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Identifying health inequalities in individuals with Major Mental Illness (MMI) using routine data

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Abstract and Summary of Thesis:

Background:

Individuals with Major Mental Illness (such as schizophrenia and bipolar disorder) experience increased rates of physical health comorbidity compared to the general population. They also experience inequalities in access to certain aspects of healthcare. This ultimately leads to premature mortality. Studies detailing patterns of physical health comorbidity are limited by their definitions of comorbidity, single disease approach to comorbidity and by the study of heterogeneous groups. To date the investigation of possible sources of healthcare inequalities experienced by individuals with Major Mental Illness (MMI) is relatively limited. Moreover studies detailing the extent of premature mortality experienced by individuals with MMI vary both in terms of the measure of premature mortality reported and age of the cohort investigated, limiting their generalisability to the wider population. Therefore local and national data can be used to describe patterns of physical health comorbidity, investigate possible reasons for health inequalities and describe mortality rates. These findings will extend existing work in this area.

Aims and Objectives:

To review the relevant literature regarding: patterns of physical health comorbidity, evidence for inequalities in physical healthcare and evidence for premature mortality for individuals with MMI. To examine the rates of physical health comorbidity in a large primary care database and to assess for evidence for inequalities in access to healthcare using both routine primary care prescribing data and incentivised national Quality and Outcome Framework (QOF) data. Finally to examine the rates of premature mortality in a local context with a particular focus on cause of death across the lifespan and effect of International Classification of Disease Version 10 (ICD 10) diagnosis and socioeconomic status on rates and cause of death.

Methods:

A narrative review of the literature surrounding patterns of physical health comorbidity, the evidence for inequalities in physical healthcare and premature mortality in MMI was undertaken. Rates of physical health comorbidity and multimorbidity in schizophrenia and bipolar disorder were examined using a large primary care dataset (Scottish Programme for

Improving Clinical Effectiveness in Primary Care (SPICE)). Possible inequalities in access to healthcare were investigated by comparing patterns of prescribing in individuals with MMI and comorbid physical health conditions with prescribing rates in individuals with physical health conditions without MMI using SPICE data. Potential inequalities in access to health promotion advice (in the form of smoking cessation) and prescribing of Nicotine Replacement Therapy (NRT) were also investigated using SPICE data. Possible inequalities in access to incentivised primary healthcare were investigated using National Quality and Outcome Framework (QOF) data. Finally a pre-existing case register (Glasgow Psychosis Clinical Information System (PsyCIS)) was linked to Scottish Mortality data (available from the Scottish Government Website) to investigate rates and primary cause of death in individuals with MMI. Rate and primary cause of death were compared to the local population and impact of age, socioeconomic status and ICD 10 diagnosis (schizophrenia vs. bipolar disorder) were investigated.

Results:

Analysis of the SPICE data found that sixteen out of the thirty two common physical comorbidities assessed, occurred significantly more frequently in individuals with schizophrenia. In individuals with bipolar disorder fourteen occurred more frequently. The most prevalent chronic physical health conditions in individuals with schizophrenia and bipolar disorder were: viral hepatitis (Odds Ratios (OR) 3.99 95% Confidence Interval (CI) 2.82-5.64 and OR 5.90 95% CI 3.16-11.03 respectively), constipation (OR 3.24 95% CI 3.01-3.49 and OR 2.84 95% CI 2.47-3.26 respectively) and Parkinson's disease (OR 3.07 95% CI 2.43-3.89 and OR 2.52 95% CI 1.60-3.97 respectively). Both groups had significantly increased rates of multimorbidity compared to controls: in the schizophrenia group OR for two comorbidities was 1.37 95% CI 1.29-1.45 and in the bipolar disorder group OR was 1.34 95% CI 1.20-1.49.

In the studies investigating inequalities in access to healthcare there was evidence of: under-recording of cardiovascular-related conditions for example in individuals with schizophrenia: OR for Atrial Fibrillation (AF) was 0.62 95% CI 0.52 - 0.73, for hypertension 0.71 95% CI 0.67 - 0.76, for Coronary Heart Disease (CHD) 0.76 95% CI 0.69 - 0.83 and for peripheral vascular disease (PVD) 0.83 95% CI 0.72 - 0.97. Similarly in individuals with bipolar disorder OR for AF was 0.56 95% CI 0.41-0.78, for hypertension 0.69 95% CI 0.62 - 0.77 and for CHD 0.77 95% CI 0.66 - 0.91.

There was also evidence of less intensive prescribing for individuals with schizophrenia and bipolar disorder who had comorbid hypertension and CHD compared to individuals with hypertension and CHD who did not have schizophrenia or bipolar disorder. Rate of prescribing of statins for individuals with schizophrenia and CHD occurred significantly less frequently than in individuals with CHD without MMI (OR 0.67 95% CI 0.56-0.80). Rates of prescribing of 2 or more anti-hypertensives were lower in individuals with CHD and schizophrenia and CHD and bipolar disorder compared to individuals with CHD without MMI (OR 0.66 95% CI 0.56-0.78 and OR 0.55 95% CI 0.46-0.67, respectively).

Smoking was more common in individuals with MMI compared to individuals without MMI (OR 2.53 95% CI 2.44-2.63) and was particularly increased in men (OR 2.83 95% CI 2.68-2.98). Rates of ex-smoking and non-smoking were lower in individuals with MMI (OR 0.79 95% CI 0.75-0.83 and OR 0.50 95% CI 0.48-0.52 respectively). However recorded rates of smoking cessation advice in smokers with MMI were significantly lower than the recorded rates of smoking cessation advice in smokers with diabetes (88.7% vs. 98.0%, p<0.001), smokers with CHD (88.9% vs. 98.7%, p<0.001) and smokers with hypertension (88.3% vs. 98.5%, p<0.001) without MMI. The odds ratio of NRT prescription was also significantly lower in smokers with MMI without diabetes compared to smokers with diabetes without MMI (OR 0.75 95% CI 0.69-0.81). Similar findings were found for smokers with MMI without CHD compared to smokers with CHD without MMI (OR 0.34 95% CI 0.31-0.38) and smokers with MMI without hypertension compared to smokers with hypertension without MMI (OR 0.71 95% CI 0.66-0.76).

At a national level, payment and population achievement rates for the recording of body mass index (BMI) in MMI was significantly lower than the payment and population achievement rates for BMI recording in diabetes throughout the whole of the UK combined: payment rate 92.7% (Inter Quartile Range (IQR) 89.3-95.8 vs. 95.5% IQR 93.3-97.2, p<0.001 and population achievement rate 84.0% IQR 76.3-90.0 vs. 92.5% IQR 89.7-94.9, p<0.001 and for each country individually: for example in Scotland payment rate was 94.0% IQR 91.4-97.2 vs. 96.3% IQR 94.3-97.8, p<0.001. Exception rate was significantly higher for the recording of BMI in MMI than the exception rate for BMI recording in diabetes for the UK combined: 7.4% IQR 3.3-15.9 vs. 2.3% IQR 0.9-4.7, p<0.001 and for each country individually. For example in Scotland exception rate in MMI was 11.8% IQR 5.4-19.3 compared to 3.5% IQR 1.9-6.1 in diabetes.

Similar findings were found for Blood Pressure (BP) recording: across the whole of the UK payment and population achievement rates for BP recording in MMI were also significantly reduced compared to payment and population achievement rates for the recording of BP in chronic kidney disease (CKD): payment rate: 94.1% IQR 90.9-97.1 vs.97.8% IQR 96.3-98.9 and p<0.001 and population achievement rate 87.0% IQR 81.3-91.7 vs. 97.1% IQR 95.5-98.4, p<0.001. Exception rates again were significantly higher for the recording of BP in MMI compared to CKD (6.4% IQR 3.0-13.1 vs. 0.3% IQR 0.0-1.0, p<0.001). There was also evidence of differences in rates of recording of BMI and BP in MMI across the UK. BMI and BP recording in MMI were significantly lower in Scotland compared to England (BMI:-1.5% 99% CI -2.7 to -0.3%, p<0.001 and BP: -1.8% 99% CI -2.7 to -0.9%, p<0.001). While rates of BMI and BP recording in diabetes and CKD were similar in Scotland compared to England (BMI: -0.5 99% CI -1.0 to 0.05, p=0.004 and BP: 0.02 99% CI -0.2 to 0.3, p=0.797).

Data from the PsyCIS cohort showed an increase in Standardised Mortality Ratios (SMR) across the lifespan for individuals with MMI compared to the local Glasgow and wider Scottish populations (Glasgow SMR 1.8 95% CI 1.6-2.0 and Scotland SMR 2.7 95% CI 2.4-3.1). Increasing socioeconomic deprivation was associated with an increased overall rate of death in MMI (350.3 deaths/10,000 population/5 years in the least deprived quintile compared to 794.6 deaths/10,000 population/5 years in the most deprived quintile). No significant difference in rate of death for individuals with schizophrenia compared with bipolar disorder was reported (6.3% vs. 4.9%, p=0.086), but primary cause of death varied: with higher rates of suicide in individuals with bipolar disorder (22.4% vs. 11.7%, p=0.04).

Discussion:

Local and national datasets can be used for epidemiological study to inform local practice and complement existing national and international studies. While the strengths of this thesis include the large data sets used and therefore their likely representativeness to the wider population, some limitations largely associated with using secondary data sources are acknowledged.

While this thesis has confirmed evidence of increased physical health comorbidity and multimorbidity in individuals with MMI, it is likely that these findings represent a significant under reporting and likely under recognition of physical health comorbidity in this population. This is likely due to a combination of patient, health professional and

healthcare system factors and requires further investigation. Moreover, evidence of inequality in access to healthcare in terms of: physical health promotion (namely smoking cessation advice), recording of physical health indices (BMI and BP), prescribing of medications for the treatment of physical illness and prescribing of NRT has been found at a national level.

While significant premature mortality in individuals with MMI within a Scottish setting has been confirmed, more work is required to further detail and investigate the impact of socioeconomic deprivation on cause and rate of death in this population. It is clear that further education and training is required for all healthcare staff to improve the recognition, diagnosis and treatment of physical health problems in this population with the aim of addressing the significant premature mortality that is seen.

Conclusions:

Future work lies in the challenge of designing strategies to reduce health inequalities and narrow the gap in premature mortality reported in individuals with MMI. Models of care that allow a much more integrated approach to diagnosing, monitoring and treating both the physical and mental health of individuals with MMI, particularly in areas of social and economic deprivation may be helpful. Strategies to engage this "hard to reach" population also need to be developed. While greater integration of psychiatric services with primary care and with specialist medical services is clearly vital the evidence on how best to achieve this is limited. While the National Health Service (NHS) is currently undergoing major reform, attention needs to be paid to designing better ways to improve the current disconnect between primary and secondary care. This should then help to improve physical, psychological and social outcomes for individuals with MMI.

Table of Contents

List of Tables

List of Figures

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Author's Declaration

This thesis is the work of the author unless specifically otherwise stated.

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Abbreviations

AADR	Age-Adjusted Death Rates
A&E	Accident and Emergency
ACE	Angiotensin Converting Enzyme
AF	Atrial Fibrillation
ARB	Angiotensin II Receptor Blocker
BHF	British Heart Foundation
BMA	British Medical Association
BNF	British National Formulary
BP	Blood Pressure
CABG	Coronary Artery Bypass Grafting
CATIE	Clinical Antipsychotic Trials of Intervention Effectiveness
CE	Community Engagement
CHD	Coronary Heart Disease
CHI	Community Health Index
CI	Confidence Interval
CKD	Chronic Kidney Disease
CMF	Comparative Mortality Factor
CMHT	Community Mental Health Team
COPD	Chronic Obstructive Pulmonary Disease
CS	Cervical Screening
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
DHSSPSNI	Department of Health, Social Service and Public Safety
GCPH	Glasgow Centre for Population Health
GP	General Practioners
GPC	General Practioners Committee
GRO	General Register Office
HALE	Healthy Life Expectancy
HDL	High Density Lipoproteins
HF	Heart Failure
HIV	Human Immunodeficiency Virus
HPPs	Health Promotion Programmes
HR	Hazard Ratios
HSCIC	Health and Social Care Information Centre
hsCRP	High Sensitivity C Reactive Protein
IBS	Irritable Bowel Syndrome
ICD-10	International Classification of Diseases Version 10
IHD	Ischaemic Heart Disease
IQR	Inter-Quartile Range
ISD	Information Services Division
LDL	Low Density Lipoproteins
LVEF	Left Ventricle Ejection Fraction
MAR	Missing at Random
MCAR	Missing Completely at Random

MMI	Major Mental Illness
MMR	Mortality Rate ratios
MS	Multiple Sclerosis
NHS	National Health Service
NHSGG&C	National Health Service Greater Glasgow and Clyde
NICE	National Institute for Clinical Effectiveness
NMAR	Not Missing At Random
NPI	Non-Pharmacological Intervention
NRT	Nicotine Replacement Therapy
OR	Odds Ratio
OSA	Obstructive Sleep Apnoea
OTD	Other Types of Depression
PAD	Peripheral Arterial Disease
PIMS	Patient information management systems
PsyCIS	Psychosis Clinical Information System
PVD	Peripheral Vascular Disease
QOF	Quality and Outcome framework
RA	Rheumatoid Arthritis
RAISE	Recovery After an Initial Schizophrenia Episode
RCGP	Royal College of General Practioners
SIMD	Scottish Index of Multiple Deprivation
SIR	Standardised Incidence Rate
SMI	Serious/ Severe Mental Illness
SMR	Standardised Mortality Ratio
SPICE	Scottish Programme for Improving Clinical Effectiveness in Primary Care
STI	Sexually Transmitted Infections
TSH	Thyroid Stimulating Hormone
UK	United Kingdom
VA	Veterans Affair
YLL	Years of Life Lost

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Physical health indicators in Major Mental Illness: Data from The Quality and Outcome Framework in the UK. 26th February 2015 Academy of Medical Sciences, London, England

Smoking Status, cessation advice and prescribing of Nicotine Replacement Therapy (NRT) in individuals with Major Mental Illness (MMI): Evidence of inequality. 16th October 2014 Royal College of Psychiatrists General Adult Meeting, Brighton, England

Comparing Blood Pressure and Body Mass Index Recording for Major Mental Illness, Diabetes and Chronic Kidney Disease. Analysis of National QOF Data for the UK. 26th June 2014 Royal College of Psychiatrists 2014 International Congress, London, England

Patterns of multimorbidity in schizophrenia: A cross-sectional study of 1.4 million participants in primary care 4th July 2013 Royal College of Psychiatrists 2013 International Congress, Edinburgh, Scotland

Premature mortality in schizophrenia and bipolar affective disorder: Age and cause of death within the Glasgow Psychosis Cohort (n=4,216) 3rd July 2013 Royal College of Psychiatrists 2013 International Congress Edinburgh, Scotland

How does socioeconomic deprivation and ICD 10 diagnosis influence mortality in psychotic disorders? 14th December 2012 SMRH Annual meeting Glasgow, Scotland

Oral Presentations

Comparing Blood Pressure and Body Mass Index Recording for Major Mental Illness, Diabetes and Chronic Kidney Disease. Analysis of National QOF Data for the UK. 14th May 2014 HERON Conference, London, England

Chapter 1 Introduction:

Since the recognition of schizophrenia in its modern concept from the early nineteenth century, the high morbidity and premature mortality associated with this severe condition has been recognised worldwide (Bleuer, 1950; Malzburg, 1934; Alstrom, 1942). The work by Emil Kraepelin as early as the 18th Century, where he dichotomised manic-depressive illness (later named bipolar disorder) and dementia praecox (later named schizophrenia) based on illness prognosis also recognised the poor outcomes associated with schizophrenia (Kraepelin, 1919). More recently the increased morbidity and premature mortality associated with bipolar disorder too has become recognised (Osby at al., 2001; Roshanaei-Moghaddam et al., 2009). Inequalities in access to and the provision of healthcare for individuals with schizophrenia and bipolar disorder have been highlighted as potential explanatory factors for the increased morbidity and premature mortality reported (Druss et al., 2001) however the exact mechanism for this is poorly understood.

While increased morbidity and premature mortality are recognised within individuals with Major Mental Illness (namely schizophrenia and bipolar disorder), there are significant gaps in the understanding of the precise patterns of physical health comorbidity and multimorbidity within these individuals. A detailed understanding of how inequalities in healthcare access and provision manifest in primary care for individuals with Major Mental Illness (MMI) is also lacking. Moreover the cause of mortality across the adult lifespan and in particular the effects of gender and socioeconomic deprivation on mortality are also poorly understood. The effect of socioeconomic deprivation is particularly pertinent at a local Glasgow and wider Scottish level, given Scotland's place as the "Sick Man of Europe" (GCPH Still the Sick Man of Europe? 2012).

This chapter provides a review of the current evidence for the increased rates of physical health comorbidity in individuals with MMI compared to individuals without MMI. The research to date investigating multimorbidity in individuals with MMI will also be explored and gaps in research within these fields will be highlighted. Evidence for the inequalities in healthcare access and provision experienced by individuals with MMI will be explored. Finally the evidence of premature mortality for individuals with MMI will also be detailed along with the evidence for the increasing gap in mortality between individuals with MMI and individuals without MMI.

1.1 Methodology:

A narrative review of the literature was undertaken. Narrative reviews are useful in providing an overview and summary of existing literature (Collins and Fauser, 2005). Although an explicit, systematic search protocol was not used, a thorough review of the literature was undertaken by using well defined search terms (detailed in Appendix 1) and multiple search engines namely: *Pubmed, Google Scholar* and *MEDLINE*. Study suitability was determined by reading the titles and abstracts of the identified papers and where necessary the full paper was retrieved. Further potential sources were identified from reference lists. All peer-reviewed publications were considered. Studies were included based on their quality and relevance as determined by: their definition of Major Mental Illness (MMI), sample size, duration of follow up, and where relevant: physical comorbidity/comorbidities included, measure of inequality in healthcare provision or access and measure of mortality. While it is recognised that narrative reviews can be prone to author bias, care was taken to minimise this by using extensive search terms and multiple databases.

1.2 Evidence for increased physical comorbidity in Major Mental Illness (MMI):

1.2.1 Evidence for increased physical comorbidity in schizophrenia:

Multiple studies reporting increased rates of physical comorbidity in individuals with schizophrenia were identified. In particular studies exploring the increased rates of: diabetes (Dixon et al., 2000), obesity (Wirshing and Meyer, 2003), hyperlipidaemia (McGreadie, 2003), hypertension and metabolic syndrome (Heiskanen et al., 2003; Cohn et al., 2004) were all found.

It is estimated that diabetes is twice as prevalent in individuals with schizophrenia compared to the general population (Vancampfort et al., 2013). While an association between antipsychotics and diabetes is well recognised, rates of diabetes are not appreciably increased in aged matched, drug naïve individuals with a first episode psychosis (Vancampfort et al., 2013; Mitchell et al., 2013). It is therefore generally appreciated that the majority of metabolic abnormalities occur fairly rapidly after the initiation of treatment (De Hert et al., 2011) and several studies have suggested that the differing weight gain potential of different antipsychotics contribute to the differing

relative risks (RRs) of diabetes associated with them (Fiedorowicz et al., 2012). However antipsychotics may also induce diabetes independently of weight gain and adiposity (Deng, 2013; Ballon et al., 2014) potentially by inducing insulin resistance (Weston-Green et al., 2013). There is also some evidence to suggest that genetic polymorphisms may increase susceptibility to both diabetes and schizophrenia (Alkelai et al., 2012).

For metabolic syndrome: Heiskenan and colleagues reported a prevalence of 37% in individuals with schizophrenia, which was 2 to 4 times that of the general population (Heiskenan et al., 2003). Similarly Vancampfort and colleagues (2013) reported an increased odds ratio (OR) of 2.35 (95% CI 1.68-3.29; $p<0.001$). Increased risk of: hypertension (OR 1.36 95%CI 1.21-1.53; $p<0.001$), reduced high-density lipoprotein (HDL) cholesterol (OR 2.35 95% CI 1.78-3.10; $p<0.001$) and hypertriglyceridemia (OR 2.73 95% CI 1.95-3.83; $p<0.001$) were also found (Vancampfort et al., 2013).

It is recognised that metabolic disturbances occur quickly after antipsychotic exposure, with data from the Recover After an Initial Schizophrenia Episode (RAISE) study observing significant cardiometabolic abnormalities (dyslipidaemia, hyperglycaemia and Blood Pressure changes) after only 47 days of antipsychotic exposure (Correll et al., 2014). This finding of accumulation of cardiometabolic risk has also been reported by Mitchell and colleagues (2013) who reported a 10% rate of metabolic syndrome in unmedicated individuals with first episode psychosis compared to 32.5% in individuals with more established schizophrenia (Mitchell et al., 2013).

Inflammation is also important in psychosis and the development of cardiometabolic risk factors. A preliminary study by Russell and colleague (2015) reported that individuals who had increased levels of inflammation (as measured by high sensitivity C-reactive protein hsCRP) early in their course of illness, had increased risk of metabolic abnormalities (such as dyslipidaemia) independent of weight gain (Russell et al., 2015). Clearly this potential relationship requires further investigation.

Rates of obesity in individuals with schizophrenia are also increased (Zipursky et al., 2005) with estimates that compared to the general population individuals with schizophrenia are 2.8-4.4 times more likely to be obese (Suburamaniam et al., 2014; Correll et al., 2015). Some studies have suggested that women with schizophrenia have higher rates of obesity that men with schizophrenia (Gardner-Sood et al., 2015) and that obesity may be a factor in non-compliance with medication, especially if associated with distress (Weiden et al.,

2004). Increased rates of obesity in individuals with schizophrenia appears be a global phenomenon, as studies from China (Suburamaniam et al., 2014), Nigeria, Japan, Switzerland, Germany and Denmark (Larsen et al., 2013) have all reported similar findings.

Higher rates of angina, compared to the general population (Filik et al., 2006) have also been reported in individuals with Severe Mental Illness (SMI) (including schizophrenia). Increased odds ratios of: arrhythmia, (OR 1.5 95% CI 1.2 -1.8); syncope, (OR 4.0 95% CI 2.0-7.9); heart failure, (OR 1.7 95% CI 1.4 - 2.2) and transient cerebral ischemia, (OR 2.6 95% CI 1.7-3.7) have also been reported in a cohort of individuals with schizophrenia compared to the general population in Canada (Curkendall et al., 2004). Risk of cerebrovascular disease has also reported to be increased- with one study estimating that young individuals (under 45) with schizophrenia had a two fold increase of developing stroke during the 5 years after hospitalisation compared to the comparison group (Lin et al., 2008).

In addition to the physical health problems associated with increased cardiometabolic risk, there is also evidence for increased rates of irritable bowel syndrome (IBS) (Gutpa et al., 1997), infections such as HIV, hepatitis (Goff et al., 2005) and tuberculosis (Mishin et al., 2008) and higher rates of smoking related diseases such as Chronic Obstructive Pulmonary Disease (COPD) (Hsu et al., 2013). Poorer lung function compared to the general population has also been reported (Filik et al., 2006). Obstructive sleep apnoea (OSA) was also found to be more common in individuals with schizophrenia compared to the general population (Naqvi et al., 2014) and there is also evidence of poorer outcomes for individuals with schizophrenia who develop pneumonia (Chen et al., 2011). Evidence for increased rates of osteoporosis (Howard et al., 2007) and fractures (Stubbs et al., 2015) for individuals with schizophrenia have also been reported.

Dental problems too have been reported to be more prevalent- with significantly more young individuals with schizophrenia being edentate compared to the general population (McGreadie et al., 2004). Skin disorders: particularly dermatitis and fungal infections are also more prevalent in individuals with schizophrenia (Wu et al., 2014). Sexual dysfunction (Schottle et al., 2009), rates of sexually transmitted infections (STIs) in part due to "risky" sexual behaviour (Carey et al., 2004) and obstetric complications during pregnancy (Leucht et al., 2007) were also more common in individuals with schizophrenia compared to the general population.

Despite high rates of obesity and other risk factors which may be associated with increased rates of cancer- such as low energy expenditure (Fair and Montgomery, 2009), the evidence for increased rates of cancer in individuals with schizophrenia was mixed- with some studies reporting increased rates (Hippisley-Cox et al., 2007: Lichtermann et al., 2001) and others reporting lower rates (Barak et al., 2005: Grinshpoon et al., 2005). A meta-analysis of incidence of cancer by Catts and colleagues (2008), reported that pooled overall rates of cancer incidence were not significantly increased in individuals with schizophrenia compared to controls (Standardised Incidence Rate (SIR) 1.05 95% CI 0.95-1.15). They also found that although incidence of lung cancer was increased, when adjusted for smoking there was no difference in incidence rates. This study also reported that the incidence of several cancers unrelated to smoking was reduced in individuals with schizophrenia (Catts et al., 2008).

1.2.2 Gaps in the evidence for increased physical comorbidity in Schizophrenia:

Although there are a number of studies detailed above, which investigate the prevalence of certain chronic diseases in individuals with schizophrenia compared to the general population, these studies are frequently carried out in small numbers of hospitalised individuals in countries outside of Europe for example in Canada (Cohn et al., 2004; Curkendall et al., 2004) and the US (Gutpa et al., 1997). Therefore their findings are limited in terms of their generalisability to the wider outpatient UK population with schizophrenia.

Although there are a few studies carried out in the UK, using primary care data, they investigate rates and patterns of one or two specific comorbidities in individuals with schizophrenia. To date there have been no studies which have systematically compared rates of a wide range of physical health problems in individuals with schizophrenia to the general population in Scotland. This thesis will systematically investigate the prevalence of a wide range of physical health problems (thirty-two common comorbidities) within a large Scottish cohort of individuals with schizophrenia within primary care. The effect of age, gender and socioeconomic status on physical health comorbidity will also be considered. This thesis will therefore add to the gaps in understanding of the patterns of physical health comorbidity in individuals with schizophrenia.

1.2.3 **Evidence for increased physical comorbidity in Bipolar Disorder:**

As described in schizophrenia, a number of conditions associated with cardiovascular disease were also increased in individuals with bipolar disorder. In particular rates of obesity were increased 1.2-1.7 fold (Goldstien et al.,2011) and rates of diabetes were increased three fold (Calkin et al., 2013). Rates of metabolic syndrome were also increased compared to the general population (OR 1.98 95% CI 1.74-2.25) (Vancampfort et al., 2013). This relationship appeared to be bi-directional, where individuals with bipolar disorder often displayed poor choices in terms of healthy living- with low rates of exercise, high calorie diets and subsequent increased risk of type II diabetes and obesity (Kilbourne et al., 2007). However there was also evidence that specific cardiometabolic conditions (such as obesity) predisposed to the development of depressive symptoms (Vogelzangs et al., 2010) and were associated with longer and more severe episodes of mood disorder and shorter times to illness recurrence (Kemp et al., 2014).

