)
Three	15(6.0)	1(2.9)	14(6.6)
Four	3(1.2)	0(0)	3(1.4)
Five	2(0.8)	0(0)	2(0.9)
Missing	5(2.0)	2(5.7)	3(1.4)
Number of Diabetes Complications- Follow-up			
None	98(39.5)	16(45.7)	82(38.5)
One	50(20.2)	3(8.6)	47(22.1)
Two	25(10.1)	4(11.4)	21(9.9)
Three	16(6.5)	0(0)	16(7.5)
Four	2(0.8)	0(0)	2(0.9)
Five	2(0.8)	0(0)	2(0.9)
Missing	55(22.2)	12(34.3)	43(20.2)
Total Medicine Burden Missing	7 (5,10) [Range 1-21] 11(4.4)	7 (4,9) [Range 1-11] 2(5.7)	7 (5,10) [Range 1-21] 9(4.2)
Total Medicine Burden – Follow-Up Missing	8 (5,10) [Range 1-20] 57(23.0)	7 (5,9) [Range 1-12] 12(34.3)	8 (5,11) [Range 2-21] 45(21.1)
Diabetes Regime:			
None	24(9.7)	4(11.4)	20(9.4)
Tablets only	145(58.5)	18(51.4)	128(60.1)
Tablets & insulin	38(15.3)	4(11.4)	33(15.5)
Insulin only	10(4)	0(0)	10(4.7)
Insulin & GLP-1	1(0.4)	0(0)	1(0.5)
Tablets, insulin & GLP-1	2(0.8)	1(2.9)	1(0.5)
Tablets and GLP-1	24(9.7)	7(20.0)	17(8.0)
Missing	4(1.6)	1(2.9)	3(1.4)
Diabetes Regime at follow-up:			
Tablets only	76(30.6)	12(34.3)	64(30.0)
Tablets & insulin	43(17.3)	2(5.7)	43(20.2)
Tablets & GLP-1	47(19.0)	6(17.1)	39(18.3)
Insulin only	7(2.8)	1(2.9)	6(2.8)
Insulin & GLP-1	3(1.2)	0(0)	5(2.3)

Tablets, insulin & GLP-1	19(7.7)	3(8.6)	14(6.6)
GLP-1 Only	3(1.2)	0(0)	3(1.4)
Missing	50(20.2)	11(31.4)	39(18.3)
Number of Diabetes medicines–Baseline:			
None	24(9.7)	4(11.4)	20(9.4)
One	68(27.4)	7(20.0)	61(28.6)
Two	101(40.7)	13(37.1)	88(41.3)
Three	48(19.4)	10(28.6)	38(17.8)
Four	3(1.2)	0(0)	3(1.4)
Missing	4(1.6)	1(2.9)	3(1.4)
Number of Diabetes medicines–Follow-Up			
One	30(12.1)	5(14.3)	24(11.3)
Two	74(29.8)	8(22.9)	67(31.5)
Three	81(32.7)	9(25.7)	73(34.3)
Four	9(3.6)	1(2.9)	7(3.3)
Five	1(0.4)	0(0)	1(0.5)
Missing	53(21.4)	12(34.3)	41(19.2)
Baseline Weight (kg)	98.35 (85.92, 118)	96.9 (86.89, 109.5)	98.6 (85.9, 118.8)
Missing	12(4.8)	2(5.7)	10(4.7)
Baseline BMI (kg/m2)	35.05 (8.70) (31.2, 39.9) [Range 22.1-61.1]	34.8 (30.0, 37.9) [Range 23.0-46.8] 2(5.7)	35.3 (31.2, 40.7) [Range 22.1-61.1]
Missing	12(4.8)		10(4.7)
Baseline HbA1c (mmol/mol)	77 (66,91.5) [Range 42-134]	82 (64.5, 98) [Range 55-114]	77 (66,90) [Range 42-134]
Missing	11(4.4)	2(5.7)	9(4.2)
Blood Pressure-Systolic	134±15	134±12	134±15
Missing	16(6.5)	4(11.4)	12(5.6)
Blood Pressure-Diastolic	76±11	77±7	75±11
Missing	16(6.5)	4(11.4)	12(5.6)
Cholesterol (mmol/L)	4.1 (3.5, 5.0)	4.2 (3.5, 4.9)	4.1 (3.5, 5.0)
Missing	50(20.2)	7(20.0)	43(20.2)
LDL (mmol/L) (n=173)	2 (1.5, 2.69)	2 (1.5, 2.5)	2 (1.5, 2.8)
Missing	75(30.2)	10(28.6)	65(30.5)
HDL (mmol/L) (n=194)	1.1 (0.9, 1.21)	1.1 (0.9, 1.3)	1.1 (0.9, 1.2)
Missing	54(21.8)	8(22.9)	46(21.6)
Triglycerides (mmol/L)	2.1 (1.5, 2.9)	1.98 (1.3, 2.7)	2.18 (1.5, 2.9)
Missing	63(25.4)	10(28.6)	53(24.9)
eGFR (ml/min) (n=226)	78.5 (60,90)	**87.5[+] (70, 90)**	**78[+] (57,90)**
Missing	22(8.9)	3(8.6)	19(8.9)
Creatinine (umol/L)	78 (31) (66,97)	**71[+] (58, 89)**	**79 [+] (67, 101)**
Missing	21(8.5)	2(5.7)	19(8.9)

+Mann-Whitney U Test, Creatinine: U=2373.0 ,z= -2.338, p=0.019, eGFR: U=2335.5, z=-2.242, p=0.025

Appendix 5.4: Cronbach's alpha, baseline standard deviation and Standard Error of Measurement for each scale

Scale	Cronbach's alpha	Baseline SD	SEM
EITQ/PITQ*	0.64	0.82	0.29
SIMS	0.90	4.83	1.49
SIMS-AU	0.86	2.25	0.83
SIMS-PPM	0.89	3.17	1.05
BMQ-Necessity	0.83	0.66	0.27
BMQ-Concerns	0.73	0.65	0.33
Necessity-Concern Differential	Based on Difference between SEM-Necessity and SEM-Concerns		0.06
BMQ-Overuse	0.79	0.78	0.35
BMQ-Benefits	0.75	0.52	0.26
BMQ-Harm	0.65	0.56	0.33
DiabMedSat	0.88	14.86	5.05
DiabMedSat-Burden	0.84	15.75	6.30
DiabMedSat-Efficacy	0.78	19.02	8.75
DiabMedSat-Symptom	0.80	21.90	9.64
TRIM-Wt-DL	0.59	17.50	11.20
TRIM-Wt-WM	0.60	21.88	13.78
TRIM-Wt-PH	0.91	27.51	8.25
MMAS-8	0.60	1.52	0.96
MMAS-8 plus 2 items	0.64	1.74	1.04
SEAMS	0.96	0.90	0.18
SEAMS-UCU	0.92	0.99	0.28
SEAMS-UDC	0.95	0.89	0.12
OWLQOL	0.98	30.92	4.33

*Cronbach's α for PITQ-EITQ change score scale and SD is for the change score (see section 4.2.4).

Appendix 5.5: Proportion of patients whose expectations were unmet, met, or exceeded by experience (EITQ-PITQ)

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Unmet Expectations <-0.29	30% (n=20)	39% (n=22)	31% (n=20)	33% (n=62)
Expectations Met ≥-0.29 and ≤0.29	25% (n=17)	24% (n=14)	30% (n=19)	27% (n=50)
Expectations exceeded by Experience >0.29	45% (n=30)	37% (n=21)	39% (n=25)	40% (n=76)
p=0.560, No significant difference between the three weight-effect groups				

Appendix 5.6: Proportion of patients whose satisfaction with information received about new medicine had improved, did not change or decreased

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Decreased SIMS ≤-1.49	15% (n=10)	26% (n=15)	25% (n=16)	22% (n=41)
No change in SIMS >-1.49 and ≤1.49	38% (n=26)	35% (n=20)	47% (n=30)	40%(n=76)
SIMS Improved SEM >1.49	46% (n=31)	39% (n=22)	28% (n=18)	38% (n=71)
P=0.089, No significant difference between the three weight-effect groups				
Decreased SIMS-AU ≤-0.83	19%(n=13) *****	33% (n=19)	31%(n=20) *****	28% (n=52)
No change in SIMS-AU >-0.83 and ≤0.83	38% (n=26)	35% (n=20)	47% (n=30)	40%(n=76)
SIMS-AU Improved >0.83	**43% (n=29)** *	32% (n=18)	**22% (n=14)** *	32% (n=61)
p=0.37, *Weight Reducing Vs Weight Increasing **p=0.012**				
Decreased SIMS-PPM ≤-1.05	12% (n=8)	21% (n=12)	17% (n=11)	16% (n=31)
No change in SIMS-PPM >-1.05 and ≤1.05	43% (n=29)	49% (n=28)	58% (n=37)	50%(n=94)
Improved SIMS-PPM >1.05	45% (n=30)	30% (n=17)	25% (n=16)	34% (n=63)
P=0.055, No significant difference between the three weight-effect groups				

Appendix 5.7: Proportion of patients whose beliefs about the new medicine had improved, did not change or decreased