The findings regarding risk of myocardial infarction (MI) in individuals with bipolar disorder was mixed. With some finding increased risk of MI in individuals with a history of a manic or hypomanic episode (OR 2.97 95% CI: 1.40 - 6.34) (Ramsey et al., 2010), and others finding no evidence for a significant increase in the risk of MI for individuals with bipolar disorder compared to controls: relative risk (RR): 1.09 95% CI 0.96-1.24 (Preito et al., 2014). However problems with heterogeneity in study methodology has been noted. For risk of stroke, there was some evidence to suggest that in individuals with bipolar disorder the risk is significantly increased compared to controls (RR 1.74 95% CI 1.29-2.35) (Preito et al., 2014). However again studies in this area are largely limited by methodological heterogeneity.

In addition to cardiometabolic disease, other physical health comorbidities have been reported; a study by Crump and colleagues (2013) reported that after adjusting for age and other sociodemographic factors, individuals with bipolar disorder had increased risk of influenza or pneumonia (2.4 fold in women and 1.9 fold in men) and COPD (2.1 fold in women and 1.7 fold in men). Higher rates of thyroid disease (Krishnan, 2005), asthma (Schoepf and Heun, 2014), lower back pain (Kilbourne et al., 2004), hepatitis C (Matthews et al., 2008), renal disease and HIV (Carney et al., 2006) in individuals with bipolar disorder have also been reported. Sleep apnoea is also thought to be prevalent in individuals with bipolar I disorder (Soreca et al., 2012) and there have been studies to

suggest an association between bipolar disorder and multiple sclerosis (MS) (Kosmidis et al., 2012).

Although bipolar disorder was previously thought to have a more benign course than schizophrenia (Kraepelin, 1918), one small study of 192 inpatients with schizophrenia and 97 inpatients with bipolar disorder reported that individuals with bipolar disorder had both more somatic (67.1% vs. 50.6%) and more psychiatric (29.9% vs. 10.9%) comorbidity than individuals with schizophrenia (Oreški et al., 2012). This is clearly worthy of further exploration given the paucity of research in this area.

1.2.4 Gaps in the evidence for increased physical comorbidity in Bipolar Disorder:

Although there are studies available which investigate the physical health of individuals with bipolar disorder, they often focus solely on bipolar I disorder. Single physical illnesses and are also often centred on distinct patient groups, such as the elderly and inpatients, and so findings may not be widely generalisable to the general adult outpatient population. Therefore similarly to that seen in schizophrenia, there remain significant gaps in the detailed understanding of patterns and rates of physical health comorbidities in a large group of individuals with bipolar disorder compared to the general population. The impact of age, gender and socioeconomic status on rates of physical health comorbidity have also not been fully explored as to date large scale, systematic population based studies describing rates of physical health comorbidity in detail in bipolar disorder are lacking. This thesis will attempt to add to the current understanding of the patterns of physical comorbidity in bipolar disorder, by investigating rates of a range of physical health comorbidities in a large primary care dataset within Scotland.

1.2.5 Multimorbidity research within Schizophrenia and Bipolar disorder:

Multimorbidity, defined as two or more long-term conditions co-occurring in an individual, is common and is often the norm rather than the exception in individuals with long-term conditions (van den Akker et al., 1998). It is a significant and growing issue for patients, health professionals and healthcare systems worldwide. Multimorbidity was previously considered a problem of elderly populations but recent work has found this not to be the case. A study of almost 1.8 million people within 314 primary care practices in Scotland found that more people with multimorbidity were aged below 65 than were aged

above 65 (Barnett et al., 2012) and similar findings have been observed internationally (Brett et al., 2013). Socioeconomic deprivation has a strong and consistent association with multimorbidity: in the Scottish primary care study, prevalence rates of physical and mental health comorbidity were almost twice as high in the most deprived areas (11.0%) compared with the most affluent areas (5.9%) (Barnett et al., 2012). Furthermore, the onset of multimorbidity occurred up to 15 years earlier in the most deprived areas compared with the most affluent areas. Therefore multimorbidity is likely an important issue for individuals with MMI, who often live in more socioeconomic deprived areas- due to both an increased incidence of psychosis in individuals living in deprived backgrounds (Dohrewend et al., 1992) and due to the socioeconomic drift of individuals with schizophrenia (Timms, 1998).

To date only a handful of studies have investigated the burden of multimorbidity in individuals with MMI. One such study investigated rates of medical comorbidity in individuals with schizophrenia and alcohol dependence (Batki et al., 2009) and found that the average number of medical diagnoses in the cohort was 2.9. A further study by Tsan and colleagues (2012) investigating mortality and guideline concordant care for veterans with schizophrenia reported that on average, four additional chronic diseases were recorded for veterans with schizophrenia. Using data from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Chwastiak and colleagues (2006) reported that 9% of individuals had four or more medical conditions. While all three studies have reported that rates of multimorbidity are increased: the groups included in these studies may not be representative of the wider outpatient adult population of individuals with schizophrenia.

For bipolar disorder, even less work exploring rates and patterns of multimorbidity has been undertaken: one study by Carney and colleagues (2006) reported that individuals with bipolar I disorder were significantly more likely to have medical comorbidity, including three or more chronic conditions compared to controls (41% vs. 12%, p<0.001). This was a retrospective study using claims data from 3,357 individuals and so generalisability may be limited.

1.2.6 **Gaps in multimorbidity research within Schizophrenia and Bipolar disorder:**

Although some preliminary work as outlined above has been undertaken, rates of multimorbidity in individuals with MMI compared to individuals without MMI have been poorly described throughout the literature. For individuals with schizophrenia, multimorbidity studies have been in individuals with comorbid alcohol dependence, in veterans and in individuals enrolled in the CATIE trial. The findings reported for these specific sub-populations may not be generalisable to the wider UK outpatient population. For individuals with bipolar disorder, only one, retrospective study has been undertaken and again generalisability may be limited. The role of age, gender and socioeconomic status in multimorbidity has also not been fully explored. Clearly further work detailing rates of multimorbidity in both individuals with bipolar disorder and schizophrenia is important. This thesis therefore aims to describe both the patterns of multimorbidity in individuals with schizophrenia and bipolar disorder in more detail and aims to investigate the role of age, gender and socioeconomic status on these patterns.

1.3 Evidence for potential inequalities in physical healthcare in individuals with Major Mental Illness (MMI):

There are many potential reasons for the adverse physical health outcomes experienced by individuals with MMI. For example it is recognised that these individuals are more likely than the wider population to lead unhealthy, physically inactive lifestyles (Faulkner et al., 2006), have poor diets in terms of high levels of fat intake (McGreadie, 2003), high rates of smoking (Myles et al., 2012) and elevated rates of alcohol misuse. The side effects of psychotropic medications are also associated with significant increased risks of physical health problems: such as obesity (O'Donoghue et al., 2013), type II diabetes (Cassidy et al., 1999) and metabolic syndrome (Correll et al., 2008). However there is also increasing evidence to suggest that unequal access to healthcare provision, plays an important role in this health inequality.

1.3.1 **Evidence for the potential inequalities in physical health investigations, treatments, prescribing and outcomes in individuals with Major Mental Illness (MMI):**

This potential health inequality has been reported across a wide range of chronic physical health problems and in both primary and secondary care. For example, while rates of

cardiometabolic risk factors are higher in individuals with MMI compared to the general population, there is evidence that individuals with MMI do not receive the same level of guideline consistent treatment. In a study by Kisely and colleagues (2009) of 49,248 admissions for ischaemic heart disease (IHD), individuals with a history of psychosis, despite experiencing a higher one year mortality rate, had lower rates of coronary artery bypass grafting (CABG) (adjusted odds ratio (OR) 0.35 95% CI 0.25-0.48) and lower rates of prescription of beta blockers and statins (adjusted OR 0.82 95% CI 0.71-0.95 and adjusted OR 0.51 95% CI 0.41-0.63). This increased mortality post myocardial infarction (MI) for individuals with schizophrenia has also been reported by Boden and colleagues, where the 30-day mortality OR was 2.58 95% CI 1.88-3.54 and 1-year mortality was OR 2.55 95% CI 1.98-3.29 when compared to individuals without MMI (Boden et al., 2015) and has been replicated in Canada (Kurdyak et al., 2012). A similar pattern was also seen for admission for strokes, where individuals with a history of psychosis were less likely to receive cerebrovascular arteriography or warfarin prescription (Kisely et al., 2009).

For individuals with MMI and diabetes there is evidence of poorer adherence to HbA_{1c} testing (OR 1.24 95% CI 1.22-1.27), Low Density Lipoprotein (LDL) testing (OR 1.25 95% CI 1.22-1.27) and retinal examination (OR 1.05 95% CI 1.03-1.07), with subsequent poorer glycaemic control (defined as $HbA_{1c} \geq 9.5\%$: OR 1.32 95% CI 1.30-1.35) and poorer lipid control (defined as LDL ≥ 3.37 mmoll^{-1} : OR 1.17 95% CI 1.15-1.20). For older individuals with MMI inequality in access to healthcare provision has also been reported; in individuals with MMI and heart failure, there was evidence of lower rates of Left Ventricle Ejection Fraction (LVEF) evaluation (53.0% vs. 47.3%, p<0.001), higher ORs for one year all cause readmission (OR 1.30 95% CI 1.21-1.39) and higher one year mortality (OR 1.20 95% CI 1.12-1.28) (Rathore et al., 2008).

In Ontario, Canada where over 1.3 million residents aged 65 or over, had their prescriptions reviewed, it was reported that individuals with psychosis were less likely to receive medical treatment for arthritis (OR 0.59 95% CI 0.57-0.62, p<0.001) and for individuals with psychosis and emphysema, rates of lipid lowering medication were also significantly lower compared to individuals with emphysema alone (OR 0.69 95% CI 0.67-0.72, p<0.001) (Redelmeier et al., 1998). The authors concluded that the differences in prescribing patterns were evidence for the under treatment of unrelated chronic physical illnesses in individuals with MMI. Similarly in the UK, Mitchell and colleagues (2012) reported that in individuals with severe mental illness the adjusted odds ratio (OR) for equitable prescription was 0.74 (95% CI 0.63–0.86), with lower than expected

prescriptions for angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs), beta-blockers and statins (Mitchell et al., 2012).

1.3.2 Evidence for the potential inequalities in health promotion and screening in individuals with Major Mental Illness (MMI):

Given the increased burden of physical illness and adverse outcomes seen in individuals with MMI, preventative healthcare and screening along with effective targeted health promotion, which addresses the environmental, behavioural and iatrogenic risks to health in individuals with MMI, may be an effective strategy in promoting the health and wellbeing of individuals with MMI.

In terms of preventative healthcare and screening, it has been reported that women with any mental disorder are significantly less likely to receive mammography compared to women without a mental disorder. Carney and Jones (2006) reported that the severity of mental illness (where high severity was defined as psychiatric hospitalisation and a dual diagnosis of substance misuse disorder and a non-substance misuse disorder and moderate severity was defined as either psychiatric hospitalisation or a dual diagnosis) contributed to the reduced rates of screening. They found that the OR for mammography was 0.38 (95% CI 0.33-0.43) in women with high severity mental illness and 0.62 (95% CI 0.59-0.66) in women with moderate severity mental illness. In another study by Xiong and colleagues (2008), which reviewed screening for breast, cervical, prostate and colorectal cancer: lifetime screening for cervical cancer was found to be higher than for breast, prostate and colorectal cancers. However the study concluded that "routine, timely cancer screening was low, especially for colorectal cancer in individuals with mental illness" (Xiong et al., 2008). In a study in Switzerland, there was also evidence that individuals with schizophrenia received less preventative care than individuals without schizophrenia (Streit et al., 2014). These studies all provide evidence of potential inequalities in healthcare screening for individuals with MMI.

Studies investigating the effectiveness of life-style interventions to promote the physical health of individuals with MMI are limited. Large, population cohort intervention studies, often exclude individuals with MMI and so the evidence base is limited. In the UK, the Department of Health, has set the improvement of the physical health of individuals with MMI as a national priority and as such the UK government has encouraged the NHS and local authorities to develop health promotion programmes (HPPs). However when these

have been evaluated, there is some evidence to suggest that they are unequally distributed and may set admission conditions which actually impede access (O'Brien et al., 2014). Therefore more work in this area is required to improve equity and access to these interventions.

There is evidence to suggest that lifestyle interventions are effective when smaller studies specifically targeting individuals with MMI are reviewed. For example one study by McCreadie and colleagues (2005) investigated the impact of giving free fruit and vegetables, with and without instruction, to a cohort of individuals with schizophrenia living in Scotland. They found that although individuals who were given free fruit and vegetables consumed more fruit and vegetables immediately after the intervention, their consumption fell back to pre-intervention levels 12 months after the intervention stopped (McGreadie et al., 2005).Studies investigating the effect of exercise intervention on weight in the form of: organised cardiovascular workouts (Scheewe et al., 2013), walking (Beebe et al., 2005; Methapatara et al., 2011), stationary cycles (Poulin et al., 2007) and football practice (Battaglia et al., 2013) have all been undertaken. All five studies, showed that exercise had a weight reducing effect as well as beneficial effects on physical health. Two further studies which investigated the effect of combination exercise (walking) and nutritional advice; reported weight loss in the intervention group compared to the control group (Jean-Baptiste et al., 2007; Direck and Ucok, 2008). Other studies using mixed interventions (such as diet, exercise and behavioural interventions) to reduce obesity in individuals with schizophrenia, found that all interventions were associated with weight loss and improved physical health parameters (Hjorth et al., 2014). A meta-analysis by Gaughran and Lally (2013), also reported that non pharmacological interventions (NPIs) were effective in reducing antipsychotic associated weight (-3.2kg 95% CI -4.03 to -2.21, p<0.0001 I^2= 42%) and BMI gain (-0.94 kg/m^2 95% CI -1.45 to -0.43, p=0.0003, I^2= 75%), but these effects were restricted to outpatients only (Gaughran and Lally, 2013).

For individuals with bipolar disorder, interventions to target obesity have also been shown to be effective. Daumit and colleagues (2013), reported that a behavioural weight-loss intervention significantly reduced weight over a period of 18 months in overweight and obese adults with serious mental illness (of which 19.4% of the intervention group had a diagnosis of bipolar disorder) (Daumit et al., 2013). These studies all clearly show that health promotion interventions can be effective in individuals with schizophrenia and bipolar disorder. However more has to be done to ensure that these individuals are given

equal opportunity to engage in health promotion and screening interventions in both an inpatient and outpatient setting.

Cigarette smoking is the leading cause of preventable poor health and premature death worldwide (Koplan and MacKay, 2012) and in Scotland alone, tobacco use is associated with over 13,000 deaths and around 56,000 hospital admissions every year (Scot PHO, 2011). Although it is recognised that the prevalence of smoking in the general population in Scotland has decreased over time (from 30.7% in 1999 to 22.9% in 2012) (The Scottish Government,2013), reducing smoking further remains a national public health priority.

It is estimated that 70% of individuals with schizophrenia and 45% of individuals with bipolar disorder smoke compared to 20% of the general population (Myles et al., 2012) and in England, a third of all cigarettes smoked, are by individuals with a mental disorder (Royal College of Psychiatrists Council Report CR178, 2013). It is also recognised that individuals with MMI are likely to smoke more cigarettes and extract more nicotine from cigarettes compared to the general population (Olincy et al., 1997). While rates of smoking have declined in the general population, rates of smoking in individuals with mental health disorders have remained static (Royal College of Psychiatrists Council Report CR178, 2013). This divergence in smoking rates between individuals with MMI and individuals without MMI is of great concern due to the negative health consequences associated with smoking.

Potential reasons for the high rates of smoking in individuals with MMI are complex and multifactorial. It has been argued that smoking has been part of psychiatry's culture. Clinicians have historically, smoked with patients (Dickerson et al., 2004), used cigarettes to reduce agitation (Lawn, 2004) and encourage treatment compliance (Wye et al., 2009). This may have partly contributed to the high smoking rates. Psychiatric patients too have not been afforded equal protection from tobacco exposure. For example while smoking within public places was banned in Scotland on the 26th of March 2006 (Smoking, Health and Social Care (Scotland) Act 2005), psychiatric units were exempt from this. This exemption for psychiatric units also occurred in the US (Brown-Johnson et al., 2014). However smoke-free psychiatric units, may act as an opportunity for discussion regarding initiation of smoking cessation therapy (Schuck et al., 2014) and this may occur when the smoking ban is extended to include psychiatric units from the 1st of October 2015 in Scotland.

Nicotine replacement therapy (NRT) is recognised as being effective in promoting smoking cessation. A meta-analysis by Stead and colleagues (2012) reported that the relative risk (RR) of abstinence using any form of NRT (including gum, lozenges, patches, inhaler and nasal spray) was 1.60 (95% CI 1.53-1.68) (Stead et al., 2012). For individuals with MMI, it has been recognised that social influences such as others' approval of treatment significantly predicted use of smoking cessation medication (Aschbrenner et al., 2015). Given that other anti-smoking medications such as varenicline are not recommended in individuals with a history of mental illness, NRT may be an especially important and effective tool in promoting smoking cessation in individuals with MMI.

One recent meta-analysis of seven studies, looking at rates of smoking cessation advice in individuals with and without a mental illness reported that there was no significance difference in rates of advice given (relative risk (RR) 1.02 95% CI 0.94-1.11) (Mitchell et al., 2015). The same was also true for individuals with schizophrenia (RR 1.09 95% CI 0.68-1.70) and bipolar disorder (RR 1.14 95% CI 0.85-1.50) (Mitchell et al., 2015). However given the disparities in prescribing of physical health medications for individuals with MMI (Mitchell et al., 2012 and Redelmeier et al., 1998) further investigation reviewing rates of prescription of NRT within primary care would be of importance given the limited evidence in this area.

Ecigarettes, too are becoming increasingly used to aid smoking cessation. While the long term health risks associated with them remain unclear, there is some evidence to suggest that they appear to be "equally effective, safe, and acceptable for people with and without mental illness" (O'Brien et al., 2015). Moreover for individuals with mental illness, Ecigarettes may be as effective and safe as patches, yet more acceptable, and associated with greater smoking reduction (O'Brien et al., 2015). Clearly further investigation into strategies to reduce the high rates of smoking in individuals with MMI is of importance.

While there is evidence for potential inequalities in healthcare in terms of: investigations, treatments, prescribing, outcomes, health promotion and screening, for individuals with MMI, reasons for the potential inequalities reported, require further consideration.

1.3.3 Evidence for the potential reasons for the inequalities in healthcare provision reported for individuals with Major Mental Illness (MMI):

Barriers to healthcare are generally considered at a patient, provider and service level. Possible barriers to healthcare for individuals with MMI and potential reasons for the inequalities seen can therefore be considered in this way.

1.3.3.1 Potential patient reasons for inequalities in healthcare provision:

A recent review by Lawrence and Kisely (2010) identified some potential patient factors which may contribute to difficulties in accessing healthcare for individuals with MMI. These included; cognitive impairment associated with the mental disorder, social isolation, lack of family support, suspiciousness or fear of seeking advice, self-neglect, poor motivation (potentially due to the negative features of a psychotic illness), socioeconomic factors and difficulties in communicating health needs. These issues are all particularly pertinent when considering Zola's help seeking model (Zola, 1973).

While there are difficulties in individuals with MMI accessing healthcare, there is also evidence to suggest that they when they do access healthcare, they are less compliant with the medical care they receive (Hennekens, 2007). This can subsequently result in premature discharge from outpatient clinics and loss to follow up. For individuals receiving care, consent issues, particularly for more complex, high risk procedures may be particularly relevant; as at times, assessing capacity in individuals with MMI can be challenging, especially when the individual refuses treatment or care while reporting residual psychotic symptoms. These factors likely contribute to the inequalities in healthcare provision that are reported.

1.3.3.2 Potential provider reasons for inequalities in healthcare provision:

Potential provider reasons for inequalities in healthcare provision are complex and multi-factorial and may include stigmatisation of individuals with mental illness. While negative attitudes to mental illness, with particular negative attitudes to schizophrenia, occur worldwide (Thornicroft et al., 2009), and are likely affected by cultural and historical factors (Fabrega Jr, 1991), stigmatisation may still play an important role in the potential reasons for inequalities in healthcare for individuals with MMI within the UK health service (Jones et al., 2008). Stigmatisation is a problem that has been reported worldwide. In a recent cross-sectional survey of 777 individuals with schizophrenia from 27 countries,

17% reported experiencing discrimination when treated for physical health problems (Harangozo et al., 2013), with higher rates in post-communist countries. Indeed stigmatisation as a barrier to healthcare has been reported in the US, Australia and The Netherlands (Happell et al., 2012).

It is also recognised that time and resource constraints play an important role in healthcare provision. For General Practioners (GPs), it is recognised that over recent years, the complexity of their consultations has increased (Freeman et al., 2002) and while in the UK the length of the average consultation has also increased: from 8.4 minutes in 1992, to 11.7 minutes in 2006/2007 (GP Workload Survey, 2007), the time to fully assess the physical health of an individual with MMI may still be impossible within this tight consultation framework. GPs, who may be inexperienced in mental health issues, may also feel uncomfortable due to a perceived inadequacy in expertise, and so this too can inadvertently result in inequalities in provision of healthcare.

The issue of diagnostic over-shadowing, whereby physical health complaints are attributed as psychosomatic symptoms (van Nieuwenhuizen et al., 2013) is also important. For example, individuals with MMI presenting with palpitations, may have their symptoms put down to anxiety rather than an arrhythmia and so may consequently miss out on appropriate healthcare and treatment. These factors all contribute to potential provider causes of the inequalities in healthcare provision experienced by individuals with MMI.

1.3.3.3 Potential system reasons for inequalities in healthcare provision:

System issues undoubtedly contribute to the inequalities in healthcare provision for individuals with MMI. Current healthcare systems throughout the world (including the UK) are predominantly organised around a 'single-disease' approach to both physical and mental disorder. Given that most individuals with long-term conditions are likely to have more than one (Barnett et al., 2012) this can lead to fragmented and disorganised care. The current separation of physical and mental healthcare facilities, can lead to a lack of clarity regarding who is responsible for the physical healthcare of individuals with MMI- as often psychiatrists are reluctant to and inadequately resourced to take responsibility for this, while GPs can feel overwhelmed.

The separation between mental and physical healthcare as a barrier to good physical healthcare of individuals with MMI has been reported worldwide in countries such as the

US, Australia and the Netherlands (Happell et al., 2012). Current under-resourcing of mental healthcare in particular, also provides little opportunity for specialists to focus on care outside their core speciality (Druss, 2007), and as a result, the physical healthcare may be delegated back to primary care.

For psychiatric inpatients the fragmentation of physical and mental healthcare has important costs both for the patient and for the health service. In a recent study by Lally and colleagues (2015) over the course of a full year, of 4676 psychiatric inpatients, 16.0% were admitted to a general hospital and 18.0% attended Accident and Emergency (A&E) while an inpatient in psychiatry. Therefore simultaneously occupying beds in both the general and psychiatric hospitals for a total of approximately 5163 bed days at a cost of £2.4 million over the year (Lally et al., 2015). While liaison psychiatrists review, assess and treat the mental health needs of individuals with physical health problems, there is a potential gap in the assessment and treatment of the physical health needs for people with MMI (Doherty and Gaughran, 2014).

The challenge therefore is to gather evidence for new integrated innovations in service organisation and delivery in order to minimise inequalities in healthcare driven by limitations in service design and improve cost.

1.3.4 Gaps in the evidence for potential inequalities in physical healthcare in individuals with Major Mental Illness (MMI):

While there have been studies detailing prescribing inequalities in individuals with MMI work in this field is limited. Redelmeier and colleagues (1998) looked at older adults (>65) and Mitchell and colleagues (2012), undertook a meta-analysis of prescribing patterns in individuals with and without severe mental illness in studies with high heterogeneity (I^2=97.2). Therefore further investigation of possible inequalities in prescribing for comorbid physical health problems within a primary care setting in Scotland would be of interest and of clinical relevance. This thesis therefore aims to examine in more detail possible inequalities in prescribing for comorbid chronic physical health problems using a large primary care data set. The chronic physical health problems investigated will include hypertension and coronary heart disease (CHD) and the drugs compared will include anti-hypertensives, statins and anti-platelets.

Smoking cessation programs are recognised as being highly cost effective (Warner, 1997) and given the high smoking rates in MMI combined with the fact that smokers with mental

disorders are as likely as those without mental disorders to want to quit (Royal College of Psychiatrists Council Report CR178, 2013), targeting individuals with mental illness, is potentially a good way to reach smokers and promote smoking cessation. Although there is evidence to suggest that smoking cessation interventions are effective in individuals with schizophrenia (Stubbs et al., 2015; Peckham et al., 2015), little work in this area has been carried out. To date there has been no investigation of the rates of recording of smoking cessation advice and NRT prescribing in a large cohort of individuals with MMI in primary care in Scotland. Given the importance of smoking cessation as a public health intervention, further investigation in this area is warranted. This thesis will attempt to explore, in detail the recording of smoking cessation advice and the prescribing equity of NRT within primary care in Scotland.

Despite evidence that lifestyle interventions appear to be effective in promoting weight loss in MMI, it is unclear to what extent health promotion and weight monitoring for individuals with MMI is occurring routinely in UK primary care. One study, compared recording of Body Mass Index (BMI), blood pressure (BP), blood glucose and cholesterol in individuals with severe mental illness to individuals with diabetes using incentivised Quality and Outcome Framework (QOF) Data from England. They found that screening was "higher among patients with diabetes than among those with severe mental illness (97.3% versus 74.7%, $p<0.001$)" (Mitchell and Hardy, 2013). Thus suggesting evidence of inequalities in incentivised healthcare. However this study used only QOF data from England. Therefore further examination of incentivised QOF data particularly in Scotland (as well as elsewhere in the UK) would be helpful to determine if this possible inequality is consistent both across the UK and compared to other chronic diseases (other than diabetes). This thesis will explore potential inequalities in health promotion and screening by investigating the rates of recording of BMI and Blood Pressure (BP) in individuals with MMI compared to individuals with other chronic diseases (namely diabetes and chronic kidney disease (CKD)), in primary care using incentivised QOF data from the whole of the UK.