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Decreased BMQ-Necessity ≤-0.27	34% (n=23)	36% (n=21)	34% (n=22)	35% (n=66)
No change in BMQ-Necessity >-0.27 and ≤0.27	39% (n=26)	36% (n=21)	47% (n=30)	41%(n=77)
Stronger BMQ-Necessity >0.27	27% (n=18)	28% (n=16)	19% (n=12)	24% (n=46)
P=0.838, No significant difference between the three weight-effect groups				
Decreased BMQ-Concerns ≤-0.33	39% (n=26)	33% (n=19)	33% (n=21)	35% (n=66)
No change BMQ-Concerns >-0.33 and ≤0.33	48% (n=32)	53% (n=31)	31% (n=20)	44%(n=83)
Stronger BMQ-Concerns >0.33	**13**% (n=9)	14% (n=8)	**36% (n=23)**	21% (n=40)
P=0.104, WR Vs WI p=0.046, but not significant after Bonferroni correction p<0.017				
Decreased Necessity–Concern Differential ≤-0.06	31% (n=21)	43% (n=25)	47% (n=30)	40% (n=76)
No change in Necessity–Concern Differential >-0.06 and ≤0.06	14% (n=9)	7% (n=4)	12% (n=8)	11% (n=21)
Stronger Necessity–Concern Differential >0.06	55% (n=37)	50% (n=29)	41% (n=26)	49% (n=92)
P=0.188, No significant difference between the three weight-effect groups				
Decreased BMQ-Overuse ≤-0.35	15% (n=10)	12% (n=7)	19% (n=12)	15% (n=29)
No change in BMQ-Overuse >-0.35 and ≤0.35	61% (n=41)	63% (n=36)	55% (n=35)	60%(n=112)
Stronger BMQ-Overuse >0.35	24% (n=16)	25% (n=14)	26% (n=17)	25% (n=47)
P=0.937, No significant difference between the three weight-effect groups				
Decreased BMQ-Benefits ≤-0.26	21% (n=14)	16% (n=9)	23% (n=15)	20% (n=38)
No change in BMQ-Benefits >-0.26 and ≤0.26	62% (n=41)	63% (n=36)	61% (n=39)	62%(n=116)
Stronger BMQ-Benefits >0.26	17% (n=11)	21% (n=12)	16% (n=10)	18% (n=33)
P=0.484, No significant difference between the three weight-effect groups				
Decreased BMQ-Harm ≤-0.33	16% (n=11)	16% (n=9)	17% (n=11)	17% (n=31)
No change in BMQ-Harm >-0.33 and ≤0.33	70% (n=47)	67% (n=38)	59% (n=38)	65%(n=123)
Stronger BMQ-Harm >0.33	14% (n=9)	17% (n=10)	24% (n=15)	18% (n=34)
P=0.663, No significant difference between the three weight-effect groups				

Appendix 5.8: Proportion of patients whose treatment satisfaction of new medicine had improved, did not change or decreased

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Decreased DiabMedSat ≤-5.05	14% (n=9)	30% (n=13)	22% (n=13)	21% (n=35)
No change in DiabMedSat >-5.05 and ≤5.05	35% (n=23)	33% (n=14)	24% (n=14)	31%(n=51)
Improved DiabMedSat >5.05	51% (n=33)	37% (n=16)	54% (n=31)	48% (n=80)
P=0.156, No significant difference between the three weight-effect groups				
Decreased DiabMedSat-Efficacy ≤-8.75	22% (n=14)	16% (n=7)	17% (n=10)	19% (n=31)
No change in DiabMedSat-Efficacy >-8.75 and ≤8.75	23% (n=15)	55% (n=24)	25% (n=15)	32%(n=54)
Improved DiabMedSat-Efficacy >8.75	55% (n=36)	**29% (n=13)**	**58% (n=34)**	49% (n=83)
P=0.087, WN Vs WI, p=0.031 but not significant after Bonferroni Correction p<0.017				
Decreased DiabMedSat-Burden ≤-6.30	17% (n=11)	14% (n=6)	25% (n=15)	19% (n=32)
No change in DiabMedSat-Burden >-6.30 and ≤6.30	45% (n=29)	58% (n=25)	48% (n=28)	49%(n=82)
Improved DiabMedSat-Burden >6.30	38% (n=25)	28% (n=12)	27% (n=16)	32% (n=53)
P=0.293, No significant difference between the three weight-effect groups				
Decreased DiabMedSat-Symptom ≤-9.64	17% (n=11)	32% (n=14)	26% (n=15)	24% (n=40)
No change in DiabMedSat-Symptom >-9.64 and ≤9.64	46% (n=30)	41% (n=18)	48% (n=28)	46%(n=76)
Improved DiabMedSat-Symptom >9.64	37% (n=24)	27% (n=12)	26% (n=15)	30% (n=51)
P=0.168, No significant difference between the three weight-effect groups				

Appendix 5.9: Proportion of patients whose impact of new medicine related to daily life, weight management and Psychological Health had improved, did not change or decreased

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Decreased TRIM-Wt-DL ≤-11.20	10% (n=6)	11% (n=5)	13% (n=8)	11% (n=19)
No change TRIM-Wt-DL >-11.20 and ≤11.20	56% (n=36)	66% (n=29)	67% (n=40)	63%(n=105)
Improved TRIM-Wt-DL>11.20	34% (n=22)	23% (n=10)	20% (n=12)	26% (n=44)
P=0.191, No significant difference between the three weight-effect groups				
Decreased TRIM-Wt-WM ≤-13.78	11% (n=7)	14% (n=6)	21% (n=13)	16% (n=26)
No change TRIM-Wt-WM >-13.78 and ≤13.78	30% (n=19)	56% (n=24)	54% (n=33)	45%(n=76)
Improved TRIM-Wt-WM >13.78	**59% (n=38)** **+++	**30% (n=13)** **	**25% (n=15)** +++	39% (n=65)
P=0.001, **WR Vs WN **p=0.009**, +++WR Vs WI, **p<0.001**				
Decreased TRIM-Wt-PH SEM≤-8.25	17% (n=11)	23% (n=10)	23% (n=14)	21% (n=35)
No change TRIM-Wt-PH >-8.25 and ≤8.25	50% (n=32)	52% (n=23)	50% (n=30)	51%(n=85)
Improved TRIM-Wt-PH >8.25	33% (n=21)	25% (n=11)	27% (n=16)	28% (n=48)
P=0.518, No significant difference between the three weight-effect groups				

Appendix 5.10: Proportion of patients whose medication adherence levels had improved, did not change or decreased

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Decreased MMAS-8 ≤-0.96	22% (n=14)	18% (n=8)	28% (n=17)	23% (n=39)
No change on MMAS-8 >-0.96 and ≤0.96	56% (n=36)	49% (n=22)	43% (n=26)	49%(n=84)
Improved MMAS-8 >0.96	22% (n=14**)**	33% (n=15)	29% (n=18)	28% (n=47)
P=0.485, No significant difference between the three weight-effect groups				

Appendix 5.11: Proportion of patients whose self-efficacy with appropriate use of new medicine had improved, did not change or decreased

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Decreased SEAMS≤-0.18	24% (n=16)	33% (n=19)	36% (n=22)	31% (n=57)
No change SEAMS >-0.18 and ≤0.18	21% (n=14)	33% (n=19)	32% (n=20)	28%(n=53)
Improved SEAMS>0.18	**55% (n=37)** **	33% (n=19)	**32% (n=20)** **	41% (n=76)
P=0.031, Weight Reducing Vs Weight Neutral p=0.032, **Weight Reducing Vs Weight Increasing **p=0.017**				
Decreased SEAMS-UDC≤-0.12	30% (n=20)	42% (n=24)	40% (n=25)	37% (n=69)
No change SEAMS-UDC >-0.12and ≤0.12	18% (n=12)	25% (n=15)	24% (n=15)	22%(n=41)
Improved SEAMS-UDC>0.12	**52% (n=35)**	**33% (n=19)**	36% (n=22)	41% (n=76)
P=0.092, Weight Reducing Vs Weight Neutral, p=0.049, but not after Bonferroni correction p<0.017				
Decreased SEAMS-UCU≤-0.28	26% (n=17)	24% (n=14)	34% (n=21)	28% (n=52)
No change SEAMS-UCU >-0.28and ≤0.28	16% (n=11)	44% (n=25)	34% (n=21)	31%(n=57)
Improved SEAMS-UCU>0.28	**58% (n=39)** **	32% (n=18)	**32% (n=20)** **	41% (n=77)
P=0.33, WR Vs WN p=0.044 not after Bonferroni correction, **WR Vs WI **p=0.016**				

Appendix 5.12: Proportion of patients whose weight related quality of life had improved, did not change or decreased

	Weight Reducing	Weight Neutral	Weight Increasing	Whole Group
Decreased OWLQOL≤-4.33	19% (n=13)	20% (n=12)	28% (n=18)	23% (n=43)
No change on OWLQOL >-4.33 and ≤4.33	24% (n=16)	40% (n=23)	42% (n=27)	35%(n=66)
Improved OWLQOL>4.33	**57% (n=39)** ***	40% (n=23)	**30% (n=19)** ***	43% (n=81)
P=0.018, ***WR Vs WI p=0.005				

Appendix 5.13 Ordinal Regression – Single Baseline (non-significant) Predictors for follow-up medication adherence