1.4 Evidence of Premature mortality in Major Mental Illness (MMI):

1.4.1 Markers of Premature Mortality:

To date the literature, which has investigated premature mortality in Major Mental Illnesses (MMI), has used a number of different measurements of premature mortality. The most commonly used measurements include mortality rate ratios (MMRs), hazard ratios (HRs), reduction in life expectancy, life expectancy at 20 years, years of potential life lost (YPLL) and average age at death. Each measurement used has its own advantages and disadvantages. Given the variety of measures of mortality used throughout the literature, interpretation and synthesis of large quantities of data has been limited. This restricts generalisability of results and limits interpretation.

1.4.1.1 Mortality Rate Ratios (MRR):

Mortality Rate Ratios (MRR) are a useful tool to quantify the increase in mortality experienced by individuals with MMI compared to the general population. The MRR is calculated by dividing the mortality rate in the group of interest by the mortality rate in a comparison population. For example the mortality rate in a cohort of individuals with schizophrenia could be divided by the mortality rate of a group of individuals living in the general population without schizophrenia to determine the MRR associated with schizophrenia. By doing this mortality rates for different population subgroups and different causes of death can be calculated; for example for males and females, for certain ages for example those under 25, or aged 25-24 and for certain causes of death for example death due to suicide, cardiovascular deaths etc. Most commonly within MRR, Standardised Mortality Ratios (SMR) are used.

SMR is a ratio between the observed number of deaths in a study population and the number of deaths which would be expected in the same population, based on the age and sex specific rates in a standard population with the same age and sex distribution as the study population (Everitt et al., 2010). If the ratio of the observed: expected deaths is greater than 1.0, there is said to be "excess deaths" in the study population. The ratio can be expressed as a percentage by multiplying by 100.

There are however a number of limitations associated with the use of MRR and SMR; firstly given the low rate of death in younger age groups in the general population, the

MRR and SMR between the group of interest and the general population are often dramatically elevated particularly at younger ages and this difference decreases as age increases. This phenomenon, known as "effect modification by age", is important to consider when calculating and interpreting MRR and SMR especially in younger age groups. This effect also needs to be carefully considered when comparing MRR and SMR across groups and between different countries, as the age distribution of the populations need to be carefully considered to avoid biasing results.

1.4.1.2 Reduction in life expectancy and Years of Potential Life Lost (YLL):

Another useful measurement tool, to quantify the increase in mortality experienced by individuals with MMI is reduction in life expectancy. Reduction in life expectancy is a similar measurement tool to Years of Potential Life Lost (YLL) (Health Knowledge Research Methods, 2009). Reduction in life expectancy is the difference in the number of years that an individual with the condition of interest lives compared to an individual living in the general population. Therefore if an individual with schizophrenia dies at 48 years of age and the expected age of death in the population is 78, there is a reduction in life expectancy of 30 years. Years of Potential Life Lost (YLL), is the sum of the gap between all premature deaths in the cohort of interest and the average life expectancy of the general population. Both measures give greater weight to deaths at younger age and a lower weight to deaths at an older age, and so are helpful in raising awareness of the common causes of death in younger people. A further advantage of these tools is that the increase in mortality represented by a reduction in life expectancy is a clear and understandable measure of the magnitude of excess mortality.

YLL and reduction in life expectancy also allows comparisons between different populations (for example individuals with schizophrenia or bipolar disorder) and comparisons of causes of death to be made: for example YLL and reduction in life expectancy associated with cardiovascular disease, suicide, cancer etc. within a well-defined population. Both reduction in life expectancy and YLL are used in public health planning to compare the relative importance of different causes of death and so can be used to identify priorities for prevention and intervention. This will then help aid distribution and allocation of healthcare resources.

1.4.1.3 **Healthy Life Expectancy (HALE):**

Healthy life expectancy (HALE) is the number of years an individual is expected to live in "full health" and therefore takes into account the years lived in less than full health due to disease and/or injury. It is recognised as an important measure of health due to its ability "to capture fatal and non-fatal health outcomes in a summary measure of average levels of population health" (WHO Health Status Statistics, 2004). Healthy Life Expectancy at birth adds up expectation of life for different health states adjusted for severity and is therefore sensitive to changes over time and differences between countries. This measure, although used by the WHO in mortality statistics, is not routinely used in the literature surrounding premature mortality in MMI.

1.4.1.4 **Hazard Ratios (HRs):**

Hazard Ratios (HRs) are another measurement of mortality that are often used to compare mortality between groups. It is defined as the hazard or chance of an event occurring in the group of interest compared to the hazard or chance of an event occurring in another (control) group. For example the chance of death in a group of individuals with bipolar disorder compared to a group of individuals without bipolar disorder. Hazard ratios are distinct from the relative risk ratio which is a measure of the proportion of events (for example deaths) which have occurred in a group (for example individuals with bipolar disorder) expressed as a ratio of the proportion of events (deaths) occurring in the control group (for example individuals without bipolar disorder). Hazard ratios allow the risk of an event occurrence between two groups within a selected timeframe to be compared and so is a useful tool to measure mortality. One disadvantage associated with this measurement is that the time until an event (such as death) is not detailed. In studies, where there is a long lag period between exposure and outcome measure (for example death), care must be taken to ensure that the timeframe is long enough to give a true measure of the increased risk. This "sleeper effect" (Hackim, 1987) can be more readily captured if the study is longitudinal in design.

1.4.1.5 **Life Expectancy:**

Life expectancy is the calculated expected duration of survival using statistical models and life tables and is often reported in the medical literature as a measure of mortality. It can be calculated at any age, by gender and by country. Life expectancy may be calculated from birth (as is commonly reported) or it can be calculated from any age, for example at age

20. Life expectancy at age 20 is used to compare life expectancy in individuals with MMI to that of individuals without MMI. The life expectancy calculated is an average and so care in its interpretation is required. For example in countries, where there is high infant and child mortality, average life expectancy at birth may be low (for example life expectancy at birth may be 40), however survival over the age of 60, may occur in the population, especially if survival of the early hazards occur. Therefore interpretation of life expectancy at birth should be taken within a wider context and often other measurements such as infant mortality rates are required to help contextualise the life expectancy calculation.

1.4.1.6 **Average age at Death:**

Average age at death is another commonly used public health statistic to compare mortality across populations and between genders. It is readily understood by clinicians and is helpful in showing disparities between cohorts. Patterns in average age of death over time can also be compared relatively easily. This measure has been used to compare average age of death in individuals with MMI to the general population.

1.4.2 **Work to date in Schizophrenia describing premature mortality:**

It is now largely well recognised that individuals with schizophrenia have increased standardised mortality rates (SMR) and reduced life expectancy compared to the general population and that the excess in mortality reported cannot be explained by increased suicide rate alone. This excess mortality has been reported throughout the literature in many different countries (Hoang et al., 2011; Wahlbeck et al., 2011; Laursen et al., 2011; Crump et al., 2013).

For example, Harris and Barraclough, (1998), reported an overall SMR of 1.6 (95% CI 1.5-1.6), using data from twenty papers on a population of almost 36,000 from nine countries. Black, (1998) using data from the Iowa Record linking study reported an overall SMR of 2.7 and a SMR of 1.8 for natural deaths for individuals with schizophrenia. In Australia the SMR for all psychotic disorders was calculated at 5.5 (Saha and Whiteford, 2013) and Mortensen and Juel, (1993) reported that the increase in SMR for both men and women with schizophrenia could be seen, across the lifespan until the age of 80 in women and 84 in men. In a landmark study by Laursen and colleagues (2007) which reported Mortality Rate Ratios, by age group and ICD 10 diagnosis for 1,480,608 deaths from a cohort of

5,558,959 individuals, an elevated MRR across both genders and all age groups for individuals with schizophrenia was found (Laursen et al., 2007).

A further study by Fors and colleagues, (2007) in Uppsala, Sweden, reported that the 10 year mortality rate for individuals with schizophrenia was higher than for the general population (23.0% vs. 11.2%) (Fors et al., 2007). A recent meta-analysis by Walker and colleagues, (2015) (using data from 65 studies) reported that for all-cause mortality, the pooled relative risk (RR) among individuals with psychoses was 2.54 (95% CI 2.35-2.75) (Walker et al., 2015).

Studies measuring premature mortality using reduction in life expectancy calculations have generally found that on average, men with schizophrenia die 20 years earlier and women die 15 years earlier than the general population (Laursen et al., 2013). A study by Morden and colleagues, (2012) which described years of potential life lost (YLL) due to cardiovascular disease found that in 2007, 14.0 years were lost due to cardiometabolic disease in individuals without Severe Mental Illness (SMI) while in individuals with SMI, 15.4 years were lost due to cardiometabolic disease (Morden et al., 2012). Studies using hazard ratios as a measure of mortality have also reinforced the premature mortality in individuals with MMI. One such study by Chen and colleagues, (2010) found that for individuals with schizophrenia, the adjusted risks of dying during the 6 year follow up were 4.6 times higher than that for the control group (Chen et al., 2010).

In terms of the causes of the premature mortality it is recognised that much of the excess mortality is due to cardiovascular disease, unnatural deaths (such as suicide), respiratory disease and cancers (Bushe et al., 2010). However it is really only in the last ten years that a heightened awareness of the contribution of the "natural" causes of death to the premature mortality has been recognised. To date, studies which examine premature mortality by cause are limited due to a combination of small sample size, differing lengths of follow up and differences in age of the cohorts described.

Nevertheless there is a growing body of evidence to suggest that cardiovascular disease (CVD) is an important cause of premature mortality in individuals with schizophrenia. Osborn and colleagues, (2007) reported that in the UK, CVD mortality was elevated almost four fold (HR 3.61) in individuals aged 18-49 years with a doubling of risk in those aged 50-75 (HR 1.96) (Osborn et al., 2007). The finding of premature cardiovascular mortality, has also been reported by Mortensen and Juel, (1993) who reported a SMR for

CVD of 1.69 in young men (modal age of diagnosis was 25-29 years with a 8 year follow up period) and Kiviniemi and colleagues, (2010) who reported a SMR of about 16 for CVD mortality of in individuals aged 20-24 years (Kiviniemi et al., 2010). These studies not only reinforce the increased cardiovascular risk and subsequent mortality in individuals with schizophrenia, but suggest that it may have a premature onset.

1.4.3 Gaps in the work to date describing premature mortality in Schizophrenia:

Despite an increased awareness of the premature mortality from "natural" causes, there remain significant gaps in not only the underlying causes of "natural" deaths but also the deeper understanding of the impact of age, gender and socioeconomic status on cause and rate of death. For example the reported contribution of death from cancer to the increased mortality experienced by individuals with schizophrenia is unclear. Data from Australia (Lawrence et al., 2001) and Denmark (Dalton et al., 2008) has reported an increase in cancer deaths in individuals with MMI compared to the general population, while work from Kredentser and colleagues, (2014) reported that although the mortality rate for individuals with schizophrenia was double that of the population (20.0% vs. 9.4%) overall cancer deaths were similar (28.6 vs. 27.3 per 1,000, p=0.42). (Kredentser et al., 2014)

Other causes of death in individuals with MMI such as: respiratory disease (Capasso et al., 2008), cerebrovascular disease (Mortensen and Juel, 1993; Dean and Thuras, 2009) and "other natural causes" (Brown et al., 2000; Chong et al., 2009) have been recognised as being increased, but the number of studies in which they are described to a significant extent are limited. Therefore detailed investigation into specific causes of deaths in individuals with schizophrenia is warranted to further aid the understanding of the elevated mortality reported in these individuals. This thesis will attempt to address these issues.

In terms of understanding the effect of age on cause of death in schizophrenia, little work has assessed different causes of mortality across the life-span. While suicide has been recognised as a major contributor to excess mortality in certain groups of individuals with schizophrenia on a population level (for example, young males) (Gunnell and Middleton, 2003), there is limited research exploring other patterns of mortality in an age-specific manner. This thesis will also attempt to explore this relationship and aim to contribute to the gaps in knowledge within this field.

The effect of socioeconomic deprivation on rate and cause of death in individuals with MMI has also not been explored in detail. While it is generally recognised that individuals from more deprived areas commonly experience more adverse outcomes and reduced life expectancy compared to individuals from more affluent areas (Hosseinpoor et al., 2012; MacIntyre and Ellaway, 2003), the impact of deprivation specifically on rate and cause of death in individuals with schizophrenia has not been examined. Given the unique mortality challenges experienced by both Glasgow and the wider Scottish population, investigation into the impact of deprivation on mortality rates in individuals with schizophrenia in a Glasgow setting is worthy of further detailed exploration. This thesis will attempt to provisionally examine this relationship.

While the evidence detailing the increased mortality associated with schizophrenia when suicide is excluded is relatively consistent, it has not been universally reported. For example Drew, (2005) in Australia, reported that although deaths due to suicide were greatly increased compared to the general population, deaths from "all cause" were only mildly increased (Drew, 2005). They highlighted the need to interpret population based mortality studies cautiously and reinforced the idea that more work in this area is required. Therefore a study of mortality in the local Scottish population which specifically addresses the impact of age and deprivation on cause and rate of death will be of significant scientific and clinical merit.

1.4.4 Work to date in Bipolar Disorder describing premature mortality:

As reported in schizophrenia, it is recognised that individuals with bipolar disorder have increased mortality compared to the general population. This finding has been described in the medical literature from as early as 1979- where SMR was noted to be elevated in individuals with unipolar or bipolar depression at 1.69 (Weeke, 1979). Most of the initial studies investigating the excess mortality associated with bipolar disorder, grouped all affective disorders together (i.e. unipolar and bipolar depression), for example in 1982 Eastwood and colleagues reported an increased SMR associated with affective disorders (1.37) (Eastwood et al., 1982) and in Denmark in 1986, an increase in SMR of 1.73 for individuals with unipolar or bipolar depression was reported (Weeke, 1986).

Later work, by Harris and Barraclough, (1998), separated unipolar and bipolar depression. Their study, a systematic review of six papers from four countries totalling 4,547

individuals with a follow up period ranging from 0-40 years, described an overall SMR for bipolar disorder for both genders of 2.02 (95% CI 1.9-2.7). They also reported that mortality from unnatural causes was nine times that of the expected mortality rate and deaths from natural causes were 1.5 times more than expected (Harris and Barraclough, 1998). A recent meta-analysis (of 19 studies) by Walker and colleagues, (2015) reported that for all-cause mortality, the pooled relative risk of mortality among individuals with bipolar disorder was 2.00 (95% CI 1.70-2.34) (Walker et al., 2015).

Tsuang and colleagues, (1980) reported that natural deaths in all individuals with bipolar disorder were increased and deaths due to cardiovascular disease were particular elevated in females with mania (Tsuang et al., 1980). This finding of increased SMR in bipolar disorder has been reproduced by Osby and colleagues, (2001) who reported a SMR of 1.9 for bipolar males and 2.1 for bipolar females for all natural causes of death (Osby et al., 2001). While Laursen and colleagues, (2007) reported a SMR of 4.5 for individuals with bipolar disorder aged under 24 (Laursen et al., 2007). Elevated hazard ratios have also been described in bipolar disorder- most notably by Chen and colleagues, (2010) who reported an adjusted hazard ratio of dying of 3.87 times that of appendectomy patients (Chen et al., 2010). Studies investigating differences in mortality using reduction in life expectancy have reported that life expectancy was reduced by approximately 10 years in men and 11 years in women with bipolar disorder (Chang et al., 2011).

More recently comparisons of rates of mortality within affective disorders have been undertaken. For example Chang and colleagues, (2012) compared mortality in bipolar depression with mortality in other types of depression (OTD). They found that bipolar depression was associated with a significantly greater risk in all-cause mortality compared to other types of depression even after controlling for demographic features and comorbid disorders (adjusted hazard ratio 1.3 95% CI 1.1-1.5). They also found that bipolar depression was associated with twice the risk of suicide and accidental death compared with other types of depression (Chang et al., 2012). This finding of increased mortality in bipolar depression compared to unipolar depression was also reported by Black, (1998) in the Iowa Record linking study. Although there is consistent evidence to suggest that mortality is significantly increased in individuals with bipolar disorder compared to both the general population and individuals with other types of depression, there remain significant gaps in our understanding of specific causes of death across the lifespan and the impact of age, gender and deprivation on rate and cause of death.

1.4.5 **Gaps in the work to date describing premature mortality in Bipolar Disorder:**

Similarly to the understanding of premature mortality in schizophrenia, there remain significant gaps in not only the underlying causes of "natural" deaths but also the deeper understanding of the impact of age, gender and socioeconomic status on cause and rate of death in individuals with bipolar disorder. In terms of specific causes of death, few large scale studies have investigated this in detail. For example Osby and colleagues, (2001) reported that SMRs for infectious diseases (3.4 and 2.4), respiratory diseases (3.1 and 3.2), cardiovascular diseases (1.9 and 2.6) and gastrointestinal diseases (2.0 and 1.9) were all increased in men and women with bipolar disorder, while SMR due to cancer was not significantly elevated (1.1 and 1.2) (Osby et al., 2001). However Kisely and colleagues, (2005) reported an increase in MRR due to cancer (1.76 and 1.50) for men and women with bipolar disorder (Kisely et al., 2005). Additionally the large scale studies investigating specific causes of death in individuals with bipolar disorder have been carried out in Scandinavia (Fors et al., 2007; Capasso et al., 2008; Crump et al., 2013; Wahlbeck et al., 2011; Laursen et al., 2007), Canada (Kredentser et al., 2014) and Australia (Saha and Whiteford, 2013; Lawrence et al., 2000) and so generalisability to the UK population may be limited.

Reports of cause of death using Scottish data are limited: one study by Sharma and Makara, (1994), of 472 individuals with bipolar disorder who were followed up retrospectively over 17 years, found that individuals with bipolar disorder had greater mortality from suicide, cardiovascular and respiratory disease than the general population (Sharma and Makara, 1994). One further study exploring mortality in a Scottish context, reported mortality for a cohort of individuals on lithium, rather than for individuals with bipolar disorder specifically (Norton and Whalley, 1984). Over 9 years for individuals on lithium, SMR was elevated at 2.83, with excess mortality attributable to suicide and cardiovascular disease. Given the limited studies to date, a detailed exploration of the specific causes and rates of death for individuals with bipolar disorder within a Scottish context will be of scientific and clinical interest. This thesis will attempt to explore this in detail.

As is seen in schizophrenia, investigation into the rate of death throughout the adult lifespan in individuals with bipolar disorder is also limited- with only one study by Laursen and colleagues, (2007), using Danish data, reporting SMR across the lifespan. To date no

studies have specifically investigated the impact of socioeconomic status on rate or cause of death in bipolar disorder. Therefore detailed understanding of how cause of death may vary by age and socioeconomic status in bipolar disorder is worthy of further investigation.

A meta-analysis by Walker and colleagues, (2015) reported higher, pooled relative risk of all-cause mortality among individuals with psychoses compared to bipolar disorder (2.54 (95% CI 2.35-2.75) vs. 2.00 (95% CI 1.70-2.34)) (Walker et al., 2015). Work directly comparing mortality in individuals with bipolar disorder and schizophrenia is limited. Further comparison of rate and cause of death between individuals with schizophrenia and bipolar disorder in a Scottish setting would be of interest, especially given the historical viewpoint that schizophrenia has a worse prognosis than bipolar disorder (Kraepelin, 1918). Consequently this thesis will attempt to address these important gaps in current understanding.

1.4.6 Recent trends in the gap in Life expectancy of individuals with MMI and the General Population:

While there is recognition of the premature mortality experienced by individuals with MMI, possibly of more concern is that recent work has suggested that the mortality gap may be getting worse. Morden and colleagues, (2012) in the United States reported that the mortality gap of individuals with schizophrenia widened from 12.8 to 15.4 years over a 7 year period (2000 to 2007) and a retrospective linked analysis of hospital admissions in England has also shown that one-year post-discharge standardised mortality ratios (SMR) for individuals with schizophrenia have increased from 1.6 (95% CI 1.5 -1.8) in 1999 to 2.2 (95% 2.0-2.4) in 2006 (Morden et al., 2012). Similar findings were reported by Dutta and colleagues, (2012), where there was an increase in SMR for circulatory disease (from 1.6 to 2.5), and respiratory disease (from 3.1 to 4.7) (Dutta et al., 2012). This increase in SMR over recent years has been replicated elsewhere by Saha and colleagues, (2007) and Hoye and colleagues, (2011) in Norway.

However an increase in the life expectancy gap has not been universally reported. Tiihonen and colleagues, (2009) reported that the gap in life expectancy between individuals with schizophrenia and the general population did not widen between 1996 (25 years), and 2006 (22·5 years) (Tiihonen et al., 2009) and Rantanen and colleagues, (2009) reported a significant reduction in mortality of individuals hospitalised for schizophrenia between 1995-1998 and 1980-1984 (Rantanen et al., 2009).

Table 1-1 summaries the evidence for a widening gap in life expectancy for individuals with schizophrenia and the general population, while Table 1-2 summaries the evidence which supports either no change in mortality or possible improvement in mortality rate for individuals with schizophrenia.

Table 1-3 summaries the evidence for a widening gap in life expectancy for individuals with bipolar disorder. To date there is no evidence to support either no change in mortality or possible improvement in mortality rate for individuals with bipolar disorder.

Table 1-1 Recent Studies in Schizophrenia suggesting that the mortality gap is widening:

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Brown, 1997 BJPsych	Meta-analysis of studies from the UK, Netherlands, Israel, Scandinavia and US	18 studies, 66,161 individuals	SMR for all cause, all unnatural, all natural and specific causes with 95% CI were calculated. SMRs for men & women calculated separately	Aggregate SMR from 1970s, 1980s and 1990s.	Significantly higher aggregate SMR in 1980 compared to the 1970s (1.91 95% CI 1.83-1.99 vs.1.52 95% CI 1.44-1.60 p<0.001).
Osby et al., 2000 BMJ	Linkage to the national causes of death register allowing comparison of mortality rates for individuals with schizophrenia to the general Stockholm population between 1976 and 1995	Residents of Stockholm (pop 1.8 million) with a first hospital admission with a diagnosis of schizophrenia: 3001 men and 2801 women	SMRs for natural, unnatural, and specific causes of death (suicide, cardiovascular disease and unspecified violence) were calculated. SMRs for men & women calculated separately	SMRs were compared by consecutive 5 year periods 76-80, 81-85, 86-90 & 91-95	SMR for all causes of death increased 1.7-fold in men and 1.3-fold in women over the study period. Death from cardiovascular causes increased 4.7-fold in men & 2.7-fold in women; Suicide increased 1.6-fold in men & 1.9-fold in women; Mortality from unspecified violence increased 3.8-fold in men & 3.4-fold in women
Lawrence et al., 2003 BMJ	Population-based record-linkage study of IHD mortality rates, hospital admission rates and rates of revascularisation procedures in MMI compared to the general population.	210,129 users of mental health services in Western Australia during 1980-1998.	Mortality rate ratio (MRR) for IHD	Poisson regression analysis of the mortality rates from 1980-1998	For the general population, the mortality rate has been decreasing by 1.9% per year (95% CI 1.7-2.1%) in males and by 0.7% per year in females (95% CI 0.5-1.0%). In contrast, in users of mental health services the mortality rate was not significantly changed in males (95% CI for annual increase -0.5% to 0.9%), and was increasing at a rate of 2.2% per year in females (95% CI 1.5-3.0%).
Saha et al., 2007 JAMA Psychiatry	Examination of the distribution of SMRs from 37 papers. Selected estimates using random-effects meta-analysis were then pooled.	37 papers drawn from 25 different nations	All cause Standardised mortality ratios (SMR).	SMRs from studies in 1970 (n=8), 1980 (n=10) & 1990 (n=7) were compared. Meta-regression was used.	Median all-cause SMR for all persons was 2.58, with 10% and 90% quintiles from 1.18 to 5.76. Median SMRs for 1970s, 1980s, and 1990s were 1.84, 2.98, and 3.20, respectively. There was a significant positive association between the follow-up period midpoint year and all-cause SMR. (Slope coefficient, 0.06; 95% CI, 0.01-0.11; z = 2.21; p =0 .03).

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Capasso et al., 2008 Schizophrenia Research	Linkage study with median follow up of 23.5 years	319 Olmsted County residents meeting DSM-IV-TR criteria for schizophrenia (n=242) or schizoaffective disorder (n=77)	Cumulative survival probabilities were estimated using the Kaplan–Meier method and compared using a one-sample log-rank test with the general life expectancy for the Caucasian population of the United States and Minnesota for persons of like age, gender, and calendar year of birth. Log-rank test was used to compare survival of groups of patients	No formalised charting of survival over time	Significant ($p < 0.001$) increase in mortality for patients with a diagnosis of schizophrenia and schizoaffective disorder compared both with the mortality of the Caucasian population of the United States and Minnesota for persons of the same age, gender, and calendar year of birth. Individual survival curves for schizophrenia and schizoaffective disorder were very similar, having the same level of significance. Coronary artery disease was the primary cause of death (20%), whereas cancers (including lung cancer) accounted for 19% of deaths

Given the improvement in life expectancy for the general population, concerns about access and availability of medical and psychiatric care in the United States and other countries, the study concluded that these factors are likely contributing to the widening gap between survival of those with serious mental illness compared to the general population |
| Brown et al., 2010, BJPsych | Prospective record linkage study of the 25 year mortality of those with schizophrenia, with focus on change over time | A community cohort of 370 people with schizophrenia | All cause Standardised mortality ratios (SMR), SMR by specific causes (suicide, lung cancer, breast cancer, diabetes, cardiovascular disease, pneumonia, COPD, accident and undetermined) and mean age at death | Change in all cause, change in natural, change in un-natural and change in cardiovascular SMR over time | Mean age at death of males was significantly lower than that of the females (57.3 *v.* 65.5 years, p<0.001). This difference remained when unnatural deaths were excluded. All-cause SMR was 289 (95% CI 247-337). Most significant contributions to the overall excess mortality came from circulatory diseases (33%) and respiratory diseases (19%).

All-cause SMR showed small but non-significant changes between 1981 and 2006, falling in the first 5 years then rising slightly from 264 (95% CI 174–384) in 1986–1991 to 292 (95% CI 212–392) in 2001–2006 (p= 0.6). SMR for cardiovascular diseases increased over the study period from 129 (95% CI 27–377) in 1981–1986 to 350 (95% CI 186–598) in 2001–2006. (p= 0.053). |

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Hoye et al., 2011 Schizophrenia Research	Linkage study using data from the University Hospital of North Norway. Follow up period of 27 years	1,111 patients with schizophrenia compared to the general population.	Age adjusted SMRs for all cause, natural cause, unnatural cause and specific causes of mortality (namely suicide, cardiovascular disease & cancer) in men and women with schizophrenia compared to the general population.	SMRs for 1980-1988, 1989-1997 and 1998-2006 were calculated and compared	Male SMR was higher than female SMR (3.5 95%CI 3.1-4.1 vs. 2.6 95%CI 2.1-3.2 p=0.01 respectively) SMR in 1998-2006 was higher than that in 1980-1988 for both men 3.8 (95% CI 3.0-4.1) vs. 2.8 (95% CI 2.1-3.6) and women 2.6 (95% CI 1.9-3.7) vs. 2.1 (95% CI 1.2-4.4).
Hoang et al., 2011 BMJ	Linked dataset of English national hospital episode statistics and data from death certification. Follow up 7 years	272,248 discharges from hospital for schizophrenia in England for 1999-2006	Age and sex adjusted SMRs for deaths from unnatural and natural causes and SMRs for specific causes of death including cardiovascular disease, respiratory disease, cancer, accidents and suicide/deaths from undetermined intent	Poisson test of trend was used to investigate whether there was a significant trend in standardised mortality ratios over time	Age and sex SMR were double the population average. In 2006 SMR was 2.2 in the population discharged with schizophrenia. SMR was higher in younger than in older people: in 2006 in those aged < 45 SMR was 6.2 (95% CI 4.9-7.5) vs. 2.0 (95% CI 1.7-2.3) in those aged 65-84 SMR increased from 1.6 (95% CI 1.5-1.8) in 1999 to 2.2 (95% CI 2.0-2.4) in 2006. Poisson test for trend confirmed that the trend in risk of mortality was significant (P<0.001).
Morden et al., 2012 General Hospital Psychiatry	Patients in the Veteran Affairs Health system with schizophrenia were linked to National Death Index and compared to individuals in the Veteran Affairs Health system without serious mental illness	65,362 patients in the Veteran Affairs (VA) health system with schizophrenia and 65,362 VA patients without serious mental illness (non-SMI)	All-cause and cause-specific mortality was compared for fiscal years 2000–2007. Mean years of potential life lost (YPLLs) were calculated annually.	Comparison of all-cause and cause-specific mortality and years of potential life lost (YPLLs) between 2000 -2007.	All cause annual mortality rate for those with schizophrenia was 257 in 2000 vs. 311 in 2007. This compared to an all cause annual mortality rate of 196 in those without SMI in 2000 and 247 in 2007. Years of potential Life lost was 12.8 years in 2000 and 15.4 years in 2007 for individuals with schizophrenia compared to 11.8 years in 2000 and 14.0 years in 2007 for individuals without SMI

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Dutta et al., 2012 Psychological Medicine	Patients with first episode psychosis in three catchment areas of the U.K. were traced after a mean of 11.5 years follow-up and death certificates were obtained. Data analysis was by indirect standardization.	2723 patients: London (1965-2004, n=2056), Nottingham (1997-1999, n=203) and Dumfries and Galloway (1979-1998, n=464)	Overall standardized mortality ratio (SMR) and specific cause SMR	Poisson regression models were used to test the difference in SMRs (for all causes of death) over calendar period of follow-up, using the expected number of deaths for each stratum as the offset and assuming multiplicative effects between the number of deaths and calendar period.	Overall SMR was 184 [95% CI 167-202]. Most deaths (84.2%,) were from natural causes. Suicide had the highest SMR (1165, 95% CI 873-1524). Respiratory system and infectious diseases had the highest SMR of the natural causes of death (232, 95% CI 183-291). Risk of death from diseases of the circulatory system was also high (SMR 139, 95% CI 117-164). There was strong evidence that the mortality gap compared with the general population for all causes of death (p<0.001) and all natural causes (p=0.01) increased over the four decades of the study. There was weak evidence that cardiovascular deaths may be increasing relative to the general population (p=0.07).
Nielsen et al., 2013 Schizophrenia Research	Longitudinal linkage study using the Danish Psychiatric Research Register and the Danish Cause of Death Register. Data were analysed using descriptive statistics and survival analysis.	14,974 patients with schizophrenia were compared to 1,311,419 controls	Average age of death was constructed for the schizophrenia population and the general population for all causes and with self-harm excluded as cause of death.	Change in age at death between 1980 and 2010 were calculated as marker of increase in mortality over time. Matched control vs. schizophrenia survival analysis, with entry defined as time of birth and Kaplan–Meier plots were obtained. Log-rank test and Cox regression were employed.	Average age of death in the schizophrenia population was lower compared to the general population (62.2 years; 95%CI 61.9-62.5 vs. 73.4 years; 95% CI, 73.4–73.4, p < 0.001). Individuals with schizophrenia had an increased mortality rate compared with the general population (hazard ratio, 2.05; 95% CI, 2.01–2.09). In the general population there was an average increase in age of death of 0.28 years/calendar year in men (95% CI, 0.27–0.28), and in women an increase of 0.31 years/calendar year (95% CI, 0.31–0.32) (both p < 0.001). Age of death decreased in the schizophrenia population: -0.04 years/calendar year for men (95% CI, – 0.09 to 0.00), and for women – 0.05 years/calendar year (95% CI, – 0.09 to 0.01) (both p < 0.05). A similar pattern was seen after acts of self-harm as cause of death were excluded from the analyses.

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Walker et al., 2015 JAMA Psychiatry	Meta-analysis of studies reporting a measure of mortality.	146 studies	Pooled mortality ratios using DerSimonian-Laird random-effects models to allow for heterogeneity across studies. Random-effects meta regression models were used to determine which study characteristics could explain heterogeneity.	Pooled Relative Risk from studies published before 1970, 1970-1979, 1980-1989, 1990-1999 and after 2000	Relative risk of death increased over time: before 1970: 1.79 (95% CI 1.49-2.15), 1970-1979: 2.07 (95% CI 1.86-2.31), 1980-1989: 2.28 (95% CI 2.07-2.50), 1990-1999: 2.43 (95% CI 2.24-2.63) and after 2000: 2.47 (95% CI 2.17-2.79). NB this is for ALL mental disorders combined.

Table 1-2 Recent Studies in Schizophrenia suggesting that there is no change in the mortality gap or it is improving:

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Heila et al., 2005 Psychological Medicine	Individuals hospitalized for schizophrenia were identified via the National Hospital Discharge Register and linked to mortality data from the National Causes of Death Register.	58,761 individuals with schizophrenia were included.	Relative risks (RR) of death adjusted for age for total mortality, mortality due to natural causes (cancer, ischaemic heart disease, respiratory disease) and unnatural causes (accident, homicide, suicide), and suicide were calculated	Trend in mortality over the whole study period (1980–1996) was tested using poisson regression models.	Individuals with schizophrenia had an increased mortality both from natural causes (RR 2.59, 95% CI 2.55–2.63) and from suicide (RR 9.9, 95% CI 9.43–10.30). The RR for both natural and unnatural deaths was highest among patients with <5 years from onset. Among them all-cause mortality rose in the 1990s, but decreased among patients with >10 years from onset. Otherwise no major changes or linear trends were found in mortality during deinstitutionalization.
Colton et al., 2006 Preventing Chronic Disease	Age-adjusted death rates, SMRs, & YPPL, for mental health clients in 8 states compared with the mortality of their state general populations over 3 years (1997-2000)	8 US states (Arizona, Missouri, Oklahoma, Rhode Island, Texas, Utah, Vermont, and Virginia)	Age-adjusted death rates (AADRs), Standardised mortality ratios (SMRs), and years of potential life lost (YPLL)	SMR over time	Public mental health clients in all eight states studied had a greater risk of dying than the general populations of their states. Individuals with schizophrenia had higher AADRs and SMRs during every year submitted than the general populations of their states. SMR was highest in Oklahoma at 4.9 in 1997. However little evidence of change in SMR over time: Missouri SMR 2.0 in 1999 & 2.2 in 2000 Oklahoma SMR 4.9 in 1997 & 2.9 in 1999 and Texas SMR 4.4 in 1997 & 1.6 in 1999
Tiihonen et al., 2009 The Lancet	Finnish Nationwide registers to compare the cause-specific mortality in patients with schizophrenia linked to the use of antipsychotic drugs	66,881 patients with schizophrenia vs. the total population (5·2 million) between 1996-2006	All-cause mortality during current & cumulative exposure to any antipsychotic drug vs. no antipsychotic, & exposure to the 6 most frequently used antipsychotic drugs vs. perphenazine use.	Comparison of life expectancy in those with schizophrenia and the general population at different ages, 10 years apart.	Although the proportional use of second-generation antipsychotic drugs rose from 13% to 64% during follow-up, the gap in life expectancy between patients with schizophrenia and the general population did not widen between 1996 (25 years), and 2006 (22·5 years)

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Rantanen et al., 2009 Social Psychiatry and Psychiatric Epidemiology	Finnish hospital discharge register (FHDR), for Individuals with first hospitalisation for schizophrenia during 1980-1998 was linked to date & cause of death from Statistics Finland over 5 years	23,959 individuals with schizophrenia were included.	5 year mortality after discharge from hospital - for all causes, due to malignancy, ischaemic disease, any somatic cause, alcohol related, suicide and other unnatural cause. 5 year mortality was calculated for males and females.	Changes in 5-year follow-up mortality during the study period were explored for both genders and for different causes of death separately using multivariate logistic regression analyses	Proportion of deaths was significantly higher in males (10.1%) than in females (5.7% p<0.001). A significant reduction in overall 5-year mortality was observed among persons hospitalized in 1995-1998 when compared to people hospitalized 1980-1984 (p=0.062). In males a significant reduction was seen in all mortality (p= 0.025) and deaths from suicide (p=0.007) but not in the case of natural deaths. In females no significant changes in mortality were found.

Table 1-3 Recent Studies in Bipolar Disorder suggesting that the mortality gap is widening:

Author, Year & Journal	Study methodology	Sample Size	Measurement of mortality used	Measurement of change in mortality rates	Main Findings
Hoang et al., 2011 BMJ	Linked dataset of English national hospital episode statistics and data from death certification	100,851 discharges from hospital for bipolar disorder in England for 1999-2006	Age and sex adjusted SMRs for deaths from unnatural and natural causes were calculated. SMRs for specific causes of death were also included namely from cardiovascular disease, respiratory disease, cancer, accidents and suicide/deaths from undetermined intent	Poisson test of trend was used to investigate whether there was a significant trend in standardised mortality ratios over time	Age and sex standardised mortality ratios were about double the population average- in 2006 SMR was 1.9 in the population discharged with bipolar disorder. SMR was higher in younger than in older people: in 2006 in those aged < 45 SMR was 3.4 (95% CI 1.7-5.1) vs. 1.8 (95% CI 1.4 - 2.2), in those aged 65-84 SMR increased from 1.3 (95% CI 1.1-1.6) in 1999 to 1.9 (95% CI 1.6- 2.2) in 2006. Poisson test of trend had results of borderline significance (p=0.06).
Walker et al., 2015 JAMA Psychiatry	Meta-analysis of studies reporting a measure of mortality.	146 studies	Pooled mortality ratios using DerSimonian-Laird random-effects models to allow for heterogeneity across studies. Random-effects meta regression models were used to determine which study characteristics could explain heterogeneity.	Pooled Relative Risk from studies published before 1970, 1970-1979, 1980-1989, 1990-1999 and after 2000	Relative risk of death increased over time: before 1970: 1.79 (95% CI 1.49-2.15), 1970-1979: 2.07 (95% CI 1.86-2.31), 1980-1989: 2.28 (95% CI 2.07-2.50), 1990-1999: 2.43 (95% CI 2.24-2.63) and after 2000: 2.47 (95% CI 2.17-2.79). NB this is for ALL mental disorders combined.

The difference in mortality rate ratios and life expectancy experienced by individuals with MMI compared to individuals without MMI is evidence of potential health inequality. However, the possible reasons underpinning this are poorly understood. Better understanding of possible explanatory factors for this health inequality will allow the development of strategies to address this. These strategies may be at a primary and secondary care level as well as at an individual and societal level.

Although differences in mortality between individuals with MMI and individuals without MMI have been explored, as outlined above, there remain significant gaps in our understanding of this complex relationship. Detailed exploration of the cause of death across the lifespan of individuals with MMI is required, along with investigation into the impact of socioeconomic deprivation on cause and rate of death. Systematic comparison of the patterns and cause of death in individuals with schizophrenia and bipolar disorder will also be helpful to better aid understanding of the prognosis and outcomes of these disorders. By undertaking a study locally, an additional cohort of individuals will be investigated, and this will add to current evidence which to date has largely been from Sweden, Denmark, Australia and London. Ultimately, this thesis will attempt to explore some of these gaps in greater detail with the aim of better informing the development of strategies and policies to address the mortality gap.

1.5 Conclusion:

While increased physical comorbidity in individuals with MMI is widely reported in the literature, it is often reported, for a narrow range of single diseases in restricted cohorts of the population. This therefore limits generalisability of findings. To date there have been few large, systematic investigations into the patterns of physical health comorbidities in individuals with MMI compared to the general population using primary care data and none have been undertaken in Scotland. Therefore further investigation of rates and patterns of physical health comorbidity in MMI is required and this thesis will describe these patterns in detail. The influence of age, sex and

socioeconomic status on rates of physical comorbidity will also be considered. To date the rate of multimorbidity in MMI has been poorly explored, and given the influence of deprivation on rates of multimorbidity, and the fact that multimorbidity is common and is often the norm rather than the exception in individuals with long-term conditions, this is an area which requires further investigation. This thesis will therefore attempt to explore patterns of multimorbidity in a systematic manner in individuals with MMI.

Given that there is some preliminary evidence for inequality in prescribing of physical health medication in individuals with MMI, further exploration of possible prescribing inequalities within a large primary care database in Scotland would be of clinical and scientific merit. In particular rates of prescription of statins, antiplatelets and anti-hypertensives in individuals with MMI and hypertension and MMI and coronary heart disease will be compared to individuals with hypertension without MMI and individuals with coronary heart disease without MMI. Given the significant burden of smoking in individuals with MMI and the modifiable nature of this risk factor, investigation to determine if there are inequalities in access to smoking cessation advice and nicotine replacement therapy (NRT) prescription for individuals with MMI will also be undertaken. It is hoped that the findings reported in this thesis will provide novel insights into potential inequalities in access to healthcare advice and prescribing in primary care in Scotland.

While health inequalities are reported in individuals with MMI, to date no studies have focused on whether there is evidence of inequality in access to the incentivised healthcare provision for individuals with MMI within Scotland; namely in the form of the Quality and Outcome framework (QOF). Given the high uptake of the QOF within primary care across the UK, investigation into potential inequalities using QOF data is likely a reflection of UK wide practice. Due to the limited investigation into this area, this thesis will provide a novel insight into potential inequalities in aspects of incentivised primary care in Scotland and across the UK.

Increased mortality of individuals with MMI has been described but there remain significant gaps in our understanding of not only the patterns of cause of mortality across the lifespan, but also the effect of socioeconomic status on mortality rates. The studies carried out to date, have largely been out with Scotland and so a local study will be of scientific and clinical merit and can add to the wider scientific evidence. A comparison of patterns of cause and rate of mortality between schizophrenia and bipolar disorder would also be advantageous to add to current understanding. This thesis will therefore attempt to address some of the gaps in these areas by using a locally linked dataset.

Finally, this thesis will provide a synthesis of these findings and focus on their clinical and scientific implications. Areas for future research will be highlighted and potential modifications to current working models will also be discussed.

Chapter 2: Aims and Research Questions:

2.1 Aims:

The aims of this thesis were:

1.To conduct a review of: a) the literature on physical health comorbidity and multimorbidity in schizophrenia and bipolar disorder relative to the general population, b) to review research which has explored possible mechanisms for health inequalities in these groups and c) the literature on premature mortality in schizophrenia and bipolar disorder relative to the general population

2. To gain a more detailed understanding of the patterns of multiple physical health comorbidities in individuals with schizophrenia and bipolar disorder.

3. To better understand possible explanations for health inequalities in individuals with schizophrenia and bipolar disorder by examining a) prescribing data in primary care and b) Quality and Outcome Framework (QOF) data in Scotland, England, Northern Ireland and Wales.

4. To gain a more detailed understanding of the causes of premature mortality in individuals with schizophrenia and bipolar disorder.

2.2 Research Questions:

1. What are the patterns of multiple physical health comorbidities in individuals with schizophrenia and bipolar disorder and how do these compare to the general population?

2. Do patterns of prescribing for hypertension and coronary heart disease (CHD) in individuals with schizophrenia and bipolar disorder differ from the patterns of prescribing for hypertension and coronary heart disease in individuals without schizophrenia and bipolar disorder?

3. Do rates of recording of smoking cessation advice and patterns of prescribing of Nicotine Replacement Therapy (NRT) in smokers with schizophrenia and bipolar disorder

differ from smokers with other chronic diseases (diabetes, coronary heart disease (CHD) or hypertension)?

4. Do rates of payment, population achievement and exception reporting for comparable QOF indicators differ in individuals with schizophrenia or bipolar disorder across Scotland, England, Wales and Northern Ireland compared to other chronic diseases?

5. What are the primary causes of death across the adult life span in individuals with schizophrenia and bipolar disorder and how do these causes of death compare to the general population?

6. Does the primary cause of death in individuals with schizophrenia differ from the primary cause of death in individuals with bipolar disorder?

7. Does socioeconomic status impact on rate and primary cause of death in individuals with MMI relative to the local (Glasgow) and wider (Scottish) populations?

Chapter 3: General Methods:

Chapter Overview

This chapter is a general overview of the approach and methods used for the studies reported in this thesis. More detailed methodological information is reported within each chapter. In order to address the aims of this thesis, a narrative review of the literature was undertaken (its methodology and findings are reported above in Chapter 1). This allowed gaps in the literature to be identified and the subsequent generation of the research questions. From there a decision regarding the statistical analyses using data from primary care, secondary care and national datasets was made. The datasets included in this thesis are-

1. The Scottish Programme for Improving Clinical Effectiveness in Primary Care (SPICE) dataset,

2. The Quality and Outcome Framework (QOF) Data- a national dataset and

3. The Glasgow Psychosis Clinical Information System (PsyCIS)- a secondary care dataset.

3.1 The Scottish Programme for Improving Clinical Effectiveness in Primary Care (SPICE) dataset

3.1.1 Overview of SPICE

The SPICE dataset is a cross sectional primary care database which contains information on 1,751,841 registered patients who were alive and permanently registered with 314 general practices on March 31, 2007. Due to its size, the dataset is a representative sample covering approximately one third of the Scottish population. Secondary analyses using the SPICE database are included in Chapters 4 and 5.

3.1.2 Research methodology undertaken using the SPICE dataset:

The SPICE dataset includes basic demographic information including age, sex and socioeconomic status. Information on socioeconomic status is measured by the Carstairs

Index (divided into quintiles) and is calculated based on the individual's address. The presence or absence of certain physical and mental health conditions (schizophrenia or bipolar disorder) were based on GP diagnostic Read Codes and/or prescription data. For example individuals with migraine were identified if four or more prescription only anti-migraine medications were prescribed in the last year. A full list of the thirty two physical health conditions included and their definitions are found in Appendix 2.

3.1.3 Statistical Analyses carried out using the SPICE dataset:

3.1.3.1 Statistical Analyses of patterns of comorbidity:

Analyses of this dataset were restricted to individuals aged 18 and over and the sample was divided into the following age groups for analysis: 18-25, 25-34, 35-44, 45-54, 55-64 and 65 and older.

Differences between groups such as individuals with schizophrenia or bipolar disorder, all other individuals (controls) and between males and females were calculated by age, deprivation and number of physical conditions. T-tests were used to analyse differences between groups and Chi squared tests were used for differences across age groups and deprivation quintiles. Logistic regression was used to calculate odds ratio (ORs) for the prevalence of the thirty two physical conditions, as well as no physical disorder, one comorbid disorder, two comorbid disorders and three or more comorbid disorders. Odds ratios (ORs) are reported with 95% confidence intervals (CIs) in individuals with either schizophrenia or bipolar disorder compared with controls and were adjusted for age, gender and deprivation. Further detail of the statistical methodology undertaken is available in Chapter 4.

3.1.3.2 Statistical analyses of prescribing patterns:

For differences in prescribing patterns standard British National Formulary (BNF) classifications of drugs such as anti-hypertensives, statins, aspirin and clopidogrel were obtained. Prescribing rates of none, one and two or more anti-hypertensives were compared in individuals with comorbid schizophrenia or bipolar disorder and hypertension with individuals with hypertension without schizophrenia or bipolar disorder. Prescribing rates of none, one and two or more anti-hypertensives, along with aspirin or clopidogrel and statin prescription rates were compared in individuals with comorbid schizophrenia or bipolar disorder and coronary heart disease (CHD) and individuals with CHD without

schizophrenia or bipolar disorder. To ensure only current prescriptions were captured, prescribing data from the 84 days prior to the date that the dataset was obtained were included. Further detail of the statistical methodology undertaken is included in Chapter 4.

3.1.3.3 Statistical analyses of risk factors:

For risk factor profiles, rates of uncontrolled Blood Pressure (BP) (defined as did not achieve target BP: where systolic BP $\geq$ 140mmHg and diastolic BP $\geq$ 90mmHg if < 80 years old and systolic BP $\geq$ 150mmHg and diastolic BP $\geq$ 90mmHg if aged 80 and over) and uncontrolled cholesterol (defined as cholesterol $\geq$ 5mmo/L) were compared across groups: namely individuals with schizophrenia or bipolar disorder and hypertension or CHD versus individuals with hypertension or CHD without schizophrenia or bipolar disorder. Odds ratio calculations were adjusted for age, gender and deprivation score and are reported with 95% confidence intervals.

3.1.3.4 Statistical analyses of recording of smoking status, smoking cessation advice and Nicotine Replacement Therapy (NRT) prescription:

Recording of smoking status was reviewed and recoded into current smoker, ex-smoker and non-smoker based on the Read Codes detailed in Appendix 3. Individuals, in whom smoking status was not recorded, were excluded. Odds ratio of current smoking, ex-smoking and non-smoking in individuals with MMI with/without diabetes, individuals with diabetes without MMI, individuals with MMI with/without hypertension, individuals with hypertension without MMI, individuals with MMI with/without CHD and individuals with CHD without MMI were calculated using logistic regression adjusted for age, sex and deprivation status. Odds Ratios are reported with 95% confidence intervals.

In smokers, recording of smoking cessation advice was reviewed and recoded into having occurred on not occurred based on Read Codes, detailed in Appendix 4. For differences in prescribing rates: standard British National Formulary (BNF) classifications of Nicotine Replacement Therapy (NRT) which included patches, gum, lozenges, inhalator or nasal spray were obtained. Further details of the Read Codes included are detailed in Appendix 5. To ensure only current prescriptions were captured, prescribing data from the 84 days prior to the date that the dataset was obtained were included.

In smokers, rate of recording of smoking cessation advice and rate of prescription of Nicotine Replacement Therapy (NRT) were then calculated. Odds ratios with 95%

confidence intervals, for recording of smoking cessation advice and prescribing of NRT for the different groups were calculated using logistic regression adjusted for age, sex and deprivation status.

A comparison of rates of smoking, ex-smoking and non-smoking, rates of recording of smoking cessation advice in smokers and rates of NRT prescription in smokers, in individuals with schizophrenia and bipolar disorder was also undertaken. Odds ratios with 95% confidence intervals were calculated using logistic regression again adjusted for age, sex and deprivation status.

All analyses were performed in STATA version 12. A further more detailed explanation of the statistical methodology undertaken is detailed in Chapter 5.

3.1.4 Ethical considerations for SPICE:

The analysis of SPICE data was conducted as part of the Living Well with Multimorbidity Programme (CSO Grant ARPG/07/1) with Professor Stewart W Mercer (Principal Investigator) and Professor Bruce Guthrie (Epidemiology Lead). Therefore individual ethical approval for each study was not required.

3.2 Quality and Outcome Framework (QOF) Data.

3.2.1 Overview of QOF Data

The General Medical Services' Quality and Outcomes Framework (QOF), was introduced into the UK in 2004, and is an annual contract for the provision of care delivered by General Practices. It was introduced to standardise the improvement in the delivery of primary care and largely forms the basis of supplementary payment for General Practioners (GPs). Work using QOF data is included in Chapters 6 and 7.

The QOF is dynamic in nature and so in Scotland, England, Northern Ireland and Wales the indicators have changed since their inception in 2004. In 2012/2013 the QOF was made up of four main components, known as domains. These four domains; clinical, organisation, patient experience and additional services, contain indicators against which the primary care practice scores points according to their level of achievement. The clinical domain contains clinical indicators across a wide variety of conditions which are managed within primary care- including heart failure, coronary heart disease (CHD), stroke, asthma,

chronic obstructive pulmonary disease (COPD) and mental illnesses. Supplementary payment of General Practices is calculated based on indicator achievement rate.

Throughout the UK, the number of General practices participating in the QOF is high and so analysis of QOF data is representative of UK wide practice. Although there are subtle differences in QOF indicators between countries within the UK, some indicators are the same and so direct comparison between consistent indicators across different countries can be made.

Within a clinical domain (for example mental health or asthma), individuals may not be suitable for all indicator measurements, and so there is a facility within the QOF to exclude and to except individuals from certain indicators. This then removes these individuals from the indicator achievement and payment calculations. This process is explained in more detail in Chapter 6.

Three measurements are therefore used to describe QOF data: indicator achievement/practice payment rate, exception rate and population achievement rate. These three measurements have been included in this thesis and are detailed below (Figure 3-1).

Indicator achievement rate aka Practice Payment Rate $=$ $\dfrac{\text{number of individuals who have successfully met the indicator criteria (numerator)}}{\text{number of individuals who could have achieved that indicator target (denominator) once exclusions and exceptions have been removed.}}$

Exception rate $=$ $\dfrac{\text{number of individuals who met the exception criteria}}{\text{number of patients who were eligible for the target with exceptions included (denominator + exceptions)}}$

Population achievement rate $=$ $\dfrac{\text{number of individuals who have successfully met the indicator criteria (numerator)}}{\text{number of patients who were eligible for the target with exceptions included (denominator + exceptions)}}$

Figure 3-1   Payment rate, Exception rate and Population achievement rate calculations.