Variable	β	significance	Test for parallelism
Health Care setting			
Primary Care	-0.461	0.103	0.389
Secondary Care	Reference		
Gender	0.159	0.554	0.905
T2D diagnosis	0.021	0.25	0.462
Single	-0.779	0.079	0.545
Married	reference		
Widowed	0.718	0.205	
Divorced	-0.588	0.233	
Higher Education	-0.061	0.897	0.47
A Level	-0.061	0.897	
GCSE	-0.500	0.18	
Diploma	-0.275	0.672	
Vocational	-0.147	0.716	
No Formal Qualification	Reference		
IMD			
20% Least Deprived	0.043	0.944	0.257
61% - 80%	0.809	0.119	
41%- 60%	-0.361	0.386	
21% - 40%	-0.442	0.267	
20% Most Deprived	Reference		
EITQ	0.227	0.214	0.628
SIMS–AU	0.050	0.402	0.695
BMQ-Necessity	0.253	0.215	0.131
Belief Groups Baseline			0.718
Sceptical	-0.625	0.175	
Ambivalent	-0.387	0.273	
Indifferent	-0.305	0.560	
Accepting	Reference		
BMQ-Overuse	-0.331	0.057	0.345
BMQ-Harm	-0.461	0.056	0.402
BMQ-Benefits	0.303	0.244	0.214
DibMedSat-Symptoms	0.008	0.212	0.714
TRIM-Wt-DL	0.005	0.521	0.973
TRIM-Wt-WM	-0.002	0.809	0.702
OWLQOL	0.007	0.124	0.968
BMI Baseline	0.019	0.307	0.699
HbA1c Change	0.011	0.292	0.565
Total Medication Burden - Baseline	0.032	0.345	0.836
Total Diabetes Medication Burden - Baseline	-0.224	0.130	0.241
Total Diabetes Complications Burden - Baseline	0.148	0.243	0.249

Appendix 5.14: Ordinal Regression – Single Change (non-significant) Predictors for follow-up medication adherence

Variable	β	significance	Test of Parallelism
SEM SIMS			
Improved	Reference		0.247
No Change	0.368	0.228	
Decreased	0.224	0.536	
SEM SIMS-AU			
Improved	Reference		0.151
No Change	0.322	0.310	
Decreased	-0.015	0.965	
SEM SIMS-PPM			
Improved	Reference		0.233
No Change	0.348	0.247	
Decreased	0.131	0.746	
SEM Necessity-Concern Differential			
Stronger	Reference		0.236
No change	-0.489	0.276	
Decreased	-0.088	0.758	
SEM BMQ-Overuse			
Stronger	Reference		0.336
No Change	0.030	0.926	
Decreased	0.016	0.971	
SEM BMQ-Harm			
Stronger	Reference		0.231
No Change	-0.479	0.182	
Decreased	-0.265	0.563	
SEM BMQ-Benefits			
Stronger	Reference		0.237
No Change	-0.101	0.172	
Decreased	0.602	0.782	
SEM DiabMedSat			
Improved	Reference		0.437
No Change	0.089	0.788	
Decreased	-0.326	0.387	
SEM DiabMedSat-Burden			
Improved	Reference		0.938
No Change	0.177	0.586	
Decreased	-0.166	0.688	
SEM DiabMedSat-Symptoms			
Improved	Reference		0.176
No Change	0.312	0.351	
Decreased	-0.096	0.806	
SEM DiabMedSat-Efficacy			0.434
Improved	Reference		

No Change	0.278	0.389	
Decreased	0.098	0.800	
SEM TRIM-Wt-DL			
Improved	Reference		0.260
No Change	0.055	0.868	
Decreased	-0.153	0.763	
SEM TRIM-Wt-WM			
Improved	Reference		0.957
No Change	-0.306	0.325	
Decreased	-0.320	0.455	
SEM TRIM-Wt-PH			
Improved	Reference		0.619
No Change	-0.402	0.228	
Decreased	-0.244	0.551	
SEM SEAMS			
Improved	Reference		0.808
No Change	0.646	0.054	
Decreased	-0.483	0.139	
SEM SEAMS-UCU			0.785
Improved	Reference		
No Change	0.031	0.924	
Decreased	-0.584	0.080	
SEM OWLQOL			
Improved	Reference		0.262
No Change	0.060	0.843	
Decreased	-0.202	0.562	
Weight Change	-0.048	0.244	0.400
HbA1c Change	0.011	0.292	0.565
Total Medication Burden change	-0.080	0.373	0.776
Total Diabetes Medication Burden change	0.178	0.386	0.704

Appendix 5.15: Correlation Matrix (Pearson Correlation)

r	Age	Baseline MMAS-8	SEAMS-UDC	SEAMS-UCU	BMQ Concern Change (Stronger Vs Decrease)	BMQ-Concern Change (Stronger Vs Stable)	SEAMS-UDC Change (Improvement Vs decrease)
Age	1	0.3	0.1	0.1	.01	-0.1	-0.02
Baseline MMAS-8	0.3	1	0.6	0.5	-0.01	-0.01	-0.001
SEAMS-UDC	0.1	0.6	1	0.8*	0.01	-0.01	0.2
SEAMS-UCU	0.1	0.5	0.8*	1	0.01	-0.1	0.2
BMQ Concern Change (Stronger Vs Decrease)	0.01	-0.01	0.01	0.01	1	-0.6	-0.1
BMQ- Concern Change (Stronger Vs Stable)	-0.1	-0.01	-0.1	-0.1	-0.6	1	0.1
SEAMS-UDC Change (Improvement Vs decrease)	-0.02	-0.001	0.2	0.2	-0.1	0.1	1

*Tolerance Statistic SEAMS- UDC= 0.3, SEAMS-UCU= 0.3, VIF SEAMS-UDC= 4.1, SEAMS-UCU= 3.7

Appendix 5.16: Multinomial Regression – Single Baseline Predictors for change in medication adherence based on SEM

Variable	β Decreased Adherence	Significance	β Increased Adherence	Significance
Gender				
Male	-0.345	0.375	-0.063	0.863
Female	Reference		Reference	
Age	-0.003	0.852	0.029	0.098
T2D diagnosis	0.035	0.167	-0.01	0.724
Higher Education	0.433	0.543	0.595	0.376
A Level	-0.666	0.426	0.526	0.367
GCSE	0.145	0.783	0.202	0.691
Diploma	0.838	0.275	-19.183	
Vocational	-0.037	0.952	0.490	0.355
No Formal Qualification	Reference		Reference	
Full time	-0.531	0.334	-0.223	0.379
Part time	-0.531	0.535	-0.336	0.127
Unemployed	0.211	0.722	-0.693	0.619
Other	0.404	0.464	-1.076	0.282
Retired	Reference		Reference	
EITQ	-0.155	0.568	-0.264	0302
SIMS	0.018	0.675	-0.038	0.313
SIMS-PPM	0.030	0.620	-0.002	0.971
BMQ-Concerns	-0.268	0.364	0.071	0.797
BMQ-Necessity	-0.223	0.442	0.156	0.571
Necessity-Concern Differential Baseline	0.022	0.921	0.049	0.814
Belief Groups Baseline				
Sceptical	-0.164	0.804	-0.077	0.900
Ambivalent	-0.619	0.222	-0.491	0.297
Indifferent	0.288	0.682	-0.606	0.448
Accepting	Reference		Reference	
BMQ-Benefits	-0.573	0.138	-0.544	0.133
DiabMedSat	-0.008	0.538	-0.024	0.056
DiabMedSat-Symptoms	-0.006	0.486	-0.014	0.106
DiabMedSat-Efficacy	-0.005	0.654	-0.005	0.631
TRIM-Wt-DL	0.002	0.888	-0.10	0.340
TRIM-Wt-WM	0.017	0.053	0.011	0.190
TRIM-Wt-PH	-0.007	0.322	-0.010	0.141
SEAMS-UDC	-0.113	0.607	-0.382	0.059
OWLQOL	0.001	0.931	0.002	0.695
Baseline BMI	-0.01	0.973	-0.008	0.758
Total Medication Burden Baseline	0.042	0.376	-0.028	0.555
Total Diabetes Medication Burden Baseline	0.024	0.919	-0.132	0.553

Total Diabetes Complications Burden Baseline	0.157	0.396	0.057	0.752
Weight Effects of New Medicine:				
WI	0.520	0.241	0.577	0.222
WN	-0.067	0.897	0.561	0.190
WR	Reference		Reference	

Appendix 5.17: Multinomial Regression – Single Change Predictors for change in medication adherence based on SEM

Variable	β Decreased Adherence	significance	β Increased Adherence	Significance
Expectation Perception Difference				
Expectations Exceeded by	Reference		Reference	
Experience	-0.103	0.821	-0.772	
Expectations Unmet	-0.216	0.661	-0.461	0.086
Expectations Met				0.306
SEM SIMS				
Improved	Reference		Reference	
No Change	0.327	0.441	-0.065	0.880
Decreased	-1.030	0.143	0.377	0.424
SEM SIMS-AU				
Improved	Reference		Reference	
No Change	0.316	0.487	-0.629	0.157
Decreased	-0.606	0.299	-0.182	0.688
SEM SIMS-PPM				
Improved	Reference		Reference	
No Change	0.216	0.608	0.662	0.127
Decreased	-0.778	0.276	0.561	0.311
SEM BMQ-Concern				
Stronger	Reference		Reference	
No Change	-0.657	0.174	-0.312	0.538
Decreased	-0.770	0.151	0.211	0.682
SEM BMQ-Necessity				
Stronger	Reference		Reference	
No Change	-0.085	0.870	-0.114	0.813
Decreased	0.707	0.179	0.647	0.190
SEM Necessity- Concern Differential				
Stronger	Reference		Reference	
No change	0.265	0.693	0.243	0.678
Decreased	0.671	0.107	0.138	0.726
SEM BMQ-Harm				
Stronger	Reference		Reference	

No Change	-0.387	0.431	-0.198	0.683
Decreased	-0.331	0.612	0.074	0.903
SEM BMQ-Benefits				
Stronger	Reference		Reference	
No Change	-0.551	0.281	-0.512	0.315
Decreased	-1.303	0.067	-0.250	0.726
SEM DiabMedSat				
Improved	Reference		Reference	
No Change	0.199	0.662	-0.518	0.238
Decreased	0.399	0.427	-0.374	0.453
SEM DiabMedSat-Symptoms				
Improved	Reference		Reference	
No Change	-0.047	0.921	-0.521	
Decreased	0.286	0.593	-0.340	0.222
SEM DiabMedSat-Efficacy				
Improved	Reference		Reference	
No Change	-0.878	0.068	-0.567	0.175
Decreased	0.028	0.955	-0.397	0.450
SEM TRIM-Wt-DL				
Improved	Reference		Reference	
No Change	0.644	0.214	-0.414	0.677
Decreased	0.711	0.325	-0.269	0.311
SEM TRIM-Wt-WM				
Improved	Reference		Reference	
No Change	0.579	0.189	-0.326	0.421
Decreased	0.405	0.506	0.047	0.931
SEM TRIM-Wt-PH				
Improved	Reference		Reference	
No Change	-0.533	0.236	-0.421	0.341
Decreased	0.121	0.834	0.680	0.196
SEM OWLQOL				
Improved	Reference		Reference	
No Change	-0.546	0.254	0.036	0.931
Decreased	0.454	0.337	0.080	0.870
Weight Change	0.076	0.212	0.006	0.907
HbA1c Change	-0.003	0.843	-0.005	0.751
Total Medication Burden change	0.078	0.513	0.076	0.530
Total Diabetes Medication Burden change	0.018	0.950	-0.187	0.497

Appendix Figures Chapter 5

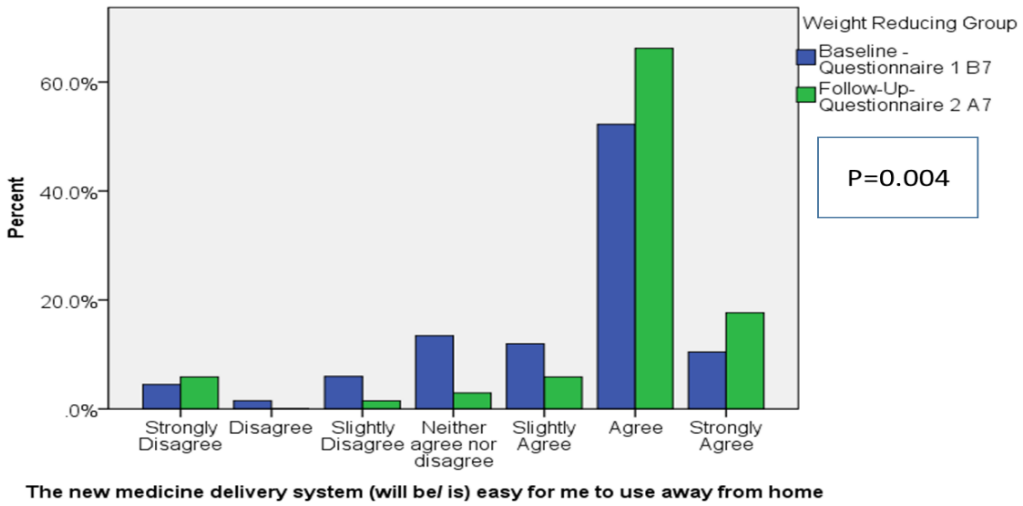


Figure 5.1: Percent agreement to EITQ/PITQ item "The new medicine delivery system (will be/ is) easy for me to use away from home" at baseline and follow-up for WR group.

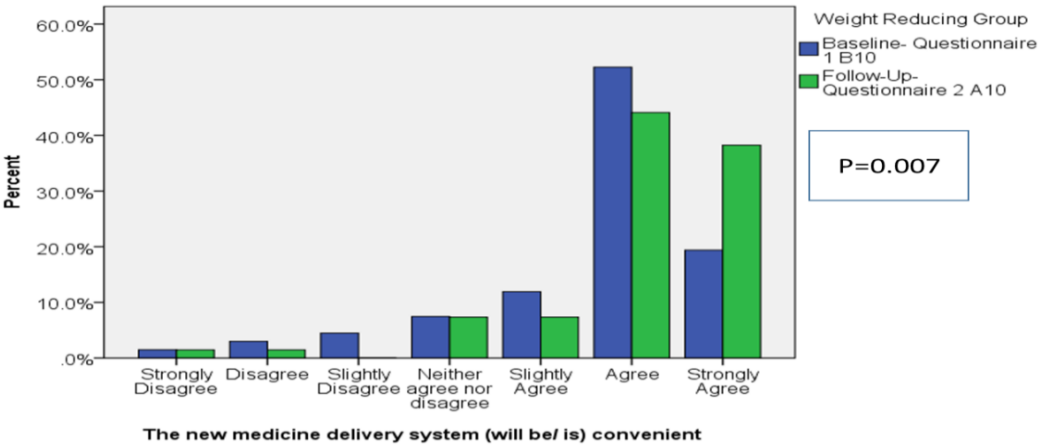


Figure 5.2: Percent agreement to EITQ/PITQ item "The new medicine delivery system (will be/ is) convenient" at baseline and follow-up for WR group.

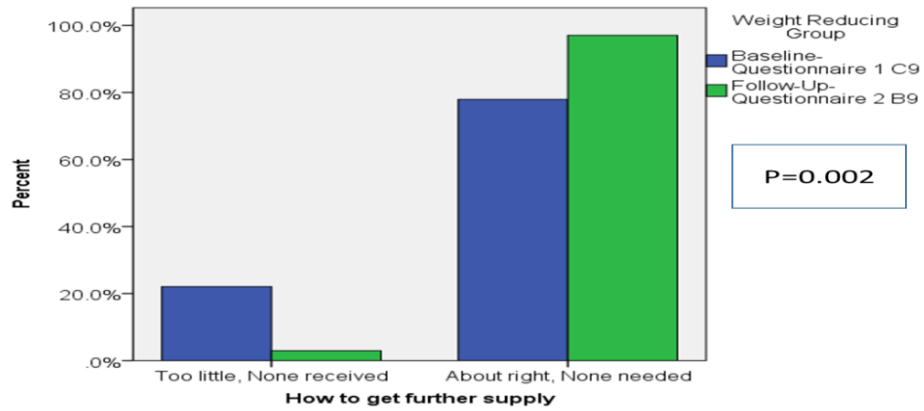


Figure 5.3: Percent agreement to SIMS item "Have received enough information about how to get further supply" at baseline and follow-up for WR group.

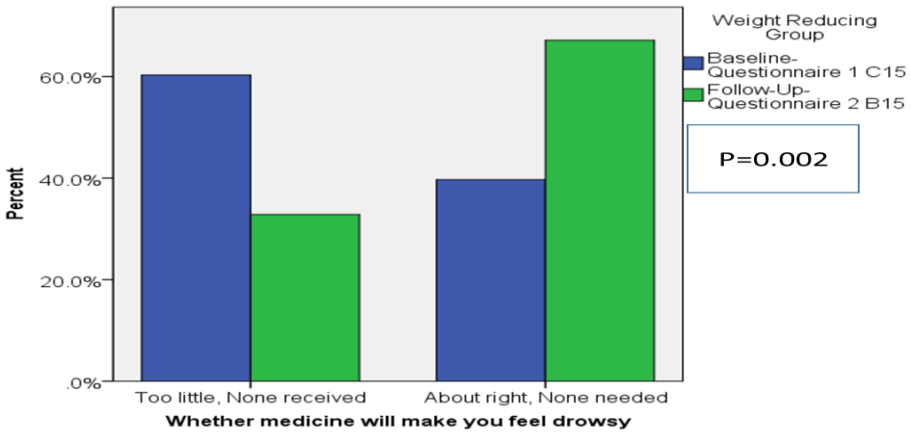


Figure 5.4: Percent agreement to SIMS item "Have received enough information about whether medicine will make you feel drowsy" at baseline and follow-up for WR group.

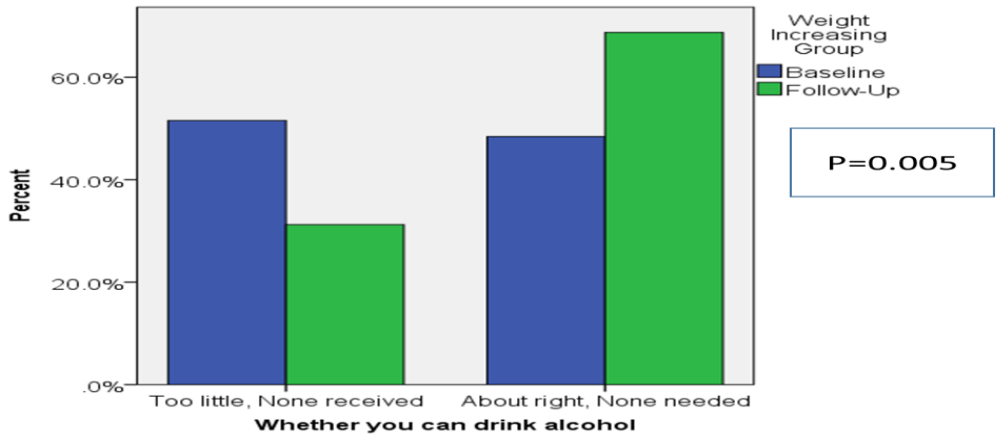


Figure 5.5: Percent agreement to SIMS item "Have received enough information about whether you can drink alcohol whilst taking this medicine" at baseline and follow-up for WI group.