3.2.2 Research methodology undertaken for cross-jurisdiction comparison of QOF Data:

To undertake a cross-jurisdiction comparison of QOF data: payment, exception and population achievement rates for two of the Mental Health indicators along with two comparator non-mental health indicators across the UK was undertaken for the years 2011/2012 and 2012/2013. Data was obtained, from the Health and Social Care

Information Service in England, the Quality and Outcome Frameworks Information Services Division (ISD) of NHS Scotland, the Department of Health, Social Service and Public Safety in Northern Ireland and the Welsh Government.

3.2.3 Statistical Analyses undertaken for cross-jurisdiction comparison of QOF Data:

Both Mental Health indicators were compared with their non-mental health comparator indicator within the same year and geographical location (i.e. within Scotland, England, Northern Ireland and Wales) and also for the UK as a whole for 2011/12 and 2012/13. As data were non-parametric and paired (within countries by practice identifier), differences in rates within the same country were compared using a sign test. Median population achievement rate, payment rate and exception rate are reported along with inter quartile range (IQR). For the UK wide figures, differences in rates were compared using a non-parametric equality of medians test. Differences in median population achievement rate between countries were compared to England using a quantile regression analysis weighted for practice denominator. Results are reported as percentage point difference with 99% confidence intervals. Further detail surrounding the statistical methodology undertaken is detailed in Chapter 6. All analyses were performed using STATA version 12.

3.2.4 Research methods undertaken using Scottish QOF data:

A retrospective analysis of exception rate data for the years 2005/2006 until 2012/2013 inclusive for all the Mental Health indicators was undertaken. Exception rate data is available on the Quality and Outcome Frameworks Information Services Division (ISD) of NHS Scotland website. Median rate of exception for each of the Mental Health indicators in the above timeframe was calculated and charted over time to determine trends in exception rate reporting.

A number of proxy comparator indicators for other chronic diseases, deemed similar to the Mental Health indicators were selected. These proxy comparator indicators were chosen after careful review and consideration of all available indicators within the QOF. Although the indicators were not always exactly the same, there were of the same type (i.e. measurement or target indicator) and used the same timeframe (for example measurements to be recorded within 12 months). The rationale for choosing the comparator indicators was discussed at supervision and agreement regarding their suitability was obtained from both supervisors. This was felt to be the most pragmatic option available to allow

comparison of indicators across a wider range of chronic diseases. Median exception rates were calculated and rates were then compared. This process is further detailed in Chapter 7.

A number of composite indicator areas were generated by combining exception rates for individual indicators within a clinical area. The clinical areas where composite indicators were generated included: mental health (MH), atrial fibrillation (AF); asthma; coronary heart disease (CHD); cancer, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), epilepsy, heart failure (HF), diabetes, hypertension, hypothyroidism, osteoporosis, peripheral artery disease (PAD), stroke, dementia and depression. The generated composite indicators included a variable number of individual indicators, for example the mental health composite indicator contained exception rates for nine individual Mental Health indicators, while the composite indicator for diabetes contained exception rates for fourteen individual diabetes indicators. Due to changes in the mental health indicators (detailed in Chapter 7) exception rate data for composite clinical indicator areas were generated for 2011/2012 and 2012/2013 only.

It has been recognised that the use of a single QOF indicator as a marker of quality of clinical care is limited and there is some evidence to suggest that composite models may be more helpful (Holmboe et al., 2010). The use of multiple QOF indicators within a composite model, has been done by others (for example de Wet and colleagues (2012)) and therefore the generation of composite indicators was felt to be useful to allow comparison of the mental health indicators with a wide range of other physical health composite indicators.

3.2.5 Statistical Analyses using Scottish QOF data:

As data was non-parametric, median exception rates were calculated and are reported with interquartile ranges (IQR) and 95% confidence intervals (95% CI). Differences between indicator exception rates and changes in median exception rates over time were compared using a non-parametric equality of medians test. Further detail surrounding the statistical methodology undertaken is included in Chapter 7. All analyses were performed using STATA version 12.

3.2.6 Ethical considerations for the QOF data:

Publically available practice level data was used and formal Ethical approval was therefore not required.

3.3 The Glasgow Psychosis Clinical Information System (PsyCIS)

3.3.1 Overview of PsyCIS

The Glasgow Psychosis Clinical Information System (PsyCIS) is an electronic database of all individuals with a psychotic illness who have been in contact with secondary care psychiatric services in NHS Greater Glasgow and Clyde (NHSGG&C). This covers a population of approximately 1.1 million (National Records of Scotland, 2013). The database initially began as a retrospective case note audit of adults aged 18-65 with an ICD10 diagnosis of a psychotic illness, diagnosed by a consultant psychiatrist. Data was initially collected retrospectively over 42 months (from February 2002 until August 2005) and demographic information was entered onto the database. The data was collected by two specifically trained research nurses. Over 8,000 case notes were audited. Work using the PsyCIS database is included in Chapter 8.

The ICD 10 diagnoses included in the PsyCIS database were: F20-29 Schizophrenia, schizotypal and delusional disorder, F30-F31 Mania and Bipolar Disorder, F32.3 Severe Depression with psychotic symptoms, F06.0 Organic Hallucinosis, F06.2 Organic delusional (schizophrenia-like) disorder, F06.30 Organic mood (affective) disorders, F06.31 Organic depressive disorder with psychotic symptoms, F53 Mental and behavioural disorders associated with the puerperium, not elsewhere classified and F1(x) Mental and behavioural disorders due to psychoactive substance with psychotic symptoms.

Detailed baseline information including ICD-10 diagnosis (as determined by a consultant psychiatrist), Community Health Index (CHI) number, ethnicity, marital status, employment status, educational attainment, accommodation status and postcode were obtained. Clinical data including family history of psychosis, current illness severity (as measured by Health of the Nation Outcome Scores (HoNOS) and Clinical Global Impression (CGI)), psychiatric admissions data, use of the Mental Health Act, psychiatric comorbidities, current and previous medications, adverse drug effects and psychosocial interventions received were also obtained.

Clinical consensus diagnostic coding was applied in cases where a diagnosis either had not been recorded by a consultant psychiatrist or where there was uncertainty over the primary diagnosis. Prospective addition of new cases to the database has occurred from August 2005 onwards using existing patient information management systems (PIMS). There is a reciprocal working relationship between the PsyCIS team and the local clinicians. All patients provide annual follow up information and this facilitates the return to consultants of clinically relevant information at an individualised caseload level. Annual review to check the accuracy of information such as postcode and current medication is undertaken and the database has undergone internal validity checking to determine the diagnostic accuracy of ICD10 diagnoses. Updates from the Health board to ensure that the data guardian is aware of any deaths of patients registered on the PsyCIS system also occurs.

Currently the database currently holds information on over 7,200 patients with a diagnosis of psychotic disorder, including: schizophrenia (n=4,787); bipolar disorder (n=1,784); organic psychosis (n=67); psychotic depression (n=452); and substance-induced psychosis (n=160) and is still being added to.

3.3.2 Research Methodology Undertaken using PsyCIS:

All individuals with schizophrenia (F20-F29) or bipolar disorder (F30-F31) aged between 18 and 65 who had died between 2006 and 2010 and lived within the Greater Glasgow area served by PsyCIS were identified. Date and cause of death were obtained by linkage to the Scottish Morbidity Records (SMR) held by the Information Services Division (ISD) of NHS Scotland. The International Statistical Classification of Diseases and Related Health Problems (ICD) was used to code cause of deaths, into nine categories using information from the Scottish Government website. The nine categories were as follows: 1) cardiovascular disease, 2) cerebrovascular disease, 3) respiratory diseases, 4) cancer, 5) alcohol related deaths, 6) mental and behavioural disorder due to drugs, 7) accidental, 8) suicide as defined by the Scottish suicide information database (which includes deaths of undetermined origin) and 9) other.

Scottish Index of Multiple Deprivation (SIMD) score was used as a measure of social deprivation. The SIMD identifies small areas of multiple deprivation (datazones) across Scotland by combining 38 indicators across 7 domains which are weighted. The domains include: current income (28%), employment (28%), health (14%), education (14%), geographic access to services (9%), crime (5%), and housing (2%) and are weighted based

on evidence from Oxford University's Social Disadvantage Research Centre. Each domain contains information gathered from multiple sources, for example the health domain contains information regarding: hospital episodes related to alcohol use, hospital episodes related to drug use, a measure of mortality (the comparative mortality factor (CMF)), a measure of morbidity (comparative illness factor), emergency admission to hospital, population proportion prescribed drugs for anxiety, depression or psychosis and proportion of singleton births of low birth weight (<2,500g). Each individual was allocated to a datazone and subsequent SIMD category based on their postcode (where 1 = most affluent and 5 = most deprived). There are 6,505 datazones covering Scotland and the SIMD score provides a relative measure of deprivation. Further detail is included in Appendix 6.

3.3.3 Statistical Analyses carried out using PsyCIS:

Cause of death by 10 year age at death ranges, i.e. <25, 25-34, 35-44, 45-54 and 55-64, were calculated for individuals with schizophrenia and bipolar disorder and compared to the local Glasgow and the wider Scottish population using annual mortality statistic data available from the General Register Office (GRO) for Scotland. Standardised mortality ratios (SMR) were calculated in the 10 year age ranges for the whole deceased population and further analysed by ICD10 diagnosis and gender.

Two SMRs were calculated; a local (Glasgow) SMR and a wider (Scotland) SMR. For the Glasgow SMR the expected rate of death was derived by applying the Glasgow death rate data stratified by age and cause, to the PsyCIS cohort. This is further detailed in Chapter 8. For the wider (Scotland) SMR the expected rate of death was derived by applying the Scottish death rate data stratified by age and cause to the PsyCIS cohort. Both background rates were available on request from the General Register Office for Scotland. Glasgow and Scotland SMRs for all causes of death, all causes excluding suicides, and causes due to cardiovascular disease, cerebrovascular disease and cancer, were then calculated.

All statistical tests were performed using STATA version 12. 95% confidence intervals for SMRs were calculated assuming that the data was normally distributed. Differences in death rates between men and women were compared using Chi squared tests. Rates of primary cause of death in schizophrenia and bipolar disorder were also compared using Chi squared tests. Difference in rate of death between the most and least affluent quintile was compared using a Chi squared test.

3.3.4 **Ethical considerations for PsyCIS:**

Ethical Approval was via Caldicott Guardian approval for NHS Greater Glasgow and Clyde.

Chapter 4: Patterns of comorbidity and prescribing trends in individuals with Schizophrenia and Bipolar Disorder- Analysis of SPICE Data:

Chapter Overview

This chapter will detail the patterns of recording of physical health comorbidities and multimorbidity in individuals with schizophrenia and bipolar disorder compared to the general population using SPICE data. It will also compare prescribing patterns in individuals with schizophrenia and bipolar disorder and comorbid hypertension or coronary heart disease (CHD) with prescribing patterns in individuals with hypertension or CHD without schizophrenia and bipolar disorder.

4.1 Background:

As outlined in Chapter 1, individuals with schizophrenia have increased rates of a number of chronic physical health problems including: diabetes (Dixon et al., 2000), metabolic syndrome (Heiskanen et al., 2013), chronic obstructive pulmonary disease (COPD) (Hsu et al., 2013) and osteoporosis (Howard et al., 2007). Similarly for individuals with bipolar disorder increased rates of: obesity (Carney and Jones, 2006a), diabetes (McIntyre et al., 2005), metabolic syndrome (Bly et al., 2013), thyroid disease (Crump et al., 2013) and renal disease (Carney and Jones, 2006a) are described. However to date, large scale epidemiological studies investigating patterns of single and multiple physical health comorbidities in these individuals within a primary care setting in Scotland are lacking.

In addition to the increased burden of disease that occurs, there may also be differences in access to healthcare for these individuals. As detailed in Chapter 1, there is evidence for differences in access to screening (Carney and Jones, 2006b), access to guideline consistent treatment (Kisely et al., 2009) and prescribing differences (Redelmeier et al., 1998).

4.2 Aims:

1. To describe the patterns of physical health comorbidities and multiple health comorbidities (multimorbidity) in individuals with schizophrenia compared to the general population.

2. To describe the patterns of physical health comorbidities and multiple health comorbidities (multimorbidity) in individuals with bipolar disorder compared to the general population.

3. To determine if there are differences in prescribing patterns in individuals with schizophrenia and a comorbid chronic disease (coronary heart disease (CHD) or hypertension) compared to individuals with a chronic disease (CHD or hypertension) who do not have schizophrenia or bipolar disorder.

4. To determine if there are differences in prescribing patterns in individuals with bipolar disorder and a comorbid chronic disease (coronary heart disease (CHD) or hypertension) compared to individuals with a chronic disease (CHD or hypertension) who do not have schizophrenia or bipolar disorder.

5. To determine if there are differences in rates of smoking, uncontrolled blood pressure and elevated cholesterol in individuals with schizophrenia and a comorbid chronic disease (coronary heart disease (CHD) or hypertension) compared to individuals with a chronic disease (CHD or hypertension) without schizophrenia or bipolar disorder.

6. To determine if there are differences in rates of smoking, uncontrolled blood pressure and elevated cholesterol in individuals with bipolar disorder and a comorbid chronic disease (coronary heart disease (CHD) or hypertension) compared to individuals with a chronic disease (CHD or hypertension) without schizophrenia or bipolar disorder.

4.3 Methods:

As detailed in Chapter 3, the Scottish Primary Care Clinical Informatics Unit dataset (SPICE) was used. The presence of thirty two of the most common chronic physical health conditions that were extracted are listed in Appendix 2.

Due to the extensive nature of the dataset, the underlying differences in the nature of the mental illnesses of interest and the opportunity to separate individuals with schizophrenia from individuals with bipolar disorder, separate analyses by mental illness for rates of physical health comorbidities, multimorbidity and prescribing patterns were undertaken.

Individuals were identified as having 'schizophrenia or related non-organic psychosis' (from here referred to as 'schizophrenia') based on the recording ever of any of the following primary care read codes (where % is noted this means "this code and any below it in the code hierarchy"): E10% schizophrenic disorders; E121 chronic paranoid psychosis; E12z paranoid psychosis NOS; E13% other non-organic psychoses; E13z non-organic psychosis/psychotic episode; NOS E1z non-organic psychosis NOS; Eu20% schizophrenia; Eu22% persistent delusional disorder; or the recording in the last 12 months of Eu23% acute/transient psychotic disorder.

Individuals were identified as having bipolar disorder based on the recording at any point of any of the following primary care Read Codes: E110% Manic disorder, single episode/hypomanic psychosis; E111% Recurrent manic episodes; E114% Bipolar affective - now manic/manic depressive - now manic; E115% Manic-depression - now depressed; E116% Manic bipolar affective disorder; E117% Unspecified bipolar affect disorder; E11y; Other manic-depressive psychosis; E11y0 Unspecified manic-depressive psychosis; E11y1 Atypical manic disorder; Eu30% Manic episode; Eu31 Bipolar affective disorder/manic depressive illness/manic depressive psychosis; Eu323 Severe depressive + psychotic; and Eu333 Recurrent depression now severe + psychosis.

Analyses of this dataset were restricted to individuals aged 18 and over and the sample was divided into the following age groups for analysis: 18-25, 25-34, 35-44, 45-54, 55-64 and 65 and older. Deprivation status was measured using the ,deprivation score (divided into quintiles) (Carstairs VMR, 1991).

Differences between individuals with schizophrenia or bipolar disorder (cases), all other individuals (controls) and between men and women with schizophrenia or bipolar disorder were calculated by age, deprivation and number of physical conditions. T-tests were used to test differences between groups. Chi squared tests were used for differences across age groups and deprivation quintiles. Logistic regression was used to calculate odds ratio (ORs) and 95% confidence intervals in individuals with schizophrenia or bipolar disorder compared to controls for the prevalence of all thirty two physical conditions, as well as no

physical disorder, one comorbid disorder, two comorbid disorders and three or more comorbid disorders. Odds ratios were adjusted for age, gender and deprivation.

For differences in risk factor profile and prescribing, individuals with CHD or hypertension and schizophrenia were compared to individuals with CHD or hypertension without schizophrenia. For this analysis individuals with bipolar disorder and CHD or hypertension were removed from the control group: the rationale being that as the control group was smaller, it was important to remove the effect of bipolar disorder on risk factor profile and prescribing trends. The reciprocal was true when comparing individuals with CHD or hypertension and bipolar disorder and individuals with CHD or hypertension without bipolar disorder- individuals with schizophrenia were removed from the analysis.

For risk factor profile, rates of current smoking, uncontrolled blood pressure (defined as did not achieve target BP: where systolic $BP \geq 140mmHg$ and diastolic $BP \geq 90mmHg$ in individuals aged < 80 and systolic $BP \geq 150mmHg$ and diastolic $BP \geq 90mmHg$ in individuals aged 80 and over) and uncontrolled cholesterol (defined as $\geq 5mmoll^{-1}$) were compared across groups. Differences in prescribing between groups were analysed by comparing the percentage of patients on aspirin/clopidogrel (for CHD only), a statin and an anti-hypertensive agent. Antihypertensive agent was defined as any angiotensin-converting enzyme inhibitor (ACE-I) (all drugs in the BNF issue 51 Chapter 2.5.5.1), any angiotensin II receptor blocker (ARB) (all drugs in BNF chapter 2.2.2.2), any beta blocker (all drugs in BNF Chapter 2.4), any calcium channel blocker (any drug in BNF chapter 2.6.2), any alpha blocker (all drugs in BNF chapter 2.5.4), spironolactone (selected drugs from BNF Chapter 2.2.3) and any other anti-hypertensive not otherwise classified (all drugs in BNF Chapter 2.5.1, 2.5.2, 2.5.3 or 2.5.4 not previously counted). To ensure only current prescriptions were captured, prescribing data from the 84 days prior to the date that the dataset was obtained were included.

4.4 Results:

4.4.1 Main Findings

9,677 individuals with schizophrenia (0.7% of the entire sample) and 1,414,701 controls were identified (Table 4-1). Individuals with schizophrenia were more likely to be male compared to controls (51.3% vs. 49.1%; p<0.001) and tended to be older than controls (mean age 51.6 years vs. 48.0 years in control; p<0.001). Individuals with schizophrenia

were more socially deprived: with 23.3% living in the most deprived quintile compared to 17.8% of controls (p<0.001) (Table 4-1).

For the bipolar disorder group, 2,582 individuals (0.2% of the entire sample) and 1,421,796 controls were identified (Table 4-1). Individuals with bipolar disorder were less likely to be male compared to controls (39.5% vs. 49.1%; p<0.001) and were older than controls (mean age 54.5 years vs. 48.0 years in controls; p<0.001). Similarly to individuals with schizophrenia, individuals with bipolar disorder were more socially deprived: with 17.9% living in the most deprived quintile compared to 15.7% of controls (p=0.003) (Table 4-1).

	Schizophrenia vs. Controls				Bipolar Disorder vs. Controls			
	Schizophrenia n=9,677		Controls n=1,414,701		p value	Bipolar Disorder n=2,582		Controls n= 1,421,796		p value
Male n, %	**4,961**	**(51.27)**	**694,468**	**(49.09)**	**<0.001**	**1,021**	**(39.54)**	**698,408**	**(49.12)**	**<0.001**
Mean Age, sd	**51.58**	**(16.54)**	**47.97**	**(18.25)**	**<0.001**	**54.46**	**(15.28)**	**47.98**	**(18.25)**	**<0.001**
Age Group									
<25	**298**	**(3.08)**	**151,395**	**(10.70)**	**<0.001**	**45**	**(1.74)**	**151,648**	**(10.67)**	**<0.001**
25-34	**1,216**	**(12.57)**	**228,180**	**(16.13)**	**<0.001**	**217**	**(8.40)**	**229,179**	**(16.12)**	**<0.001**
35-44	**2,140**	**(22.11)**	**276,853**	**(19.57)**	**<0.001**	**445**	**(17.23)**	**278,548**	**(19.59)**	**<0.001**
45-54	**2,079**	**(21.48)**	**251,715**	**(17.79)**	**<0.001**	**626**	**(24.24)**	**253,168**	**(17.81)**	**<0.001**
55-64	**1,771**	**(18.30)**	**217,562**	**(15.38)**	**<0.001**	**547**	**(21.19)**	**218,786**	**(15.39)**	**<0.001**
65+	**2,173**	**(22.46)**	**288,996**	**(20.43)**	**<0.001**	**702**	**(27.19)**	**290,467**	**(20.43)**	**<0.001**
Deprivation Status									
Least deprived-1	**1,260**	**(13.02)**	**270,769**	**(19.14)**	**<0.001**	513	(19.87)	271,516	(19.10)	0.316
2	**1,714**	**(17.71)**	**302,440**	**(21.38)**	**<0.001**	570	(22.08)	303,584	(21.35)	0.374
3	2,263	(23.39)	319,984	(22.62)	0.073	581	(22.50)	321,666	(22.62)	0.906
4	**2,190**	**(22.63)**	**269,194**	**(19.03)**	**<0.001**	514	(19.91)	270,870	(19.05)	0.270
Most deprived 5	**2,250**	**(23.25)**	**252,314**	**(17.84)**	**<0.001**	404	(15.65)	254,160	(17.88)	0.003

Table 4-1   Age, gender and deprivation score, schizophrenia versus controls and bipolar disorder versus controls.

Bold if significant (p<0.001) difference between groups Adjusted for age, sex and deprivation status

Recorded physical health comorbidities were significantly more common in individuals with schizophrenia, even after adjusting for age, gender and deprivation. Compared to individuals without schizophrenia, individuals with schizophrenia were significantly less likely to have no recorded comorbidity (OR 0.61, 95% CI 0.58-0.64) and significantly more likely to have one comorbidity (OR 1.22, 95% CI 1.16-1.28), two comorbidities (OR 1.37, 95% CI 1.29-1.45) and three or more comorbidities (OR 1.19, 95% CI 1.13-1.27) (Table 4-2).

A similar pattern was seen for the individuals with bipolar disorder, who compared to individuals without bipolar disorder were: significantly less likely to have no recorded comorbidity (OR 0.54, 95% CI 0.49-0.59) and significantly more likely to have one comorbidity (OR 1.25, 95% CI 1.44-1.36), two comorbidities (OR 1.34, 95% CI 1.20-1.49) and three or more comorbidities (OR 1.31, 95% CI 1.18-1.46) (Table 4-2).

	Schizophrenia vs. Controls							Bipolar Disorder vs. Controls					
	Schizophrenia		Controls		Odds Ratio	95% Confidence Interval	p value	Bipolar Disorder		Controls		Odds Ratio	95% Confidence Interval	p value
	n	(%)	n	(%)				n	%	n	%			
No comorbidity	4,069	(2.05)	796,039	(56.27)	**0.61**	**0.58-0.64**	<0.001	929	(35.98)	799,179	(56.21)	**0.54**	**0.49-0.59**	<0.001
1 comorbidities	2,363	(24.42)	290,950	(20.57)	**1.22**	**1.16- 1.28**	<0.001	662	(25.64)	292,651	(20.58)	**1.25**	**1.14- 1.36**	<0.001
2 comorbidities	1,493	(15.43)	148,231	(10.48)	**1.37**	**1.29- 1.45**	<0.001	427	(16.54)	149,297	(10.50)	**1.34**	**1.20-1.49**	<0.001
3 comorbidities	1,752	(18.10)	179,481	(12.69)	**1.19**	**1.13- 1.27**	<0.001	564	(21.84)	180,669	(12.71)	**1.31**	**1.18- 1.46**	<0.001

Table 4-2   Odds Ratios of No, 1, 2 and 3 Comorbidities in Schizophrenia vs. Controls and Bipolar Disorder vs. Controls. Controlled for age, sex and deprivation

Bold if significant (p<0.001) difference between groups Adjusted for age, sex and deprivation status

For each of the thirty two individual physical health conditions assessed, the reported prevalence was significantly higher in individuals with schizophrenia for sixteen conditions including: viral hepatitis, constipation, Parkinson's disease, epilepsy, dyspepsia, liver disease, Irritable Bowel Syndrome (IBS), Diabetes, blindness, thyroid disease, chronic pain, psoriasis/eczema, bronchitis/COPD, migraine, asthma and hearing loss. Reported prevalence was lower for six conditions including: atrial fibrillation (AF), hypertension, coronary heart disease (CHD), cancer, peripheral vascular disease (PVD) and rheumatoid arthritis (RA). (Tables 4-3 and 4-4 and Figure 4-1).

Similarly for individuals with bipolar disorder fourteen conditions were reported more prevalently including: viral hepatitis, constipation, Parkinson's disease, thyroid disease, CKD, epilepsy, multiple sclerosis (MS), chronic pain, psoriasis/eczema, prostate disease, IBS, bronchitis/COPD, dyspepsia and Diabetes. The reported prevalence was lower for four chronic conditions including: AF, glaucoma, hypertension and CHD. (Tables 4-3 and 4-4 and Figure 4-1).