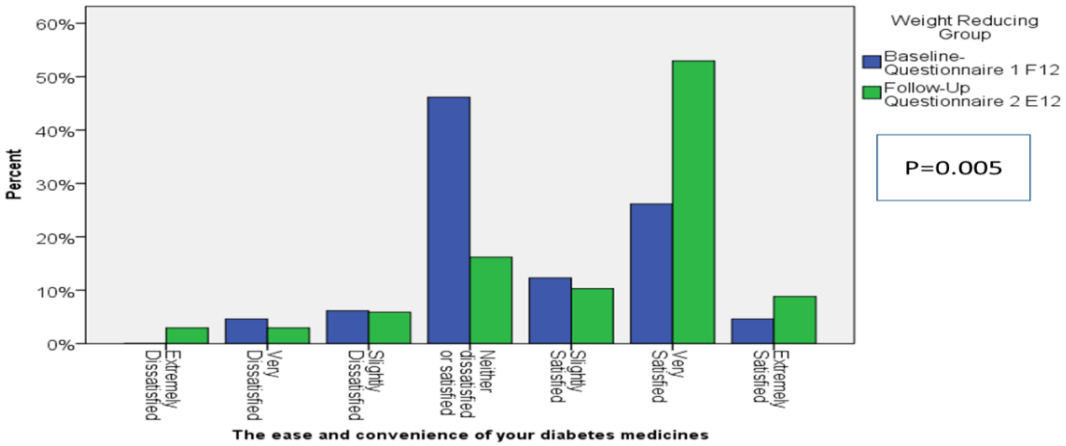


Figure 5.6: Percent agreement to DiabMedSat item "How satisfied or dissatisfied have you been with the ease and convenience of your diabetes medicine(s)" at baseline and follow-up for WR group.

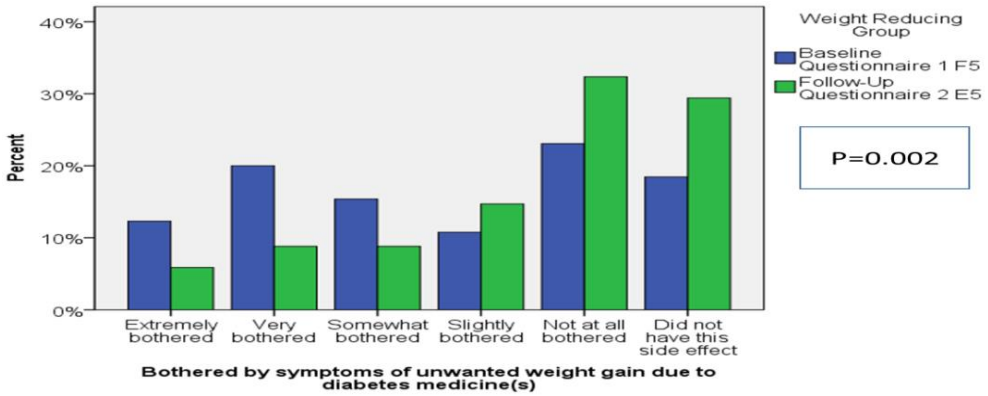


Figure 5.7: Percent agreement to DiabMedSat item "Have you been bothered by symptoms of unwanted weight gain due to your diabetes medicine(s)" at baseline and follow-up for WR group.

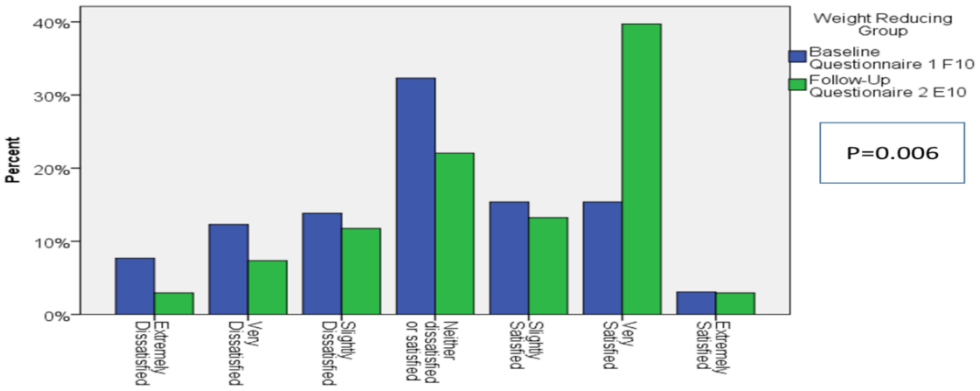


Figure 5.8: Percent agreement to DiabMedSat item "How satisfied or dissatisfied have you been with your diabetes medicine(s) ability to keep your blood sugars stable (avoid highs and lows)" at baseline and follow-up for WR group.

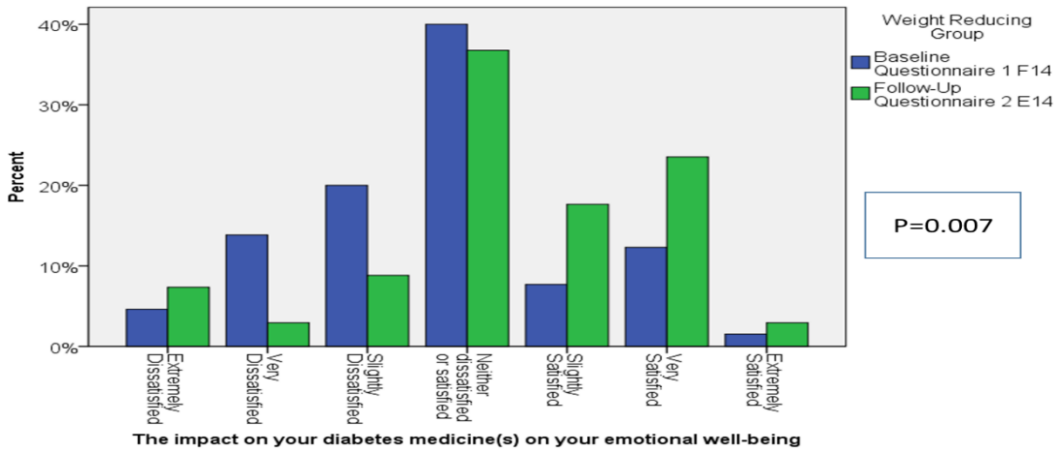


Figure 5.9: Percent agreement to DiabMedSat item "How satisfied or dissatisfied have you been with the impact of your diabetes medicine(s) on your emotional well-being" at baseline and follow-up for WR group.

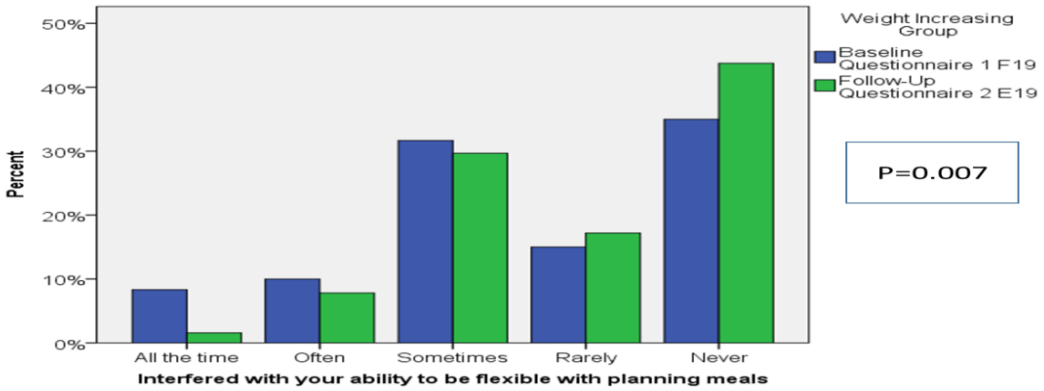


Figure 5.10: Percent agreement to DiabMedSat item "How often has taking your diabetes medicine(s) as prescribed interfered with your ability to be flexible with planning meals (when to eat and what you are able to eat)" at baseline and follow-up for WI group.

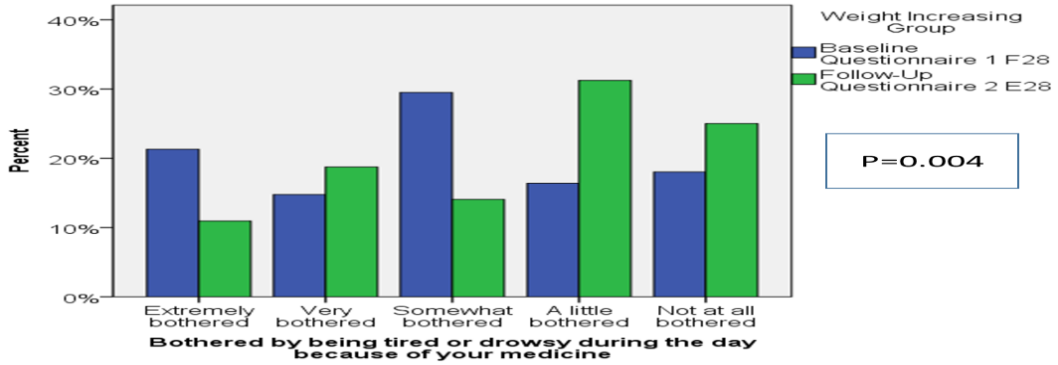


Figure 5.11: Percent agreement to TRIM-Weight item "How bothered or not bothered are you by being tired or drowsy during the day because of your medicine(s)" at baseline and follow-up for WI group.