	Schizophrenia (n, %)		Controls (n ,%)		Bipolar Disorder (n, %)		Controls (n, %)	
Atrial Fibrillation (AF)	137	(1.42)	23,839	(1.69)	39	(1.51)	23,937	(1.68)
Hypertension	1,551	(16.03)	232,763	(16.45)	462	(17.89)	233,852	(16.45)
Coronary Heart Disease (CHD)	579	(5.98)	80,888	(5.72)	170	(6.58)	81,297	(5.72)
Cancer	288	(2.98)	43,376	(3.07)	115	(4.45)	43,549	(3.06)
Peripheral Vascular Disease (PVD)	167	(1.73)	23,073	(1.63)	59	(2.29)	23,181	(1.63)
Rheumatoid Arthritis (RA)	389	(4.02)	57,619	(4.07)	119	(4.61)	57,889	(4.07)
Prostate Disease	114	(1.18)	15,119	(1.07)	46	(1.78)	15,187	(1.07)
Glaucoma	123	(1.27)	15,796	(1.12)	28	(1.08)	15,891	(1.12)
Multiple Sclerosis (MS)	23	(0.24)	3,824	(0.27)	16	(0.62)	3,831	(0.27)
Chronic Kidney Disease (CKD)	291	(3.01)	33,275	(2.35)	189	(7.32)	33,377	(2.35)
Diverticular Disease	283	(2.92)	33,530	(2.37)	89	(3.45)	33,724	(2.37)
Bronchiectasis	23	(0.24)	2,791	(0.20)	5	(0.19)	2,809	(0.20)
Crohn's Disease	71	(0.73)	9,680	(0.68)	27	(1.05)	9,724	(0.68)
Stroke	350	(3.62)	36,195	(2.56)	89	(3.45)	36,456	(2.56)
Sinusitis	69	(0.71)	9,096	(0.64)	17	(0.66)	9,148	(0.64)
Heart Failure	196	(2.03)	18,703	(1.32)	47	(1.82)	18,852	(1.33)
Hearing Loss	495	(5.12)	54,239	(3.83)	134	(5.19)	54,600	(3.84)
Asthma	696	(7.19)	83,809	(5.92)	179	(6.93)	84,326	(5.93)
Migraine	79	(0.82)	9,172	(0.65)	18	(0.70)	9,233	(0.65)
Bronchitis/Chronic Obstructive Pulmonary Disease (COPD)	577	(5.96)	52,530	(3.71)	169	(6.55)	52,938	(3.72)
Psoriasis or Eczema	101	(1.04)	10,268	(0.73)	31	(1.20)	10,338	(0.73)
Pain	1,332	(13.76)	124,799	(8.82)	451	(17.47)	125,680	(8.84)
Thyroid Disease	738	(7.63)	71,205	(5.03)	376	(14.56)	71,567	(5.03)
Blindness	104	(1.07)	8,274	(0.58)	30	(1.16)	8,348	(0.59)
Diabetes	870	(8.99)	73,961	(5.23)	218	(8.44)	74,613	(5.25)
Irritable Bowel Syndrome (IBS)	540	(5.58)	51,597	(3.65)	148	(5.73)	51,989	(3.66)
Liver Disease	36	(0.37)	2,578	(0.18)	6	(0.23)	2,608	(0.18)
Dyspepsia	1,106	(11.43)	78,098	(5.52)	237	(9.18)	78,967	(5.55)
Epilepsy	213	(2.20)	12,171	(0.86)	47	(1.82)	12,337	(0.87)
Parkinson's Disease	73	(0.75)	2,668	(0.19)	19	(0.74)	2,722	(0.19)
Constipation	873	(9.02)	35,543	(2.51)	249	(9.64)	36,167	(2.54)
Viral Hepatitis	33	(0.34)	1,142	(0.08)	10	(0.39)	1,165	(0.08)

Table 4-3   Percentage reported prevalence of the 32 Common Physical Conditions in Schizophrenia Compared to Controls and Bipolar Disorder Compared to Controls

	Schizophrenia vs. Controls			Bipolar Disorder vs. Controls		
	Odds Ratio	95% Confidence Interval	p value	Odds Ratio	95% Confidence Interval	p value
Atrial Fibrillation (AF)	*0.62*	*0.52-0.73*	<0.001	*0.56*	*0.41-0.78*	<0.001
Hypertension	*0.71*	*0.67-0.76*	<0.001	*0.69*	*0.62- 0.77*	<0.001
Coronary Heart Disease (CHD)	*0.76*	*0.69- 0.83*	<0.001	*0.77*	*0.66-0.91*	0.002
Cancer	*0.81*	*0.72-0.92*	0.001	1.09	0.90- 1.32	0.38
Peripheral Vascular Disease (PVD)	*0.83*	*0.72- 0.97*	0.021	1.03	0.80 -1.34	0.81
Rheumatoid Arthritis (RA)	*0.83*	*0.75- 0.92*	<0.001	0.85	0.71-1.03	0.1
Prostate Disease	0.86	0.71- 1.04	0.11	**1.44**	**1.07-1.94**	0.02
Glaucoma	0.88	0.73-1.05	0.15	*0.63*	*0.43-0.92*	0.02
Multiple Sclerosis (MS)	0.89	0.59-1.34	0.564	**2.02**	**1.23- 3.31**	0.005
Chronic Kidney Disease (CKD)	0.96	0.85-1.08	0.484	**2.12**	**1.81-2.48**	<0.001
Diverticular Disease	0.97	0.86- 1.09	0.605	0.94	0.76-1.17	0.59
Bronchiectasis	1.00	0.66- 1.51	0.992	0.71	0.30-1.72	0.45
Crohn's Disease	1.03	0.81 - 1.30	0.803	1.38	0.94-2.01	0.1
Stroke	1.08	0.96- 1.20	0.196	0.89	0.72- 1.11	0.29
Sinusitis	1.10	0.87-1.40	0.422	0.92	0.57- 1.48	0.72
Heart Failure	1.15	1.00-1.33	0.057	0.90	0.67-1.21	0.48
Hearing Loss	**1.14**	**1.04- 1.26**	0.004	1.06	0.89- 1.27	0.49
Asthma	**1.22**	**1.13-1.31**	<0.001	1.13	0.97- 1.32	0.111
Migraine	**1.28**	**1.02- 1.60**	0.031	0.94	0.59- 1.50	0.8
Bronchitis/Chronic Obstructive Pulmonary Disease (COPD)	**1.31**	**1.20- 1.43**	<0.001	**1.38**	**1.18-1.62**	<0.001
Psoriasis or Eczema	**1.35**	**1.11-1.64**	0.003	**1.56**	**1.09-2.22**	0.02
Pain	**1.39**	**1.30-1.47**	<0.001	**1.72**	**1.55- 1.91**	<0.001
Thyroid Disease	**1.43**	**1.32- 1.55**	<0.001	**2.40**	**2.14- 2.70**	<0.001
Blindness	**1.44**	**1.18- 1.75**	<0.001	1.35	0.94-1.94	0.1
Diabetes	**1.49**	**1.39- 1.61**	<0.001	**1.30**	**1.13- 1.50**	<0.001
Irritable Bowel Syndrome (IBS)	**1.58**	**1.45-1.72**	<0.001	**1.41**	**1.19- 1.66**	<0.001
Liver Disease	**1.67**	**1.20-2.32**	0.002	1.18	0.53- 2.62	0.69
Dyspepsia	**1.93**	**1.81- 2.06**	<0.001	**1.35**	**1.18- 1.55**	<0.001
Epilepsy	**2.42**	**2.11-2.77**	<0.001	**2.05**	**1.53- 2.7**	<0.001
Parkinson's Disease	**3.07**	**2.43-3.89**	<0.001	**2.52**	**1.60-3.97**	<0.001
Constipation	**3.24**	**3.01 -3.49**	<0.001	**2.84**	**2.47-3.26**	<0.001
Viral Hepatitis	**3.99**	**2.82-5.64**	<0.001	**5.90**	**3.16- 11.03**	<0.001

Table 4-4   Odds Ratios of the 32 Common Physical Conditions in Schizophrenia Compared to Controls and Bipolar Disorder Compared to Controls
Italic- statistically less prevalent, normal font- no difference, **bold statistically more prevalent** Adjusted for age, sex and deprivation
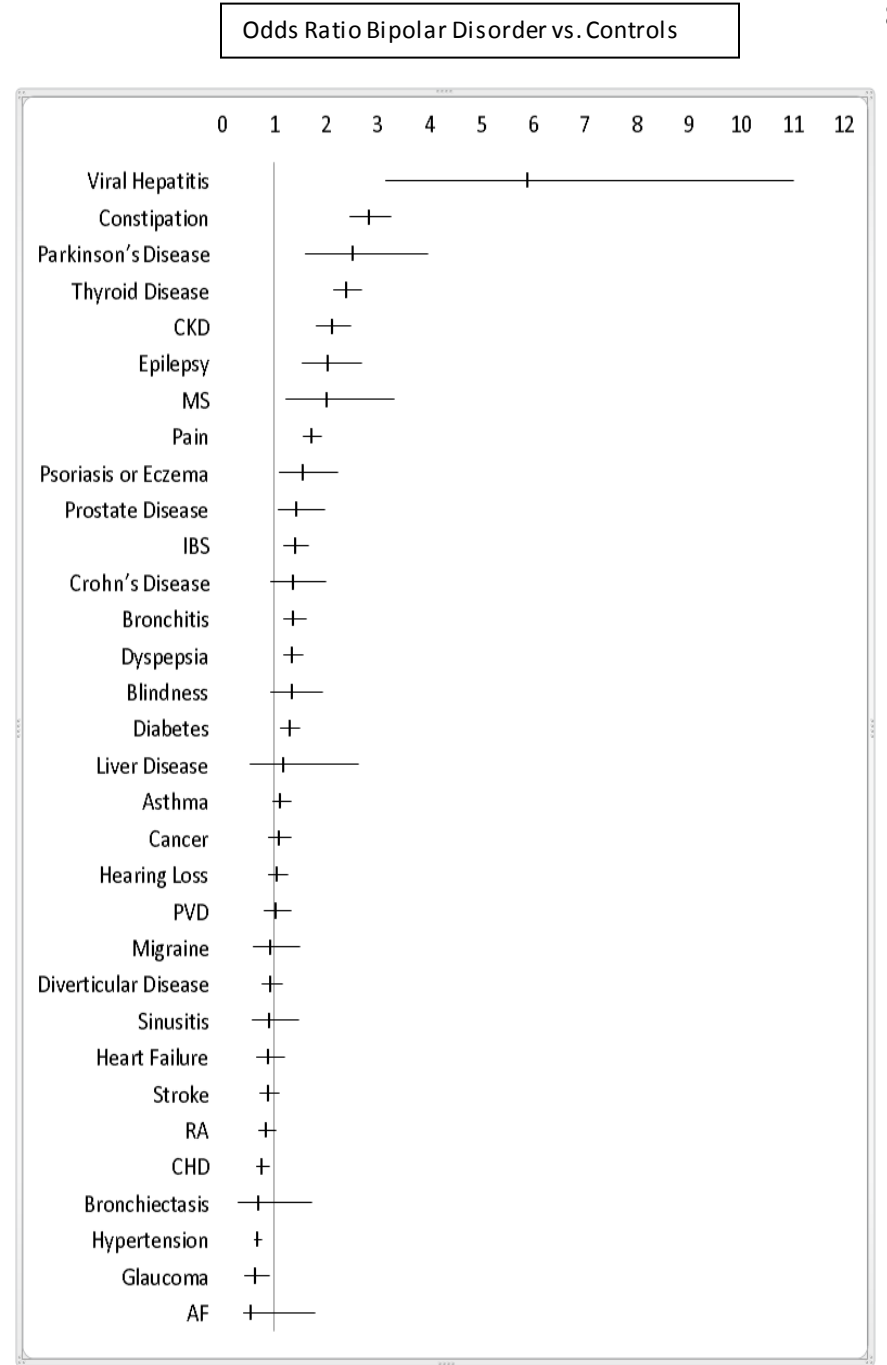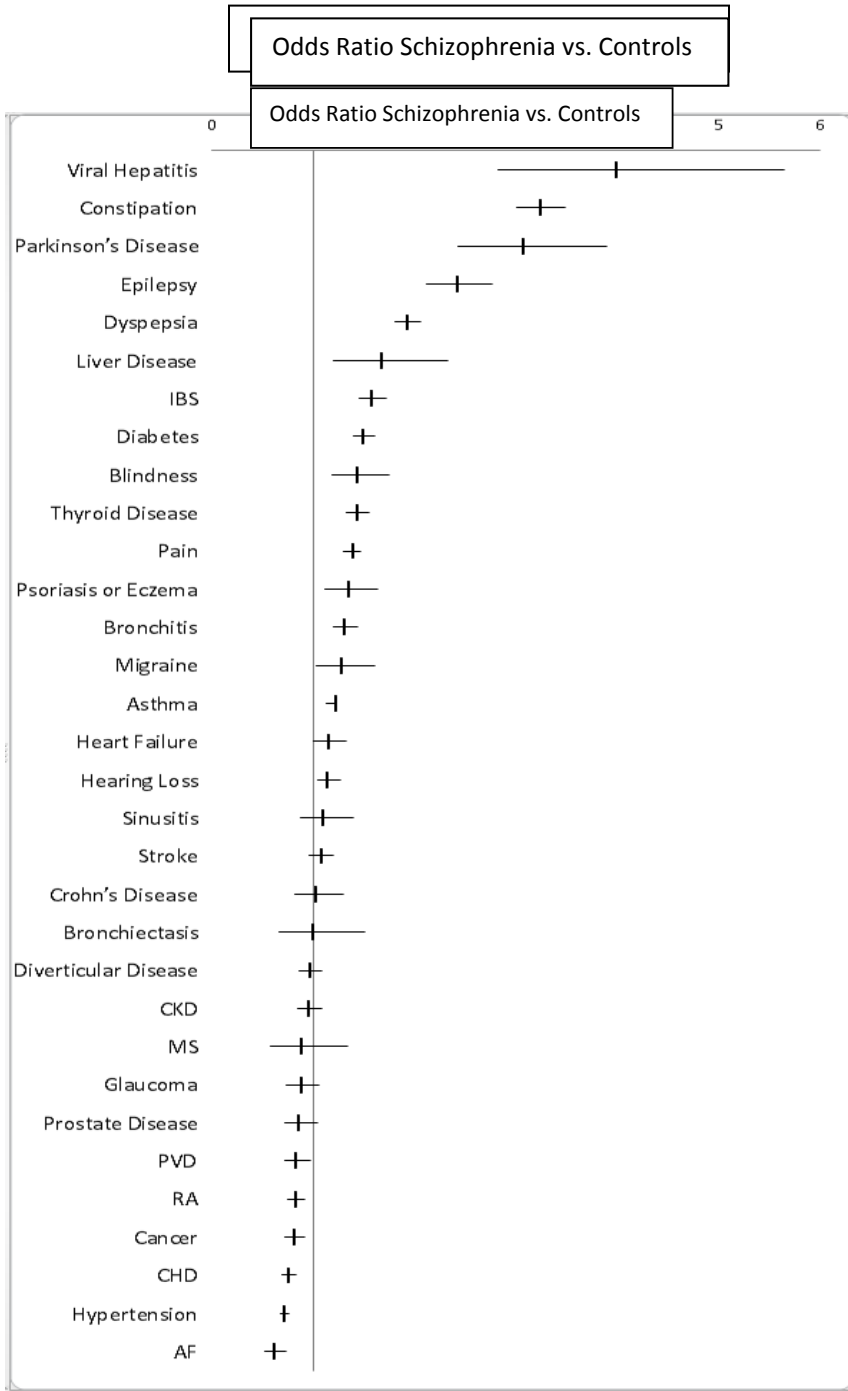
Figure 4-1 ORs for physical health comorbidities: Schizophrenia vs. Controls & Bipolar Disorder vs. Controls. Adjusted for age, gender & deprivation status.

The most recorded chronic physical health conditions in both individuals with schizophrenia and bipolar disorder were: viral hepatitis (OR 3.90 95% CI 2.82-5.64 and OR 5.90 95% CI 3.16-11.03 respectively), constipation (OR 3.24 95% CI 3.01-3.49 and OR 2.84 95% CI 2.47-3.26 respectively) and Parkinson's disease (OR 3.07 95% CI 2.43-3.89 and OR 2.52 95% CI 1.60-3.97 respectively) (Table 4-4).

Both groups had higher recorded rates of other chronic health conditions including: diabetes (9.0% vs. 5.2% p<0.001 and 8.4% vs. 5.3% p<0.001), bronchitis/COPD (6.0% vs. 3.7%, p<0.001 and 6.6% vs. 3.7%, p<0.001) and chronic pain (13.8% vs. 8.8%, p<0.001 and 17.5% vs. 8.8%, p=0.001). For individuals with bipolar disorder, Chronic Kidney Disease (CKD) was recorded much more frequently compared to controls (7.3% vs. 2.4%, p<0.001) (Table 4-3).

For the six conditions in which the relative reported prevalence in individuals with schizophrenia was lower, four were cardiovascular-related: AF (OR 0.62 95% CI 0.52-0.73), hypertension (OR 0.71 95% CI 0.67-0.76), CHD (OR 0.76 95% CI 0.69-0.83) and peripheral vascular disease (PVD) (OR 0.83 95% CI 0.72-0.97). Similarly in bipolar disorder of the four conditions where the relative reported prevalence was lower, three were cardiovascular-related: namely AF (OR 0.56 95% CI 0.41-0.78), hypertension (OR 0.69 95% CI 0.62-0.77) and CHD (OR 0.77 95% CI 0.66-0.91) (Table 4-3).

4.4.2 Gender Differences:

Differences between men and women with schizophrenia and bipolar disorder in terms of the number of recorded physical health comorbidities as well as age and deprivation status were assessed.

In the both groups on average women were older than men (55.6 vs. 47.8 years, p<0.001 schizophrenia group and 55.8 vs. 52.4 years, p<0.001 bipolar disorder group).

Recorded physical comorbidity was particularly common in women with schizophrenia, with over two thirds of women having at least one recorded comorbid physical condition, compared to half of men (Table 4-5). Women with schizophrenia

were significantly more likely to have two and three or more recorded physical health conditions than men with schizophrenia (18.1% vs. 12.9%, p<0.001 for two physical health conditions and 23.9% vs. 12.6%, p<0.001 for three or more physical health conditions) (Table 4-5).

Recorded physical comorbidity was also common in the bipolar disorder group, with over half of men and women having at least one recorded comorbid physical condition (Table 4-5). Women with bipolar disorder were significantly more likely to have three or more physical conditions recorded than men with bipolar disorder (25.0% vs. 17.0%, p<0.001) (Table 4-5).

	Schizophrenia Group					Bipolar Disorder Group				
	Male		Female			Male		Female		
Number, (%)	4,961	(51.27)	4,716	(48.73)		1,021	(39.54)	1,561	(60.46)	
Mean Age, sd	**47.78**	**(15.17)**	**55.59**	**(16.97)**	**Diff 7.80 (95%CI 7.16 to 8.44) p<0.001**	52.43	(15.08)	55.79	(15.28)	**Diff 3.36 (95% CI 2.16 to 4.56) p=<0.001**
Deprivation Mean	**0.77**	**(3.53)**	**0.29**	**(3.36)**	**Diff -0.48 (95% CI -0.62 to -0.34) p<0.001**	-0.40	(3.2)	-0.25	(3.33)	Diff 0.15 (95% CI -0.11 to 0.40) p=0.2687
Age Group (n,%)										
<25	**196**	**(3.95)**	**102**	**(2.16)**	**p<0.001**	20	(1.96)	25	(1.6)	p=0.498
25-34	**816**	**(16.45)**	**400**	**(8.48)**	**p<0.001**	**111**	**(10.87)**	**106**	**(6.79)**	**p<0.001**
35-44	**1,275**	**(25.70)**	**865**	**(18.34)**	**p<0.001**	**195**	**(19.10)**	**250**	**(16.02)**	**p<0.001**
45-54	1,111	(22.39)	968	(20.53)	p=0.025	253	(24.78)	373	(23.89)	p=0.608
55-64	**836**	**(16.85)**	**935**	**(19.83)**	**p<0.001**	214	(20.96)	333	(21.33)	p=0.821
65+	**727**	**(14.65)**	**1,446**	**(30.66)**	**p<0.001**	**228**	**(22.33)**	**474**	**(30.37)**	**p<0.001**
Deprivation Status (n,%)										
Least deprived-1	**582**	**(11.73)**	**678**	**(14.38)**	**p<0.001**	207	(20.27)	306	(19.60)	p=0.676
2	852	(17.17)	862	(18.28)	p=0.155	228	(22.33)	342	(21.91)	p=0.846
3	1,117	(22.52)	1,146	(24.30)	p=0.038	230	(22.53)	351	(22.49)	p=0.980
4	1,130	(22.78)	1,060	(22.48)	p=0.723	213	(20.86)	301	(19.28)	p=0.326
Most deprived 5	**1,280**	**(25.80)**	**970**	**(20.57)**	**p<0.001**	143	(14.01)	261	(16.72)	p=0.063
Multimorbidity (n,%)										
None	**2,492**	**(50.23)**	**1,577**	**(33.44)**	**p<0.001**	**430**	**(42.12)**	**499**	**(31.97)**	**p<0.001**
1	1,208	(24.35)	1,155	(24.49)	p=0.872	263	(25.76)	399	(25.56)	p=0.910
2	**638**	**(12.86)**	**855**	**(18.13)**	**p<0.001**	154	(15.08)	273	(17.49)	p=0.0108
3 or more	**623**	**(12.56)**	**1,129**	**(23.94)**	**p<0.001**	**174**	**(17.04)**	**390**	**(24.98)**	**p<0.001**

Table 4-5 Differences between men and women with schizophrenia and bipolar disorder Bold if significant (p<0.001) difference between groups Adjusted for age, sex and deprivation status

4.4.3 **Risk factor and prescribing differences**

4.4.3.1 **Coronary Heart Disease (CHD)**

579 individuals with recorded comorbid schizophrenia and CHD, 170 individuals with recorded comorbid bipolar disorder and CHD and 80,718 individuals with recorded CHD without schizophrenia or bipolar disorder were identified. Mean age of individuals with recorded comorbid schizophrenia and CHD and recorded comorbid bipolar disorder and CHD was lower than the mean age of individuals with recorded CHD only (69.3 years vs. 71.4 years, $p<0.001$ and 68.8 years vs. 71.4 years, $p=0.002$ respectively). Rate of smoking was higher in individuals with recorded schizophrenia and CHD (OR 1.92 95% CI 1.59-2.31, $p<0.001$) and in individuals with recorded bipolar disorder and CHD (OR 1.74 95% CI 1.24-2.45, $p<0.002$) compared to individuals with recorded CHD without MMI. Rates of recording of uncontrolled blood pressure and cholesterol were similar (Table 4-6).

There was no difference in rates of prescribing of aspirin or clopidogrel between individuals with recorded comorbid schizophrenia and CHD, individuals with recorded comorbid CHD and bipolar disorder and individuals with recorded CHD without MMI. Rate of prescribing of statins for individuals with recorded schizophrenia and CHD occurred significantly less frequently than in individuals with recorded CHD without MMI (OR 0.67 95% CI 0.56-0.80, $p<0.001$). Although prescribing of statins, tended to occur less frequently in individuals with recorded comorbid bipolar disorder and CHD compared to individuals with recorded CHD without MMI, the difference did not reach statistical significance (OR 0.72 95% CI 0.52-1.10, $p=0.059$) (Table 4-6).

Rates of prescribing of no anti-hypertensive were higher in individuals with recorded CHD and schizophrenia and recorded CHD and bipolar disorder compared to individuals with recorded CHD without MMI, when adjusted for age, sex and deprivation (OR 1.98 95% CI 1.63-2.40, $p<0.001$ and OR 2.53 95% CI 1.81-3.54, $p<0.001$ respectively). Rates of prescribing of 2 or more anti-hypertensives were lower in individuals with recorded CHD and schizophrenia and recorded CHD and bipolar disorder compared to individuals with recorded CHD without MMI, again

when adjusted for age, sex and deprivation (OR 0.66 95% CI 0.56-0.78, p<0.001 and OR 0.55 95% CI 0.46-0.67, p<0.001 respectively (Table 4-6).

	Schizophrenia & CHD (n=579)		CHD no MMI (n=80,718)		Odds Ratio (95% CI)	p value	Bipolar Disorder & CHD (n=170)		CHD no MMI (n=80,718)		Odds Ratio (95% CI)	p value
Male n, %	**288**	**(49.7)**	**46,101**	**(57.1)**		**<0.001**	84	(49.4)	46,101	(57.1)		0.043
Mean Age, sd	**69.3**	**(0.52)**	**71.4**	**(0.04)**		**<0.001**	68.8	(0.87)	71.4	(0.04)		0.002
Smoking	**204**	**(35.2)**	**16,809**	**(20.8)**	**1.92 (1.59-2.31)**	**<0.001**	55	(32.3)	16,809	(20.8)	1.74 (1.24-2.45)	0.002
Mean Carstairs Score, sd	0.19	(0.15)	0.07	(0.01)		0.3825	-0.38	(0.24)	0.07	(0.01)		0.073
Cholesterol >5 mmoll^{-1}	123 (n=501)	(24.6)	15,683 (n=73,034)	(19.4)	1.11 (0.90-1.36)	0.326	32	(18.8)	15,683	(19.4)	0.93 (0.63-1.38)	0.720
Uncontrolled BP	27	(4.7)	3,927	(4.9)	0.92 (0.62-1.366)	0.673	7	(4.1)	3,927	(4.9)	0.80 (0.37-1.71)	0.563
Aspirin/clopidogrel	435	(75.1)	59,275	(73.4)	1.09 (0.90-1.32)	0.359	119	(70.0)	59,275	(73.4)	0.85 (0.62-1.19)	0.350
Statin	**393**	**(67.9)**	**60,364**	**(74.8)**	**0.67 (0.56-0.80)**	**<0.001**	119	(70.0)	60,364	(74.8)	0.72 (0.52-1.01)	0.059
No Antihypertensive	**135**	**(23.3)**	**10,877**	**(13.5)**	**1.98 (1.63-2.40)**	**<0.001**	**48**	**(28.2)**	**10,772**	**(13.3)**	**2.53 (1.81-3.54)**	**<0.001**
1 Antihypertensive	155	(26.8)	21,294	(26.4)	1.01 (0.84-1.21)	0.953	50	(29.4)	21,294	(26.4)	1.14 (0.82-1.58)	0.444
2 or more Antihypertensive	**289**	**(49.9)**	**48,547**	**(60.1)**	**0.66 (0.56-0.78)**	**<0.001**	**72**	**(42.4)**	**48,547**	**(60.1)**	**0.49 (0.36-0.67)**	**<0.001**

Table 4-6   Differences between individuals with CHD & schizophrenia, Bipolar Disorder & CHD and individuals with CHD without MMI
ORs adjusted for Age, Sex and Socioeconomic Deprivation Status, Bold if significant.

4.4.3.2 **Hypertension**

1,551 individuals with recorded comorbid schizophrenia and hypertension, 462 individuals with recorded comorbid bipolar disorder and hypertension and 232,301 individuals with recorded hypertension without MMI were identified. There was no difference in mean age of individuals with recorded schizophrenia and hypertension or recorded bipolar disorder and hypertension compared to the mean age of individuals with recorded hypertension without MMI (66.0 years vs. 66.9 years, p=0.005 and 65.5 years vs. 66.9 years, p=0.016 respectively) (Table 4-7). Rate of smoking was higher in individuals with recorded schizophrenia and hypertension and recorded bipolar disorder and hypertension (OR 1.80 95% CI 1.60-2.02, p<0.001 and OR 2.04 95% CI 1.66-2.50, p<0.001 respectively). Rates of uncontrolled blood pressure were similar between the three groups (Table 4-7).