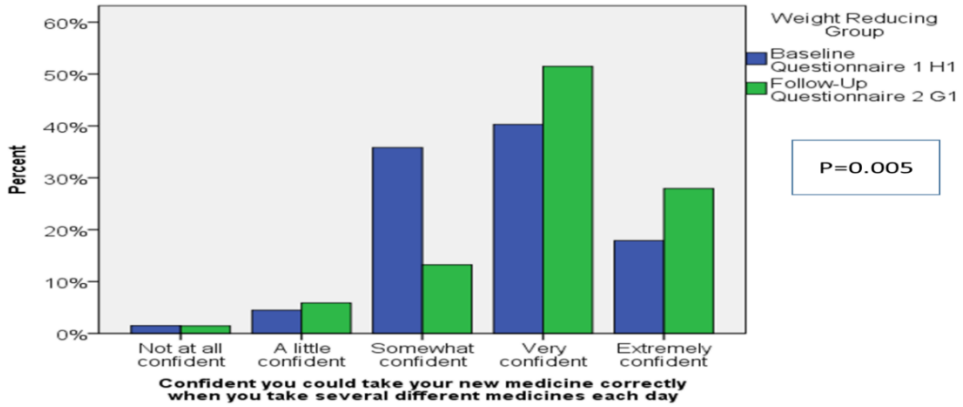


Figure 5.12: Percent agreement to SEAMS item "How confident are you that you could take your new medicine correctly when you take several different medicines each day" at baseline and follow-up for WR group.

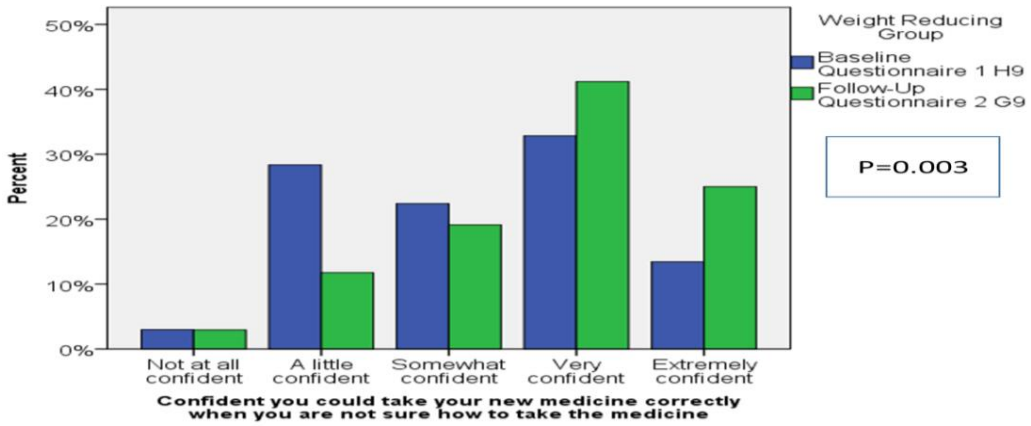


Figure 5.13: Percent agreement to SEAMS item "How confident are you that you could take your new medicine correctly when you are not sure how to take the medicine" at baseline and follow-up for WR group.

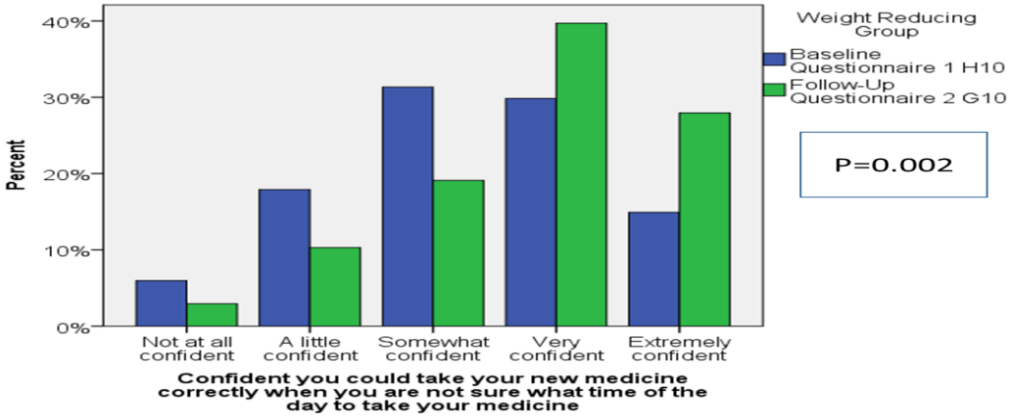


Figure 5.14: Percent agreement to SEAMS item "How confident are you that you could take your new medicine correctly when you are not sure what time of the day to take your medicine" at baseline and follow-up for WR group.

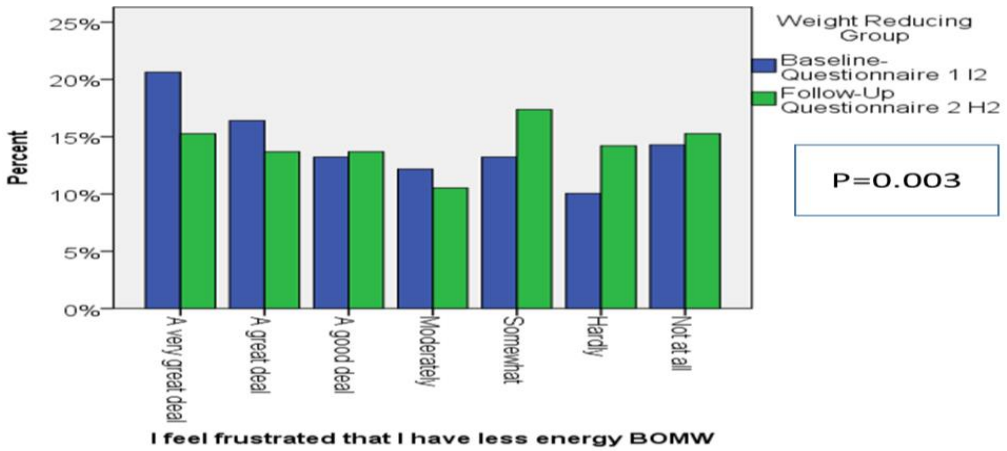


Figure 5.15: Percent agreement to OWLQOL item "I feel frustrated that I have less energy because of my weight" at baseline and follow-up for WR group.

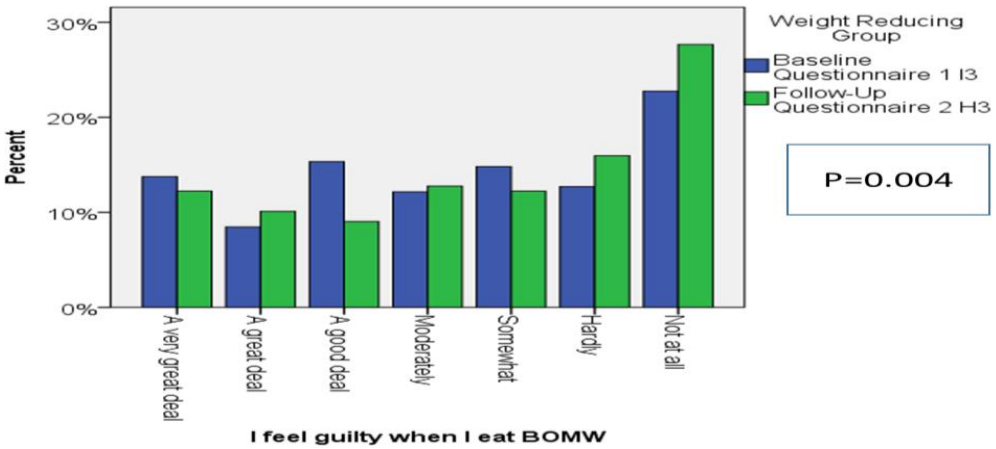


Figure 5.16: Percent agreement to OWLQOL item "I feel guilty when I eat because of my weight" at baseline and follow-up for WR group.

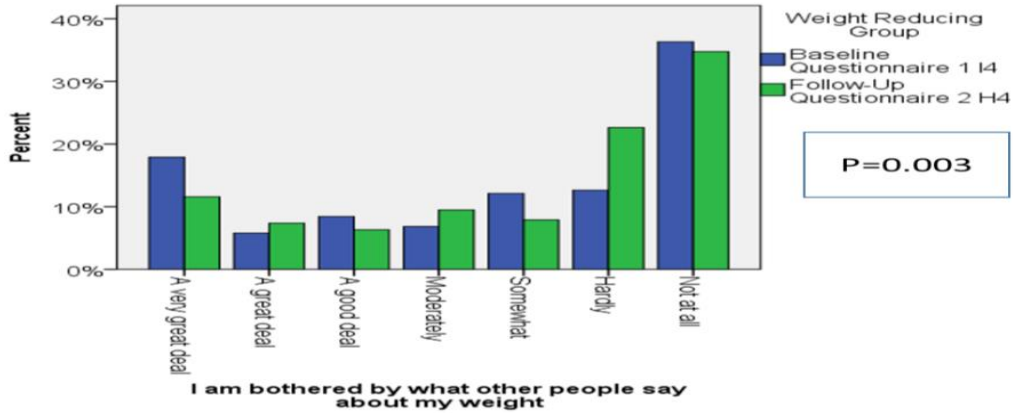


Figure 5.17: Percent agreement to OWLQOL item "I am bothered by what other people say about my weight" at baseline and follow-up for WR group.