There was no difference in rates of prescribing of statins between individuals with recorded schizophrenia or bipolar disorder and hypertension and individuals with recorded hypertension without MMI. Rates of prescribing of no anti-hypertensive were higher in individuals with recorded hypertension and schizophrenia and recorded hypertension and bipolar disorder compared to individuals with recorded hypertension without MMI, when adjusted for age, sex and deprivation (OR 1.60 95% CI 1.41-1.82, p<0.001 and OR 1.59 95%CI 1.26-2.01, p<0.001 respectively). Rates of prescribing of two or more anti-hypertensives were lower in individuals with recorded hypertension and schizophrenia and recorded hypertension and bipolar disorder compared to individuals with recorded hypertension without MMI, when adjusted for age, sex and deprivation (OR 0.71 95% CI 0.64-0.78, p<0.001 and OR 0.55 95% CI 0.46-0.67, p<0.001 respectively) (Table 4-7).

	Schizophrenia & Hypertension (n=1,551)		Hypertension no MMI (n=232,301)		Odds Ratio (95% CI)	p value	Bipolar Disorder & Hypertension (n=462)		Hypertension no MMI (n=232,301)		Odds Ratio (95% CI)	p value
Male n, %	**581**	**(37.5)**	**102,713 (44.2)**			**<0.001**	168	(36.4)	102,713 (44.2)			0.0007
Mean Age, sd	66.0	(0.34)	66.9	(0.03)		0.0046	65.5	(0.55)	66.9	(0.03)		0.0156
Smoking	**433**	**(27.9)**	**39,755**	**(17.1)**	**1.80 (1.60-2.02)**	**<0.001**	**133**	**(28.8)**	**39,755**	**(44.2)**	**2.04 (1.66-2.50)**	**<0.001**
Mean Carstairs Score, sd	**0.18**	**(0.09)**	**-0.22**	**(0.01)**		**<0.001**	-0.61	(0.14)	-0.22	(0.01)		0.009
Uncontrolled BP	180	(11.6)	25,826	(11.1)	1.01 (0.87-1.19)	0.805	50	(10.8)	25,826	(11.1)	0.94 (0.70-1.27)	0.704
Statin	651	(42.0)	96,284	(41.4)	1.06 (0.96-1.18)	0.257	168	(36.4)	96,284	(41.4)	0.87 (0.72-1.06)	0.160
No Antihypertensive	**304**	**(19.6)**	**30,183**	**(13.0)**	**1.60 (1.41-1.82)**	**<0.001**	**91**	**(19.7)**	**30,183**	**(13.0)**	**1.59 (1.26-2.01)**	**<0.001**
1 Antihypertensive	504	(32.5)	70,089	(30.2)	1.10 (0.99-1.23)	0.073	**180**	**(39.0)**	**70,089**	**(30.2)**	**1.44 (1.19-1.74)**	**<0.001**
2 or more Antihypertensive	**743**	**(47.9)**	**132,029 (56.8)**		**0.71 (0.64-0.78)**	**<0.001**	**191**	**(41.3)**	**132,029 (56.8)**		**0.55 (0.46-0.67)**	**<0.001**

Table 4-7 Differences in individuals with Hypertension and Schizophrenia, Hypertension and Bipolar Disorder and individuals with Hypertension without MMI

Odds ratios adjusted for Age, Sex and Socioeconomic Deprivation Status. Bold if significant

4.5 Discussion:

4.5.1 General Findings:

In keeping with several other reports (Laursen et al., 2011; Crump et al., 2013; Carney et al., 2016; De Hert et al., 2011a) multiple physical health comorbidity was common in individuals with schizophrenia and bipolar disorder. Almost half (43.7%) of individuals with recorded schizophrenia had at least one recorded chronic physical comorbidity and one third had two or more. Almost two thirds (64.0%) of individuals with bipolar disorder had a least one recorded chronic physical health comorbidity. The finding of increased recorded comorbidity in individuals with bipolar disorder compared to individuals with schizophrenia has been reported elsewhere (Oreški et al., 2012), although in a small cohort (197 individuals with schizophrenia and 92 individuals with bipolar disorder). Our findings therefore added to the limited studies in this area.

4.5.2 Specific Conditions:

Three chronic physical health conditions were found to be particularly more commonly recorded in individuals with schizophrenia and bipolar disorder (viral hepatitis, constipation and Parkinson's disease). High recording rates of epilepsy, chronic pain, IBS and dyspepsia in individuals with schizophrenia and bipolar disorder were also found. Individuals with schizophrenia and bipolar disorder often have higher rates of drug misuse compared to the general population (Tohen et al., 1998) and so may be at higher risk of viral hepatitis through drug taking behaviours. This may partly explain the higher recorded rates of viral hepatitis. Constipation is an important though often under-recognised side-effect of antipsychotic medication (Nielsen and Meyer, 2012; De Hert et al., 2011b) and lithium treatment and was more commonly recorded in individuals with schizophrenia and bipolar disorder compared to controls. It is estimated that between 20 and 30% of all individuals taking antipsychotic medications will have constipation and so these findings may be an under-estimate. Recording of Parkinson's disease (which included Parkinsonism) was also significantly more common in the schizophrenia and bipolar disorder groups than in controls. This may partially be explained by an increase in Read Codes of Parkinsonism due to extra-pyramidal side-effects of antipsychotic medication.

Recorded rates of diabetes, chronic pain and bronchitis in individuals with bipolar disorder and schizophrenia were also found to be higher compared to controls even when controlling for age, sex and deprivation status. This is perhaps not unexpected, partly due

to the high rates of obesity and high rates of smoking that is often reported in individuals with bipolar disorder and schizophrenia (Myles et al., 2012). High recorded rates of chronic kidney disease (CKD) and thyroid disease were also found in the bipolar disorder cohort and may be partly as a consequence of known treatment side effects. For example lithium is known to cause both thyroid and renal dysfunction.

4.5.3 Cardiovascular comorbidity:

Of the six conditions which were recorded less frequently in individuals with schizophrenia four were for cardiovascular disorders: namely AF, hypertension, CHD and PVD. Similarly in the bipolar disorder cohort recorded rates of AF, hypertension and CHD were significantly lower compared to the control population. This was somewhat unexpected, especially in the context of several studies reporting high rates of cardiovascular morbidity and mortality in individuals with schizophrenia and bipolar disorder (Laursen et al., 2011; Crump et al., 2013).

However a population-based study of administrative claims data in the United States had similar findings: they found that rates of hypertension and ischaemic heart disease were lower than expected in individuals with schizophrenia compared to controls (Carney et al., 2006). Similarly, a recent meta-analysis of prescribing data for individuals with and without major mental illness (including schizophrenia) found that individuals with severe mental illness had lower than expected rates of being prescribed medications for cardiovascular disease (Mitchell et al., 2012). Furthermore, in a recent Swedish national cohort study, although individuals with schizophrenia were more likely to die prematurely than the general population and the leading causes of death were cardiovascular disease and cancer, rates of recording of cardiovascular disease and cancer were not particularly elevated in individuals with schizophrenia (Crump et al., 2013). This was despite an increase in healthcare system contacts, suggesting that cardiovascular disease and cancer were significantly under-diagnosed and/or under-recorded in this population. This may also be true for the SPICE cohort and may partly explain the findings.

However there may be several other possible explanations for these findings. Although rates of consultation in individuals with MMI are generally comparable to the general population (Dickerson et al., 2003) information on number of healthcare contacts was not available for this dataset. It is possible that in this cohort, individuals with schizophrenia or bipolar disorder may not consult their GP as frequently as the general population, due to an

expectation that their physical health needs will be met by their community mental health team (CMHT). Some individuals may also have low awareness of symptoms of cardiac or vascular disease and so may not present to their GP, leading to under-recording and under-diagnosis of physical health problems (De Hert, 2011c).

It is also possible that relatively asymptomatic conditions such as hypertension and AF are less likely to be identified than constipation, IBS, Parkinson's disease, dyspepsia and epilepsy and this too may partly explain these findings. It is also possible that, even when these individuals attend, GPs may not be assessing and/or recording cardiac problems as often as they might (Mackell et al., 2005). It has been recognised that individuals with mental illness and comorbid physical health problems do not receive the same level of assessment and treatment for their physical problems as individuals without mental illness (Thornicroft et al., 2009; Druss et al., 2001). There is also the additional difficulty of diagnostic over-shadowing- whereby symptoms of physical illnesses may be attributed to the individual's mental illness (Nash, 2013). These factors may all contribute to the lower than expected recording rates of AF, hypertension and CHD in this cohort.

Hypertension was the most commonly recorded comorbidity in individuals with schizophrenia and bipolar disorder, but it was significantly less commonly recorded than in the control group. This may be due to the use of antihypertensive agents for symptoms such as anxiety or akathisia in individuals with schizophrenia and bipolar disorder or the hypotensive effect of some antipsychotic medications. However it may also be due to the occurrence of less frequent monitoring of blood pressure (BP) in primary care for individuals with schizophrenia and bipolar disorder relative to controls. This would be of concern given the NICE guidelines which recommend BP monitoring for individuals with schizophrenia who are prescribed antipsychotic medication (NICE Clinical Guideline 82, 2009).

4.5.4 Risk factors and Prescribing Differences:

Rates of smoking in individuals with comorbid schizophrenia and hypertension, comorbid schizophrenia and CHD, comorbid bipolar disorder and hypertension and comorbid bipolar disorder and CHD were significantly higher than in individuals with hypertension and CHD without schizophrenia and bipolar disorder. The finding of high smoking rates in individuals with schizophrenia and bipolar disorder compared to the general population has been reported elsewhere (Myles et al., 2012). However this specific finding of higher

smoking rates in individuals with schizophrenia or bipolar disorder and comorbid physical health problems is of clinical concern given the adverse effects on health smoking is known to have.

For the prescribing data, a significantly lower rate of statin prescribing in individuals with comorbid CHD and schizophrenia compared to individuals with CHD without schizophrenia and bipolar disorder was found. A trend towards lower rates of statin prescribing in individuals with comorbid CHD and bipolar disorder compared to individuals with CHD without schizophrenia and bipolar disorder was also found. This is of clinical significance as for individuals with CHD; statins are recommended for all individuals regardless of their pre-treatment cholesterol. Therefore a reduction in statin prescription is indicative of a missed opportunity to deliver a specific evidence based intervention.

For individuals with CHD and schizophrenia and CHD and bipolar disorder, significantly higher rates of no anti-hypertensive prescription and significantly lower rates of two or more anti-hypertensives being prescribed were found; this potentially points towards less intensive treatment of blood pressure in individuals with schizophrenia and bipolar disorder. This finding of possible reduced intensity of treatment was replicated in the hypertensive cohort: where individuals with schizophrenia and hypertension and bipolar disorder and hypertension had higher rates of none and one anti-hypertensive being prescribed but lower rates of two or more anti-hypertensives being prescribed compared to individuals with hypertension without schizophrenia and bipolar disorder.

The findings of disparities in prescribing patterns have been reported elsewhere (Mitchell et al., 2012) and possible reasons for this are complex, multifactorial and may arise at both a primary and secondary care level. GPs, who initiate most pharmacological treatments for cardiovascular disease, may not feel confident in managing potential drug interactions between psychotropic medications and pharmacological treatments for cardiovascular disease. Concerns about suicide risk and the potential toxicity of some of the anti-hypertensive medications should they be taken in overdose may also contribute to over-cautious prescribing.

GPs may not feel confident in their interactions with individuals with MMI and so may be less likely to follow up individuals with comorbid MMI and physical health problems (Fleury et al., 2009). Physical health problems (such as hyperlipidaemia) may occur at a

young age in individuals with MMI, and GPs may be unsure about the necessity to treat given the current cardiovascular risk algorithms that are used to estimate cardiovascular risk. Cardiovascular risk in individuals with schizophrenia and bipolar disorder may be under-estimated by existing cardiovascular risk estimation tools (which include Framingham, ASSIGN and QRISK and are weighted heavily by age). These tools have not been validated in individuals with MMI (Holt, 2014) and so under-estimation of risk, may add to the difficulties of under-recognition and under-treatment of these conditions.

Mental health professionals also may not be confident in prescribing medications for primary and secondary prevention and may not appropriately diagnose physical health problems in their patients (Koranyi 1979; Felker et al., 1996) potentially due to incomplete physical examinations (Koran et al., 1989).

The issue of rates of attendance at GP appointments and outpatient clinics in order to initiate medications to treat physical illness in individuals with MMI is also unclear. Some studies report that individuals with MMI have a higher frequency of healthcare visits and so are more likely to experience guideline recommended care for their comorbid physical health condition (Kurdyak and Gnam, 2004) while other reports suggest that attendance at such appointments and concordance with treatment may be reduced. Nonetheless it is likely that adherence to the cardiovascular medications prescribed may be even less than this data suggests and so the disparity in health care provision may be even wider than is reported here.

4.6 Strengths and limitations:

Strengths include the large sample size and so it is likely to be representative of the wider Scottish population. The rate of a recorded diagnosis of schizophrenia or related psychotic disorder of 0.7% is similar to most estimates of the prevalence of schizophrenia of around 1% (Saha et al., 2008). Estimates of the incidence and prevalence of schizophrenia varies widely by geographical location, largely due to differences in population characteristics and diagnostic assessment. However it is probable that some individuals with schizophrenia or a related psychotic disorder are known only to secondary care services (and so are not recorded within primary care) and therefore are not recorded in this dataset. It is also possible that a small additional proportion may not be in contact with either primary or secondary care and thus are missing from the study population. Both possibilities represent a limitation of this data.

The rate of a recorded diagnosis of bipolar disorder was 0.2%. Most estimates of the prevalence of bipolar disorder are 1% (Ferrari et al., 2011) and so this is lower than predicted. Possible reasons for this may include the under-diagnosis of bipolar disorder within primary care, which may potentially reflect the considerable debate and variation in the definition of this condition. As is the case with schizophrenia, it is also possible that some individuals with bipolar disorder are known only to secondary care services and are not recorded within primary care and additionally a small proportion may not be in contact with either primary or secondary care. Data from 314 primary care practices was included in the SPICE dataset and it is likely that there is variation in the diagnostic coding for bipolar disorder within the practices. Given the relatively low prevalence of bipolar disorder, in this sample, it is likely that the individuals included represent the more severe end of the bipolar spectrum. However it must also be acknowledged that the lower than expected rates of recording of Bipolar Disorder, may introduce a potential risk of bias, perhaps due to increased illness severity. It is also possible that a small number of individuals on lithium, may have been coded as Bipolar Disorder without the consideration of a diagnosis of possible treatment resistant depression. This may also be reflected in the increased recorded prevalence of Chronic Kidney Disease (CKD) in the Bipolar group.

Within the Read Code definitions used, a number of individuals in the bipolar disorder group had a Read code of 'severe/psychotic depression'. Severe or psychotic depression may be an early manifestation of bipolar disorder (Joseph et al., 2001) however psychotic features are present in a minority of cases of major unipolar depression (Johnston et al., 1991). Due to limitations in the way data was extracted it was not possible to separate out the individuals with psychotic depression from the bipolar disorder group. However given that 11 out of the 13 Read Codes were for definite bipolar disorder diagnoses, it is estimated that the proportion of individuals in this sample with psychotic unipolar depression as opposed to bipolar disorder would have been very low. However this does represent a further limitation of this data.

The data utilised, is routine primary care data from 314 practices and there is likely to be variability of diagnostic coding for the thirty two conditions of interest. While routine data is reflective of 'real world' practice, there are some limitations associated with this type of study. The use of primary care Read Codes to identify bipolar disorder, schizophrenia and a combination of Read Codes and where relevant prescribing data to identify the thirty two medical comorbidities also has limitations. While this method represents a balance between diagnostic accuracy and real-world representativeness, some of the Read Code

estimates for certain conditions may have been prone to bias: for example, higher recorded rates of thyroid disease for bipolar individuals may be related to more frequent venepuncture associated with medication (lithium) monitoring. It is also possible that in addition to the under-recognition and under-recording of cardiovascular disease in individuals with schizophrenia and bipolar disorder, some of the prevalence rates for the other physical health comorbidities included may be underestimates. This is a limitation of the design of the study in general, whereby Read Codes and/or prescribing data without confirmatory interviews were used to define diagnoses.

4.7 Conclusions:

Overall, these data suggest that individuals with schizophrenia and bipolar disorder in a Scottish Primary Care setting have high rates of recorded multiple comorbid physical health problems but lower rates of recording of certain cardiovascular diseases. The data also suggests that individuals with schizophrenia and bipolar disorder are less likely to have their cardiovascular illnesses treated as intensively as individuals without MMI. Further investigation of possible reasons for the differences in healthcare provision is required. Further training for GPs, Psychiatrists and Physicians to build confidence in prescribing and addressing the lifestyle risk factors of these individuals is recommended to ensure that a multidisciplinary focus on improving physical health investigation, diagnosis, treatment and monitoring occurs. This may then help to address the inequality in life expectancy experienced by individuals with MMI.

Given the interaction between physical and mental health problems leading to prolonged hospitalisation, treatment failure, poor quality of life (de Hert, 2011a) and premature mortality, these findings highlight the need for an integrated approach to care (Leucht et al., 2007; Truyers et al., 2011). The current separation between specialist physical and mental health services, and between primary and secondary care services in the UK and in other countries, makes the care of the physical health of individuals with schizophrenia and bipolar disorder difficult to co-ordinate. This can lead to fragmented, disjointed care. Several reports have highlighted that more integrated services are needed but the best way to achieve this remains unclear (The Kings Fund, 2012: Department of Health, 2011: London School of Economics, 2012: Schizophrenia Commission, 2012).

Integrated care, defined as the delivery of preventive and curative health services which vary according to the individual's needs over time and across different levels of the

healthcare system, can be difficult to achieve. Given that cardiovascular risk assessment is acceptable to many people with psychosis (Osborn et al., 2003), potentially a more systematic use of such screening in both primary and secondary care may improve early detection and treatment of hypertension and CHD. However further research is needed to evaluate the effectiveness of such approaches.

Chapter 5: Smoking Status, cessation advice and prescribing of Nicotine Replacement Therapy (NRT) in individuals with Major Mental Illness (MMI):

Chapter Overview:

This chapter uses the SPICE dataset to describe in detail recorded rates of current smoking, ex-smoking and non-smoking in individuals with: Major Mental Illness (MMI), individuals with MMI and comorbid diabetes, coronary heart disease (CHD) or hypertension and individuals with diabetes, coronary heart disease (CHD) or hypertension without MMI. Rates of current smoking, ex-smoking and non-smoking in individuals with bipolar disorder and schizophrenia are also compared. Within these groups, rates of recording of smoking cessation advice and prescribing of nicotine replacement therapy (NRT) are compared as a marker of potential inequality in access to healthcare advice and treatment.

5.1 Background:

As highlighted in Chapter 1, tobacco use remains the single leading cause of preventable disease and premature death in the world (WHO Report, 2011). Despite a considerable reduction in tobacco use in developed countries, over the past few decades it remains particularly common in individuals with MMI, with estimates that 70% of individuals with schizophrenia and 45% of individuals with bipolar disorder smoke compared to 20% of the general population (Myles et al., 2012). Additionally there is evidence that individuals with MMI smoke more cigarettes compared to the general population and individuals with schizophrenia extract more nicotine from each cigarette compared to the general population (Olincy et al., 1997). Given the fact that individuals with MMI have increased standardised mortality rates (SMR) compared to the general population (Hoang et al., 2011; Wahlbeck et al., 2011; Laursen et al., 2011; Crump et al., 2013) and approximately two-thirds of this premature mortality is due to cardiovascular disease, smoking-related lung disease and type II diabetes (Tiihonen et al., 2009; Saha et al., 2007; Laursen et al., 2007; Heila et al., 2005) strategies to improve the health of this cohort of individuals is imperative.

In the UK, where cigarette smoking accounts for over 100,000 deaths annually (Doll et al., 2004), cessation of smoking is thought to be the single most important and cost effective method for improving an individual's health and wellbeing (Peto et al., 2005). Primary care health professionals in particular have an important role in helping smokers stop smoking. Recording of smoking status is important as it is recognised that in cases where smoking is recorded prominently in medical records, physicians are more likely to address issues regarding smoking (Boyle et al., 2010). Moreover, brief advice against smoking is recognised as not only a simple intervention to deliver, but also as an effective intervention in promoting abstinence (Stead et al., 2008a).

Prescribing of Nicotine Replacement Therapy (NRT) in the form of patches, lozenges, gum, tablets, nasal or mouth spray in primary care, is an important and effective lifestyle modification intervention which is known to increase the chance of smoking cessation compared to placebo or no NRT use (Stead et al., 2008b; Silagy et al., 2002). Anti-craving medications including varenicline and bupropion are also effective strategies in smoking cessation (Cahill et al., 2007) but their use is limited in individuals with a history of mental illness, due to the risk of mood disturbance and suicidal behaviour particularly with varenicline (BNF, 2014). Given the particularly high rates of smoking and high nicotine load in individuals with MMI, NRT may be particularly helpful in promoting abstinence.

There is evidence to suggest that despite the increased physical health problems experienced by individuals with MMI, there are inequalities for both the access to and the quality of a range of physical healthcare services as detailed in Chapter 1. However it is unknown if these inequalities occur in either the recording of smoking cessation advice or in NRT prescribing trends within primary care in Scotland. These questions are therefore the focus of this chapter.

5.2 Aims:

1. To describe the rates of recording of smoking, ex-smoking and non-smoking in individuals with MMI compared to other chronic diseases (namely diabetes, coronary heart disease (CHD) and hypertension) in primary care.

2. To determine whether rates of recording of smoking cessation advice in individuals with MMI differ from the rates of recording of smoking cessation advice in individuals with other chronic diseases (diabetes, CHD and hypertension).

3. To determine whether rates of Nicotine Replacement Therapy (NRT) prescription in individuals with MMI differ from the rates of NRT prescription in individuals with other chronic diseases (diabetes, CHD and hypertension).

4. To determine if there are differences in: rates of smoking, ex-smoking and non-smoking, rates of recording of smoking cessation advice and rates of Nicotine Replacement Therapy (NRT) prescription in individuals with schizophrenia compared to bipolar disorder.

5.3 Methodology:

The dataset from the Scottish Primary Care Clinical Informatics Unit at the University Of Aberdeen (SPICE), detailed in Chapter 3 was used. As in the previous studies, individuals were identified as having Major Mental Illness (MMI) based on the recording ever of the schizophrenia and bipolar disorder Read Codes listed in Chapter 4.

Individuals with diabetes, without MMI were identified from the Read Codes C10E.% and C10F.% (with C10F8 excluded). Individuals with coronary heart disease, without MMI were identified from Read codes G3... - G330z, G33z. - G3401, G342. - G366., G38.. – G3z..and Gyu3 and individuals with hypertension without MMI were identified using their appropriate Read Codes (G2..., G20..%, G24.. - G2z.. (Excluding G24z1)). Individuals with comorbid MMI and diabetes, comorbid MMI and CHD and comorbid MMI and hypertension were analysed as a separate group. Within the MMI cohort individuals with schizophrenia and bipolar disorder were compared as a separate analysis.

As before, analyses of this data were restricted to individuals aged 18 and over and the sample was divided into the following age groups for analysis: <25, 25-34, 35-44, 45-54, 55-64 and 65 and older. Deprivation status was measured using the Carstairs deprivation score. Rates of multimorbidity were also noted. Smoking status was coded as current smoker, ex-smoker or non-smoker using the Read Codes included in Appendix 3. Where tobacco consumption was unknown or not recorded, smoking status was coded as missing. Smoking cessation advice was coded as being given if the Read Codes included in Appendix 4 were recorded in the primary care record. Prescription of NRT was coded if there was a recording of prescribing of NRT in the form of patches, gum, lozenges, inhalator or nasal spray included in an individual's primary care record. These are detailed in Appendix 5. To ensure only current prescriptions were captured, prescribing data from the 84 days prior to the date that the dataset was obtained were included.

Logistic regression was used to calculate odds ratio (ORs) and 95% confidence intervals (CI) of smoking, ex-smoking and non-smoking in individuals with MMI with and without the comorbid chronic disease (diabetes, CHD and hypertension) compared to individuals with the chronic disease without MMI. Differences in individuals with MMI without the chronic disease, individuals with comorbid MMI and the chronic disease and individuals with the chronic disease without MMI were calculated by age, deprivation and number of physical health conditions. T tests were used to analyse differences between groups and Chi squared tests for differences across age groups and deprivation quintiles. Odds ratios (ORs) with 95% confidence intervals for recording of smoking cessation advice and NRT prescription for smokers with MMI with and without the chronic disease of note compared to individuals with the chronic disease without MMI were also calculated. Odds ratio calculations were adjusted for age, gender and deprivation.

The analyses were then repeated comparing rates of smoking, ex-smoking and non-smoking along with rates of recording of smoking cessation advice and NRT prescription in individuals with schizophrenia and bipolar disorder.

5.4 Results:

5.4.1 Rates of Smoking in MMI compared to the Controls

From 1,426,670 individuals aged over 18: 12,259 individuals with MMI (0.9%) and 1,414,411 individuals without MMI (99.1%) were identified. Recording of smoking status was available in the majority of cases, however missing data occurred significantly more frequently in individuals without MMI (controls) (10.0%) compared to individuals with MMI (3.8%) (Table 5-1).

	MMI (n=12,259)		Controls (n=1,414,411)	
Smoking recorded	**11,788**	**(96.2)**	1,272,289	(90.0)
Missing data on smoking	**471**	**(3.8)**	142,122	(10.0)

Table 5-1   Rates of recording of smoking status in individuals with/without MMI
Bold if significant (p<0.001)

When smoking status was recorded, rates of smoking were higher in individuals with MMI compared to the individuals without MMI (47.5% vs. 27.0% p<0.001). Rates of ex-smoking and non-smoking were significantly lower in individuals with MMI compared to individuals without MMI (18.8% vs. 21.4%, p<0.001 and 33.7% vs. 51.6%, p<0.001 respectively) (Table 5-2).

The odds ratio for smoking, was higher in individuals with MMI (2.53 95% CI 2.44-2.63) compared to individuals without MMI and was particularly increased in men (2.83 95% CI 2.68-2.98). Odds ratio for ex-smoking and non-smoking were lower for individuals with MMI compared to individuals without MMI (0.79 95% CI 0.75-0.83 and 0.50 95% CI 0.48-0.52) (Table 5-2).