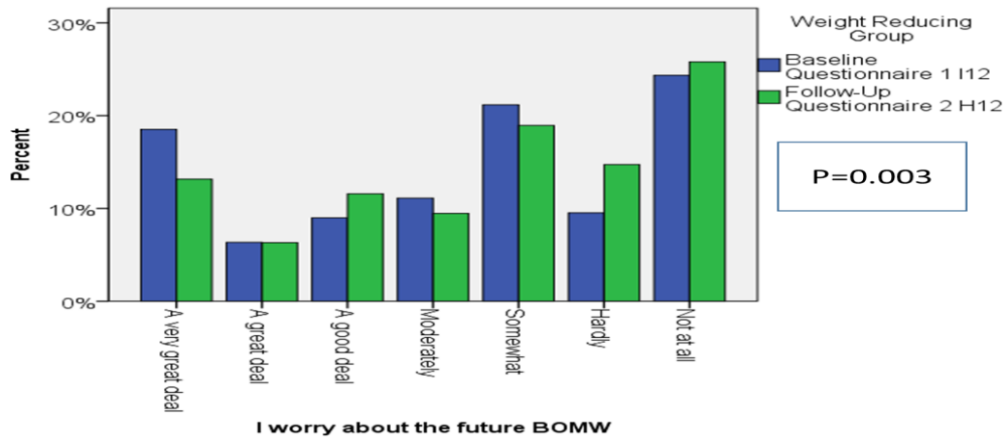


Figure 5.18: Percent agreement to OWLQOL item "I worry about the future because of my weight" at baseline and follow-up for WR

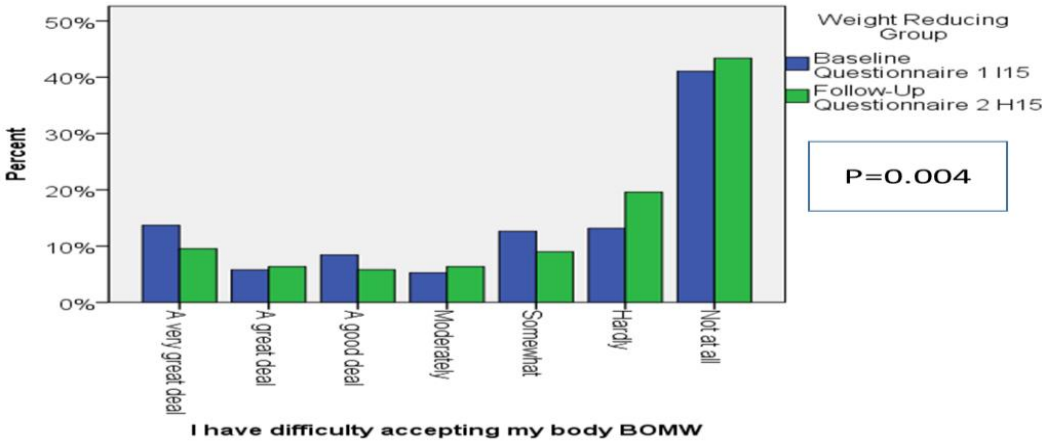


Figure 5.19: Percent agreement to OWLQOL item "I have difficulty accepting my body because of my weight" at baseline and follow-up for WR group.

Appendix 6.1: Interview Sample Characteristics and Scale scores

	Baseline n(%)	**Follow-up (n%)**
Centre Site:		
GP Practice	16 (67)	
SCDC	5 (21)	
CP	3 (12)	
Age (yrs)	63.5 (55, 69) [Range 46-78]	
Gender		
Men	13 (54)	
Women	11(46)	
Marital Status		
Alone/Single	3 (13)	
Married/ with partner	19 (79)	
Divorced/Separated	2 (8)	
Widowed	0 (0)	
Level of Education		
University /Higher Degree	1 (4)	
Diploma	0 (0)	
Vocational	2 (8)	
A level	4 (17)	
GCSE	7(29)	
No Formal Qualifications	10 (42)	
IMD		
20% most deprived	12 (50)	
21% to 40%	2 (8)	
41% to 60%	5 (21)	
61% to 80%	1 (4)	
20% least deprived	4 (17)	
Employment Status		
Full time	4 (17)	
Part-time	3 (13)	
Unemployed	3 (13)	
Retired	13 (54)	
Other [most on benefits]	1 (4)	
Years Diagnosed with T2D	8.5 (6, 13) [Range: 2 weeks- 19yrs]	
No of Diabetes Complications Missing Data	1 (0, 2)	1 (0, 2) 2 (8.3%)
New Medicine Prescribed- Weight Effect		
WR	11 (46)	
WN	6 (25)	
WI	7 (29)	
Total Medicine Burden (number/day) Missing Data	7 (5,10) [Range 1-19] 1 (4.2%)	7 (5,11) [Range 2-21] 1(4.2%)
Total Diabetes Medicine Burden (number per day) Missing Data	2 (1,3) Range (0-4)	2 (2,3) Range (1-3) 1(4.2%)

BMI (kg/m2) Missing Data	35.3 (30.8, 40.2) [Range28.4-51.8]	33.6 (30.2, 39.5) [Range 27.4-49.70] 1 (4.2%)
HbA1c (mmol/mol) Missing Data	78 (65, 91) [Range 52-110]	65 (56, 81) [Range 43-104] 4 (16.7%)
Adherence Levels Low Medium High Not Applicable Missing Data	 9 (41) 9 (41) 4 (18) 1 (4.2) 1 (4.2)	 6 (25) 10 (42) 8 (33)
Total N	24	23
EITQ (baseline)/PITQ (Follow-up)	5.8 (5.5, 6.3)	5.5 (5.1, 6.1)
SIMS	11 (7.3, 15.5)	13 (8, 16)
SIMS-AU	7 (5,8)	8 (7,9)
SIMS-PPM	4 (0.8, 6.8)	5 (2, 8)
BMQ-Concerns	3 (2.5, 3.4)	2.7 (2.3, 3.1)
BMQ-Necessity	3.9 (3.4, 4.4)	4 (3.6, 4.4)
BMQ Necessity–Concern Differential		
BMQ-Overuse	2.7 (2.3, 3.3)	3.3 (2.7, 3.7)
BMQ-Harm	2.4 (2, 2.8)	2.3 (2, 2.8)
BMQ-Benefits	4 (3.5, 4.4)	4 (3.8, 4.3)
SEAMS	3.7 (3.0, 4.0)	3.9 (2.9, 4.7)
SEAMS-UCU	3.4 (2.7, 4.0)	3.8 (2.7, 4.8)
SEAMS-UDC	3.9 (3.4, 4.1)	4 (3.1, 5.0)
OWLQOL	57.4 (27.7, 88)	77.5 (29.4, 90.2)
Total N	22	24
MMAS-8	6.8 (5.3, 7.2)	6.9 (5.6, 8)
DiabMedSat	67.1 (55.5, 78.6)	74.6 (63.3, 77.8)
DiabMedSat-Efficacy	53.3 (35.0, 72.5)	61.7 (47.5, 79.2)
DiabMedSat-Burden	89.0 (66.5, 95.5)	88.3 (76, 97.2)
DiabMedSat-Symptoms	70 (50, 80)	66 (56, 79)
TRIM-Wt-DL	70.8 (56.3, 83.3)	72.9 (58.3, 79.2)
TRIM-Wt-WM	33.3 (20.8, 50)	50 (25, 66.7)
TRIM-Wt-PH	84.4 (56.3, 100)	81.3 (64.1, 100)

Data are % or Median, IQR (Q1, Q3) or mean±SD

Appendix 6.2: Key aspects showed change or not change for the duration of the study per participant

Case	What changed	How has it changed	Why has it changed?	What has NOT changed
Irene	Support from both husband and health care services Clinical/Physical Outcomes Psychological Outcomes Treatment Routine	Increased- compliments about weight loss, reminders to take injection from husband, regular appointments, seen dietitian, DSN, Dr, GP Blood sugars improved, retained kidney function, Lost weight, less swollen legs Feeling good in herself Started liraglutide Convenient new medicine	Longing for a new lease of life Key motivation to lose weight Fear of consequences of abnormal sugars (physical evidence of medicines effectiveness & food on blood sugars)	Self-monitoring Motivation to change
Linda	Support from health care services Clinical/Physical Outcomes Treatment Routine	Increased - regular appointments, seen DSN, Dr, GP Blood sugars improved, lost weight, some minor side effects Started dapagliflozin, stopped sitagliptin Convenient new medicine	Key motivation to lose weight & stop taking medicines Fear of consequences of abnormal sugars	Still suffers unexplained pain which impacts lifestyle & wellbeing Concerns over taking medicines long term Missing other medicines
Alison	Support from health care services Clinical/Physical Outcomes Psychological Outcomes Treatment Routine	Increased- regular appointments/ telephone contact, seen DSN, Dr, GP Lost weight, some side effects Concerns over increased blood sugars Started exenatide, reduced insulin amount then increased Convenient new medicine	Key motivation to lose weight and reduce amount of insulin and Metformin	Continuous family support
Angela	Support health care services Clinical/Physical Outcomes Psychological Outcomes Treatment	Increased- regular appointments/ telephone contact, Seen DSN, Dr, GP Eventually blood sugars improving Concerns over increased blood sugars Started twice daily insulin- dose increased over time, stopped liraglutide and once daily insulin, stopped gliclazide	To improve post meal blood sugars and stopped liraglutide Concerns over increased blood sugars- she was not concerned at the beginning, but became concerned after change in treatment	Perceptions about seriousness of diabetes

	Routine	Sometimes delayed taking new medicine, considers eating patterns to reduce hypoglycaemia risk		
Oliver	Support from health care services Clinical/Physical Outcomes Treatment	Increased- regular appointments/ telephone contact, testing HbA1c, seen DSN Blood sugar improvement, lost weight Started liraglutide, stopped sitagliptin	Wants to control diabetes and lose weight Wants to live life without making lifestyle changes	Routine Views about support from GP and health care organisation
Christopher	Support from family and health care services Clinical/Physical Outcomes Psychological Outcomes Treatment Routine	Increased- all family members mentioned, regular appointment/ telephone contact, testing HbA1c, seen DSN Eventually blood sugars improving, gain weight, retained kidney function, experienced hypoglycaemic episodes, increased self-monitoring Injecting in public uncomfortable, annoyed with amount of self-monitoring Started once daily Insulin- dose increased over time, takes less Metformin and more gliclazide Convenient new medicine- becomes inconvenient	Concerned about health- diabetes and other issues. Does not want to keep changing medicines. Motivation to preserve kidney function. Insulin means takes less metformin	Beliefs about necessity and benefits of medicines Continuous family support
Philip	Support from health care services Clinical/Physical Outcomes Psychological Outcomes Treatment	Increased- regular appointment/ telephone contact, testing HbA1c, seen DSN High blood sugars, weight gain, increased self-monitoring Frustrated with support and increased blood sugars, concerned about weight gain Started Exenatide and insulin dose increased, stopped metformin and gliclazide	Wants to live his life, live longer Wants to be independent and control diabetes, wants to be normal Motivation to reduce amount of tablets	Concerns over taking medicines long term Routine
Adam	Support from health care services	Increased- regular appointment/ telephone contact, testing HbA1c, monitoring kidney function, seen DSN	Concerned about health- Diabetes and other issues	Continuous family support, trust doctors, belief in benefits of medicines

	Clinical/Physical Outcomes Psychological Outcomes Treatment Routine	Eventually blood sugars improving, kidneys deteriorated, experienced hypoglycaemic episodes, increased self-monitoring Surprised with slow effectiveness of insulin Started once daily insulin- dose increased overtime, stopped metformin, less gliclazide Convenient new medicine	Motivation to preserve kidney function	
Elizabeth	Support from health care services Clinical/Physical Outcomes Treatment	Increased- regular appointment/ telephone contact, testing HbA1c, seen DSN, GP, Matron nurse Slight improvement on blood sugars, less hypoglycaemic episodes Started twice daily insulin- dose increased overtime, stopped previous twice daily insulin, takes less medicines after GP review – not T2D medicines	Concerned of health- Diabetes and other issues Motivation to prevent weight gain, take less medicines and minimise side effects and Hypoglycaemia	Continuous family support Concerns re: symptoms of itchiness, blood sugars and weight Self-monitoring Routine
Kate	Support from health care services Clinical/Physical Outcomes Treatment	Increased- regular appointment/ telephone contacts, seen dr, DSN, PN Slight improvement on blood sugars, weight gain Never started Sitagliptin, Insulin dose increased and frequency of injections, more heart medicines	Motivation to take less insulin	Unsure of medicines' benefits Continuous family/friend support Routine
Keith	Support from wife and health care services Clinical/Physical Outcomes Psychological Outcomes Treatment	Increased- remind to self-monitor blood sugars and take injection, regular appointments/ telephone contact, seen DSN, GP, PN Weight loss, relatively stable blood sugars, short term side effects Made up with weight loss, frustrated with GP support Started Exenatide	Wants to live a normal life Key motivation to lose weight Wants to look after wife	Concerns over taking medicines long term

	Routine	Convenient new medicine- although sometimes forgets to inject		
Karen	Support from family and health care services Clinical/Physical Outcomes Treatment Routine	Increased- parent support experienced with injections, regular appointments/ telephone contacts , seen DSN, GP Blood sugars improvement, weight loss, body bruises at injection site, side effects Started Liraglutide More organised/ Increased adherence to tablets	Keen motivation to lose weight	Injectable medicines more important than tablets
Teresa	Support from family and health care services Clinical/Physical Outcomes Psychological Outcomes Treatment Routine	Increased- husband aware of hypoglycaemia, regular appointment/ telephone contact, seen DSN Improved blood sugars, experienced hypoglycaemic episodes Disappointed with no weight loss Started Exenatide extended release Convenient new medicine	Key motivation to lose weight and avoid insulin	Body weight Concerns over amount of tablets taken and risk of hypoglycaemia
Robert	Support from health care services Clinical/Physical Outcomes Psychological Outcomes Treatment	Decreased- not regular contact, unable to make appointment, unaware of HbA1c results Blood sugars may have improved, may have gained weight, experienced hypoglycaemic episodes Disappointed with new medicine- not as expected, frustrated with GP service Started gliclazide, changed eating patterns and food amount due to hypoglycaemia	Key motivation to control diabetes Wants to function as a normal person Wants to look after wife	Continuous family support
Kelly	Support from health care services Clinical/Physical Outcomes Psychological Outcomes	Increased- regular appointment/ telephone contact, changes in treatment, seen DSN Blood sugars improved then deteriorated, Weight lost then gained, experienced side effects	Key motivation to lose weight and stop taking medicines Wants to go back to her old self	Continuous family support

	Treatment Routine	Disappointed with changes and effectiveness of medicines Started exenatide then changed to liraglutide, stopped pioglitazone, changes to eating patterns due to side effects Convenient new medicine		
Andrew	Support from health care services Clinical/Physical Outcomes Treatment	Increased- regular appointment / telephone contact, testing HbA1c, monitoring kidney function, seen DSN, dietitian Blood sugar improvement, Started gliclazide, changes in types and portions of food in order to lose weight	Wants to live a normal life for his age Wants to control diabetes and kidney function Key motivation to lose weight	Continuous family support Difficulty in breathing Views about medicines Body weight
Edward	Support from health care services Clinical/Physical Outcomes Psychological Outcomes Treatment Routine	Increased- regular appointments, testing HbA1c Seen DSN Blood sugars improved Happy with changes to treatment and effectiveness Started twice daily insulin- dose increased over time, stopped once daily insulin, changes in eating patterns due to injections Convenient new medicine		Concerns of complications with Diabetes
Vanessa	Support from family and health care services Clinical/Physical Outcomes Psychological Outcomes Treatment	Increased- family provides cooked meals, regular appointments/ telephone contacts, seen DSN, Dr, dietitian, testing HbA1c Decreased- seen GP less due to increase in other services Blood sugars improved, weight loss, more energy Feels better in herself Started liraglutide and levemir, stopped novorapid and lantus, eating patterns & food	Key motivation to lose weight and stop taking medicines wants to live a normal life	Concerns over the number of medicines taken Omission of tablets

	Routine	amount changed due to side effects from medicines Convenient new medicines		
Gareth	Support from health care services Clinical/Physical Outcomes Treatment	Increased Blood sugar improvement, retained kidney function Started linagliptin, stopped sitagliptin	Trust in doctors	Continuous family support Routine
Julie	Support from health care services Clinical/Physical Outcomes Psychological Outcomes Treatment Routine	Increased- regular appointments/ telephone contact, seen dietitian, DSN Unsure about blood sugars as stopped self-monitoring, lost weight, more energetic Feels good about herself Started liraglutide, stopped gliclazide, changes to eating patterns, amount and type of foods due to side effects of medicine and motivation to lose weight Convenient new medicine	Key motivation to lose weight, avoid insulin and stop medicines	Fear of diabetes complications Continuous family support
Daniel	Support from health care services Clinical/Physical Outcomes Treatment Routine	Increased- regular support , seen practice nurse, GP, attended course on diabetes Unsure if improvement in blood sugars, lost weight, more energetic Started metformin dose increased over time, lifestyle changes due to effect of medicine Convenient new medicine	Wants to combat diabetes and eventually stop taking medicines	Diabetes is serious Concerns over taking medicines long term
Patrick	Support from health care services Clinical/Physical Outcomes Psychological Outcomes	Increased- regular appointments, seen DSN, DM Dr, Kidney Dr Blood sugar improvement, retained kidney function, weight loss, blood pressure improvement Happy with weight loss	Key motivation to lose weight and retain kidney function	Views about support from GP and health care organisation Routine

	Treatment	Started linagliptin, stopped sitagliptin, insulin dose reduced, started orlistat at reduced dose		
David	Support from health care services Clinical/Physical Outcomes Treatment	Increased- regular appointments, seen DSN, testing HbA1c, shown how to self-monitor Blood sugar improvement, weight loss, more energetic, self-monitors Started metformin MR	Wants to control diabetes	Continuous family support Views about support from GP and health care organisation Routine
James	Support from health care services Clinical/Physical Outcomes Treatment	Increased- regular appointments, seen DSN, testing HbA1c Slight improvement of blood sugar, lost weight, more energetic, self-monitors Started sitagliptin, reduced dose of gliclazide	Wants to control diabetes and forgets he has it	Routine Fear of insulin, concerns over hypoglycaemia risk