	MMI (n=11,788) (%)	Controls (n=1,272,289) (%)	Odd Ratio MMI vs. Controls	
Smoker	5,604 (47.5)	343,804 (27.0)	All[1] 2.53 (2.44-2.63) Males[2] 2.83 (2.68-2.98) Females[2] 2.28 (2.16-2.40)	
Ex-Smoker	2,213 (18.8)	271,957 (21.4)	All[1] 0.79 (0.75-0.83) Males[2] 0.76 (0.71-0.81) Females[2] 0.87 (0.81-0.92)	
Non Smoker	3,971 (33.7)	656,528 (51.6)	All[1] 0.50 (0.48-0.52) Males[2] 0.42 (0.40-0.45) Females[2] 0.55 (0.53-0.58)	

Table 5-2   Odds Ratio of smoking, ex-smoking and non-smoking in individuals with/without MMI

Bold if significant (p<0.001) [1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

5.4.2 MMI compared to Diabetes:

From 1,426,670 individuals aged over 18: 73,743 individuals with diabetes without MMI (5.2%), 11,171 individuals with MMI without diabetes (0.8%) and 1,088 individuals with MMI and diabetes (0.08%) were identified. Recording of smoking status was available in the majority of cases, however missing data occurred significantly more frequently in individuals with MMI (4.1%) compared to individuals with MMI and diabetes (0.7%) and individuals with diabetes without MMI (0.6%) (Table 5-3).

	MMI No Diabetes (n=11,171) (%)		MMI & Diabetes (n=1,088) (%)		Diabetes No MMI (n=73,743) (%)	
Missing data on smoking	**463**	**(4.1)**	8	(0.7)	423	(0.6)
Smoking recorded	**10,708**	**(95.9)**	1,080	(99.3)	73,311	(99.4)

Table 5-3   Rates of recording of smoking status in individuals with/without MMI with/without diabetes

Bold if significant (p<0.001) compared to those with Diabetes without MMI

In individuals who had their smoking status recorded, men with diabetes made up a greater proportion compared to individuals with MMI without diabetes (53.1% vs. 48.9%, p<0.001) and MMI and diabetes (53.1% vs. 41.1%, p<0.001). Mean age of individuals with diabetes who had their smoking status recorded was higher than the mean age of individuals with MMI without diabetes (63.5 vs. 51.5 years, p<0.001) and MMI and diabetes (63.5 vs. 60.6 years, p<0.001). Rate of having three or more additional physical health problems was most common in individuals with MMI and diabetes (60.3%) (Table 5-4).

All	MMI No Diabetes (n=10,708)		p value	MMI & Diabetes (n=1,080)		p value	Diabetes No MMI (n=73,311)	
Male n, %	5,231	(48.9)	<0.001	444	(41.1)	<0.001	38,917	(53.1)
Mean Age, sd	51.5	(0.16)	<0.001	60.6	(0.43)	<0.001	63.5	(0.05)
Age Group								
<25	294	(2.7)	<0.001	14	(1.3)	0.719	1,046	(1.4)
25-34	1,315	(12.3)	<0.001	63	(5.8)	<0.001	2,133	(2.9)
35-44	2,371	(22.1)	<0.001	183	(16.9)	<0.001	5,154	(7.0)
45-54	2,398	(22.4)	<0.001	240	(22.2)	<0.001	10,001	(13.6)
55-64	1,997	(18.6)	<0.001	163	(24.4)	<0.001	16,840	(23.0)
65+	2,333	(21.8)	<0.001	317	(29.4)	<0.001	38,137	(52.0)
Mean Carstairs Score, sd	0.35	(0.03)	<0.001	0.43	(0.11)	<0.001	0.05	(0.01)
Deprivation Status								
Least deprived-1	1,554	(14.5)	0.009	157	(14.5)	0.393	11,351	(15.5)
2	2,006	(18.7)	<0.001	187	(17.3)	0.003	15,437	(21.1)
3	2,499	(23.3)	0.118	251	(23.2)	0.548	17,615	(24.0)
4	2,339	(21.8)	<0.001	252	(23.3)	0.004	14,510	(19.8)
Most deprived 5	2,310	(21.6)	<0.001	253	(21.6)	0.002	14,398	(19.6)
Additional morbidities								
0	2,084	(19.5)	<0.001	74	(6.9)	<0.001	9,760	(13.3)
1	2,790	(26.1)	<0.001	146	(13.5)	<0.001	14,934	(20.2)
2	2,266	(21.2)	<0.001	209	(19.4)	0.885	14,316	(19.5)
3+	3,568	(33.3)	<0.001	651	(60.3)	<0.001	34,401	(46.9)

Table 5-4 **Demographics of individuals with/without MMI with/without diabetes who have had their smoking status recorded**
Bold if significant (p<0.001) compared to those with Diabetes without MMI

5.4.2.1 Rate of Smoking in MMI vs. Diabetes:

When smoking was recorded, rates of smoking were highest in individuals with MMI without diabetes (48.6%) followed by MMI and diabetes (37.1%). Rates of ex-smoking were highest in individuals with diabetes without MMI (35.8%) as were rates of non-smoking (44.3%) (Table 5-5).

In individuals with comorbid MMI and diabetes, rates of smoking were significantly lower and rates of ex-smoking significantly higher compared to individuals with MMI without diabetes. There was no difference in non-smoking rates between individuals with MMI without diabetes and individuals with comorbid MMI and diabetes (Table 5-5).

The odds ratio for smoking, was highest in individuals with MMI without diabetes (2.68 95% CI 2.5-2.80). In individuals with MMI and diabetes OR for smoking was 2.23 (95% CI 1.96-2.53). In both cohorts OR for smoking was higher in men (3.10 95% CI 2.91-3.30 and 2.42 95% CI 2.00-2.94) (Table 5-5).

Odds ratio for ex-smoking, was lowest in individuals with MMI without diabetes (0.53 95% CI 0.50-0.55) and was particularly low in men (0.46 95% CI 0.43-0.50). Odds ratio for non-smoking, was lowest in individuals with MMI without diabetes (0.56 95% CI 0.53-0.58) and was particularly low for men (0.46 95% CI 0.43-0.49) (Table 5-5).

	MMI No diabetes (n=10,708)	MMI & Diabetes (n=1,080)	Diabetes No MMI (n=73,311)	Odd Ratio MMI no DM vs. DM no MMI	Odds ratio MMI & DM vs. DM no MMI
Smoking	5,203 (48.6)	401 (37.1)	14,570 (19.9)	All[1] 2.68 (2.56-2.80) Males[2] 3.10 (2.91-3.30) Females[2] 2.33 (2.19-2.48)	All[1] 2.23 (1.96-2.53) Males[2] 2.42 (2.00-2.94) Females[2] 2.11 (1.77-2.50)
Ex-Smoker	1,927 (18.0)	286 (26.5)	26,278 (35.8)	All[1] 0.53 (0.50-0.55) Males[2] 0.46 (0.43-0.50) Females[2] 0.63 (0.59-0.68)	All[1] 0.76 (0.66-0.87) Males[2] 0.77 (0.63-0.95) Females[2] 0.77 (0.64-0.92)
Non Smoker	3,578 (33.4)	393 (35.5)	32,463 (44.3)	All[1] 0.56 (0.53-0.58) Males[2] 0.46 (0.43-0.49) Females[2] 0.62 (0.59-0.66)	All[1] 0.66 (0.58-0.75) Males[2] 0.54 (0.44-0.67) Females[2] 0.71 (0.61-0.84)

Table 5-5   Odds Ratio of smoking, ex-smoking and non-smoking in individuals with/without MMI with/without diabetes
Bold if significant (p<0.001) compared to those with Diabetes without MMI [1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

For individuals who had diabetes and were identified as smokers, the majority were male (54.8%). Mean age was 58.6 years (sd 0.12) which was similar to individuals who smoked and had comorbid MMI and diabetes (56.4 years). There was no significant difference in deprivation distribution between the three groups. Rates of comorbidity were high in all three cohorts, but were highest in individuals with MMI and diabetes (94.3%) followed by individuals with diabetes without MMI (83.6%) (Table 5-6).

All Smokers	MMI No Diabetes (n=5,203)		p value	MMI & Diabetes (n=401)		p value	Diabetes No MMI (n=14,570)	
Male n, %	2,923	(56.2)	0.077	189	(47.1)	0.002	7,978	(54.8)
Mean Age, sd	**47.1**	**(0.19)**	**<0.001**	56.4	(0.65)	0.002	58.6	(0.12)
Age Group								
<25	**172**	**(3.3)**	**<0.001**	1	(0.2)	0.023	252	(1.7)
25-34	**828**	**(15.9)**	**<0.001**	15	(3.7)	0.438	664	(4.6)
35-44	**1,412**	**(27.1)**	**<0.001**	57	(14.2)	0.026	1,562	(10.7)
45-54	**1,278**	**(24.6)**	**<0.001**	**114**	**(28.4)**	**<0.001**	2,721	(18.7)
55-64	**906**	**(17.4)**	**<0.001**	99	(24.7)	0.231	3,991	(27.4)
65+	**606**	**(11.6)**	**<0.001**	**115**	**(28.7)**	**<0.001**	5,380	(36.9)
Mean Carstairs Score, sd	0.97	(0.05)	0.043	0.95	(0.18)	0.614	0.86	(0.03)
Deprivation Status								
Least deprived-1	525	(10.1)	0.445	44	(12.0)	0.744	1,525	(10.5)
2	861	(16.6)	0.454	63	(15.7)	0.497	2,477	(17.0)
3	1,188	(22.8)	0.007	86	(21.5)	0.386	3,395	(23.3)
4	1,225	(23.5)	0.060	98	(24.4)	0.304	3,245	(22.3)
Most deprived 5	1,404	(27.0)	0.972	106	(26.4)	0.815	3,928	(27.0)
Additional Multimorbidities	**1,007**	**(19.4)**	**<0.001**	**23**	**(5.7)**	**<0.001**	2,273	(15.6)
0	**1,420**	**(27.3)**	**<0.001**	69	(17.2)	0.087	3,018	(20.7)
1	**1,134**	**(21.8)**	**<0.001**	88	(22.0)	0.089	2,708	(18.6)
2	**1,642**	**(31.6)**	**<0.001**	**221**	**(55.1)**	**<0.001**	6,571	(45.1)
3+								

Table 5-6 Demographics of smokers with/without MMI with/without diabetes
Bold if significant (p<0.001) compared to those with Diabetes no MMI

5.4.2.2 Rates of Smoking Cessation Advice in Smokers in MMI vs. Diabetes

In smokers with MMI, rate of recording of smoking cessation advice was significantly lower compared to smokers with diabetes without MMI (88.7% vs. 98.0%, OR 0.22 95% CI 0.19-0.25, p<0.001). Smokers with comorbid MMI and diabetes had the highest recorded rates of smoking cessation advice, although when compared to smokers with diabetes without MMI- the OR did not reach significance (98.5% vs. 98.0%, OR 1.37 95% CI 0.61-3.11) (Table 5-7).

	MMI No Diabetes (n=5,203)	MMI & Diabetes (n=401)	Diabetes No MMI (n=14,570)	Odd Ratio MMI no DM vs. DM no MMI	Odds ratio MMI & DM vs. DM no MMI
Offered Smoking cessation	**4,616** **(88.7)**	395 (98.5)	14,275 (98.0)	**All[1]** **0.22 (0.19-0.25)** **Males[2]** **0.22 (0.18-0.27)** **Females[2]** **0.22 (0.17-0.27)**	All[1] 1.37 (0.61-3.11) Males[2] 1.17 (0.41-3.08) Females[2] 1.94 (0.48-7.93)
Not Offered Smoking cessation	**587** **(11.3)**	6 (1.5)	295 (2.0)		

Table 5-7 **Rates of recording of smoking cessation advice in individuals with/without MMI with/without Diabetes**

Bold if significant (p<0.001) compared to diabetes no MMI [1]**Adjusted for age, sex and deprivation status** [2]**Adjusted for age and deprivation status**

5.4.2.3 **Rates of NRT Prescription in Smokers in MMI vs. Diabetes:**

In smokers with MMI without diabetes rate of NRT prescription was lower (25.4%) compared to smokers with diabetes without MMI (29.1%) and smokers with comorbid MMI and diabetes (27.4%) (Table 5-8).

The odds ratio of NRT prescription was significantly lower in smokers with MMI without diabetes compared to smokers with diabetes without MMI (OR 0.75 95% CI 0.69-0.81). There was no significant difference in the odds ratio of NRT prescription in smokers with comorbid MMI and diabetes compared to smokers with diabetes without MMI (OR 0.87 95% CI 0.70-1.09) (Table 5-8).

	MMI No Diabetes (n=5,203)	MMI & DM (n=401)	Diabetes No MMI (n=14,570)	Odd Ratio MMI no DM vs. DM no MMI	Odds ratio MMI & DM vs. DM no MMI
Prescribed NRT	**1,323** **(25.4)**	110 (27.4)	4,234 (29.1)	**All[1]** **0.75(0.69-0.81)** **Males[2]** **0.67 (0.60-0.75)** **Females[2]** **0.83 (0.75-0.93)**	All[1] 0.87 (0.70-1.09) Males[2] 0.77 (0.54-1.10) Females[2] 0.95 (0.71-1.28)
Not Prescribed NRT	**3,880** **(74.6)**	291 (72.6)	10,336 (70.9)		

Table 5-8 **Rates of Nicotine Replacement Therapy (NRT) in smokers with/without MMI with/without Diabetes**
Bold if significant (p<0.001) compared to diabetes no MMI [1]**Adjusted for age, sex and deprivation status** [2]**Adjusted for age and deprivation status**

5.4.3 MMI compared to Coronary Heart Disease (CHD):

From 1,426,670 individuals aged over 18: 80,718 individuals with CHD without MMI (5.7%), 11,510 individuals with MMI without CHD (0.8%) and 749 individuals with MMI and CHD (0.05%) were identified (Table 5-9).

Recording of smoking status occurred in the majority of cases. Missing data was more frequent in individuals with MMI without CHD (4.0%) compared to individuals with MMI and CHD (0.7%) and individuals with CHD without MMI (0.5%) (Table 5-9).

	MMI No CHD (n=11,510)		MMI & CHD (n=752)		CHD No MMI (n=80,718)	
Smoking Recorded	**11,044**	**(96.0)**	744	(98.9)	80,309	(99.5)
Missing	**466**	**(4.0)**	8	(1.1)	409	(0.5)

Table 5-9   Rates of recording of smoking status in individuals with/without MMI with/without Coronary Heart Disease (CHD)
Bold if significant (p<0.001) compared to those with CHD no MMI

Mean age of individuals with CHD without MMI who had their smoking status recorded was higher than the mean age of individuals with MMI without CHD (71.3 vs. 51.2 years, p<0.001) and MMI and comorbid CHD (71.3 vs. 69.1 years, p<0.001). Mean Carstairs score for individuals with MMI without CHD was highest (0.37) compared to individuals with MMI and CHD (0.06) and CHD without MMI (0.08). Rate of additional multimorbidity was common. Having three or more additional physical health problems was most common in individuals with MMI and CHD (71.9%) (Table 5-10).

All	MMI No CHD (n=11,044)		p value	MMI & CHD (n=744)		p value	CHD no MMI (n=80,309)	
Male n, %	**5,305**	**(49.7)**	**<0.001**	**370**	**(49.7)**	**<0.001**	45,898	(57.2)
Mean Age, sd	**51.2**	**(0.15)**	**<0.001**	**69.1**	**(0.45)**	**<0.001**	71.3	(0.04)
Age Group								
<25	**296**	**(2.7)**	**<0.001**	0	(0)	0.773	9	(0.01)
25-34	**1,347**	**(12.2)**	**<0.001**	1	(0.1)	0.654	69	(0.09)
35-44	**2,459**	**(22.3)**	**<0.001**	15	(2.0)	0.003	759	(0.9)
45-54	**2,549**	**(23.1)**	**<0.001**	**80**	**(10.8)**	**<0.001**	5,048	(6.3)
55-64	2,096	(19.0)	0.330	177	(23.0)	0.002	15,555	(19.4)
65+	**2,297**	**(20.8)**	**<0.001**	**477**	**(64.1)**	**<0.001**	58,869	(73.3)
Mean Carstairs Score, sd	**0.37**	**(0.03)**	**<0.001**	0.06	(0.13)	0.8841	0.08	(0.01)
Deprivation Status								
Least deprived-1	1,589	(14.4)	0.001	122	(16.4)	0.528	12,492	(15.5)
2	**2,053**	**(18.6)**	**<0.001**	140	(18.8)	0.125	16,961	(21.1)
3	2,553	(23.1)	0.508	197	(26.5)	0.049	18,793	(23.4)
4	**2,443**	**(22.1)**	**<0.001**	148	(19.9)	0.747	16,360	(20.4)
Most deprived 5	**2,406**	**(21.8)**	**<0.001**	137	(18.4)	0.435	15,70	(73.3)
Additional Multimorbidities								
0	**2,084**	**(18.9)**	**<0.001**	**27**	**(3.6)**	**<0.001**	7,024	(8.8)
1	**2,837**	**(25.7)**	**<0.001**	**72**	**(9.7)**	**<0.001**	13,198	(16.4)
2	**2,340**	**(21.2)**	**<0.001**	110	(14.8)	0.003	15,296	(19.1)
3+	**3,783**	**(34.3)**	**<0.001**	**535**	**(71.9)**	**<0.001**	44,791	(55.8)

Table 5-10   Demographics of individuals with/without MMI with/without CHD who have had their smoking status recorded
Bold if significant (p<0.001) compared to individuals with CHD no MMI

5.4.3.1 Rate of Smoking in MMI vs. CHD:

When smoking status was recorded there were higher rates of smoking in individuals with MMI without CHD (48.4%) and individuals with MMI and CHD (34.8%) compared to individuals with CHD without MMI (20.9%). Highest rates of ex-smoking occurred in individuals with CHD without MMI (44.3%) compared to individuals with MMI and CHD (34.3%, p<0.001) and individuals with MMI without CHD (17.7%, p<0.001) (Table 5-11).

No significant difference in rate of non-smoking was seen across the three cohorts (33.9% MMI no CHD vs. 30.8% MMI and CHD and 34.8% CHD no MMI) (Table 5-11).

The OR of smoking, when adjusted for age, sex and deprivation status was highest in individuals with comorbid MMI and CHD (1.88 95% CI 1.59-2.21) (Table 5-11).

The OR of ex-smoking, when adjusted for age, sex and deprivation status was lowest in individuals with MMI without CHD (0.53 95% CI 0.33-0.37), and was particularly low in men (0.31 95% CI 0.28-0.33) (Table 6-13). When adjusted for age, sex and deprivation

status the odds ratio of non-smoking, was 1.44 (95% CI 1.38-1.52) in individuals with MMI without CHD and 0.82 (95% CI 0.70-0.96) in individuals with MMI and CHD (Table 5-11).

	MMI No CHD (n=11,044)	MMI & CHD (n=744)	CHD no MMI (n=80,309)	Odd Ratio MMI no CHD vs. CHD no MMI	Odds ratio MMI & CHD vs. CHD no MMI
Smoking	**5,345 (48.4)**	**259 (34.8)**	16,809 (20.9)	**All[1] 1.27 (1.20-1.33)** **Males[2] 1.51 (1.41-1.63)** Females[2] 1.03 (0.96-1.11)	**All[1] 1.88 (1.59-2.21)** **Males[2] 1.84 (1.47-2.30)** **Females[2] 1.94 (1.53-2.46)**
Ex-Smoker	**1,958 (17.7)**	**255 (34.3)**	35,554 (44.3)	**All[1] 0.53 (0.33-0.37)** **Males[2] 0.31 (0.28-0.33)** **Females[2] 0.40 (0.37-0.43)**	**All[1] 0.70 (0.60-0.82)** Males[2] 0.73 (0.59-0.90) Females[2] 0.69 (0.55-0.87)
Non-Smoker	3,741 (33.9)	230 (30.9)	27,946 (34.8)	**All[1] 1.44 (1.38-1.52)** **Males[2] 1.33 (1.24-1.43)** **Females[2] 1.58 (1.48-1.69)**	All[1] 0.82 (0.70-0.96) Males[2] 0.76 (0.59-0.98) Females[2] 0.85 (0.68-1.05)

Table 5-11   Odds Ratio of smoking, ex-smoking and non-smoking in individuals with/without MMI with/without CHD
Bold if significant (p<0.001) compared to CHD no MMI [1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

Of individuals with CHD without MMI identified as smokers, the majority were male (59.7%). Mean age was 65.7 (sd 0.08) which was significantly older than individuals with MMI without CHD (47.0 sd 0.19, p<0.001). Deprivation distribution of smokers with CHD without MMI, smokers with MMI without CHD and smokers with MMI and comorbid CHD was similar. Rates of comorbidity were high in all three cohorts, but were highest in individuals with MMI and CHD (94.6%) followed by individuals with CHD without MMI (89.4%) (Table 5-12).

All smokers	MMI No CHD (n=5,345)		p value	MMI & CHD (n=259)		p value	CHD No MMI (n=16,809)	
Male n, %	**2,972**	**(55.6)**	**<0.001**	140	(54.1)	0.064	10,041	(59.7)
Mean Age, sd	**47.0**	**(0.19)**	**<0.001**	63.6	(0.69)	0.002	65.7	(0.08)
Age Group								
<25	**173**	**(3.2)**	**<0.001**	0	(0)	0.781	5	(0.03)
25-34	**843**	**(15.8)**	**<0.001**	0	(0)	0.496	30	(0.2)
35-44	**1,458**	**(27.3)**	**<0.001**	11	(4.2)	0.023	365	(2.2)
45-54	**1,350**	**(25.3)**	**<0.001**	42	(16.2)	0.096	2,141	(12.7)
55-64	**918**	**(17.2)**	**<0.001**	88	(34.0)	0.168	5,045	(30.0)
65+	**603**	**(11.3)**	**<0.001**	118	(45.6)	0.003	9,223	(54.9)
Mean Carstairs Score, sd	**0.97**	**(0.05)**	**<0.001**	1.04	(0.24)	0.519	1.18	(0.03)
Deprivation Status								
Least deprived-1	**549**	**(10.3)**	**<0.001**	24	(9.3)	0.782	1,475	(8.8)
2	876	(16.4)	0.428	48	(18.5)	0.257	2,678	(15.9)
3	1,210	(22.6)	0.406	64	(24.7)	0.314	3,714	(22.1)
4	1,278	(23.9)	0.978	45	(17.4)	0.015	4,016	(23.9)
Most deprived- 5	1,432	(26.8)	0.004	78	(30.1)	0.776	4,926	(29.3)
Additional Multimorbidities								
0	**2,601**	**(48.7)**	**<0.001**	14	(5.4)	0.007	1,788	(10.6)
1	**1,370**	**(25.6)**	**<0.001**	30	(11.6)	0.013	2,936	(17.5)
2	**750**	**(14.0)**	**<0.001**	41	(15.8)	0.231	3,153	(18.8)
3+	**624**	**(11.7)**	**<0.001**	174	**(67.2)**	**<0.001**	8,932	(53.1)

Table 5-12   Demographics of smokers with/without MMI with/without CHD
Bold if significant (p<0.001) compared to CHD No MMI

5.4.3.2 Rates of recording of smoking cessation advice in smokers in MMI vs. CHD:

In smokers with MMI without CHD rates of recording of smoking cessation advice were significantly lower compared to smokers with CHD without MMI (88.9% vs. 98.7%, p<0.001, OR 0.12 95% CI 0.10-0.15). Although rates of recording of smoking cessation advice were lower in smokers with comorbid MMI and CHD (97.7%) the OR was not significant (OR 0.52 95% CI 0.23-1.19) (Table 5-13).

	MMI No CHD (n=5,345)	MMI & CHD (n=259)	CHD No MMI (n=16,809)	Odd Ratio MMI no CHD vs. CHD No MMI		Odds ratio MMI & CHD vs. CHD No MMI	
Offered Smoking cessation	**4,754** **(88.9)**	253 (97.7)	16,589 (98.7)	All[1] **0.12 (0.10-0.15)** Males[2] **0.12 (0.09-0.15)** Females[2] **0.14 (0.10-0.19)**		All[1] 0.52 (0.23-1.19) Males[2] 0.42 (0.15-1.16) Females[2] 0.74 (0.18-3.08)	
Not offered Smoking cessation	**591** **(11.1)**	6 (2.3)	220 (1.3)				

Table 5-13   Rates of recording of smoking cessation advice in individuals with/without MMI with/without CHD Bold if significant (p<0.001) compared to CHD No MMI [1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

5.4.3.3 Rate of NRT prescription in smokers in MMI vs. CHD:

Rate of NRT prescription was lowest in smokers with MMI without CHD (25.3%) compared to smokers with CHD without MMI (33.4%) and smokers with comorbid MMI and CHD (31.7%) (Table 5-14).

Odds ratio of NRT prescription was significantly lower in smokers with MMI without CHD compared to smokers with CHD without MMI (OR 0.34 95% CI 0.31-0.38). There was no significant difference in the OR of NRT prescription in smokers with MMI and CHD compared to smokers with CHD without MMI (Table 5-14).

	MMI No CHD (n=5,345)	CHD & MMI (n=259)	CHD No MMI (n=16,809)	Odd Ratio MMI no CHD vs. CHD No MMI		Odds ratio MMI & CHD vs. CHD No MMI	
Prescribed NRT	**1,351 (25.3)**	82 (31.7)	5,614 (33.4)	**All[1]**	**0.34 (0.31-0.38)**	All[1]	0.91 (0.62-1.07)
Not Prescribed NRT	**3,994 (74.7)**	177 (68.3)	11,195 (66.0)	**Males[2]** **Females[2]**	**0.30 (0.26-0.34)** **0.40 (0.35-0.45)**	Males[2] Females[2]	0.69 (0.47-1.02) 0.97 (0.66-1.42)

Table 5-14   Rates of Nicotine Replacement Therapy (NRT) in smokers with/without MMI with/without CHD
 Bold if significant (p<0.001) compared to CHD No MMI [1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

5.4.4 MMI compared to Hypertension:

From 1,426,670 individuals aged over 18: 232,201 individuals with hypertension without MMI (16.3%), 10,246 individuals with MMI without hypertension (0.7%) and 2,013 individuals with MMI and hypertension (0.14%) were identified.

Recording of smoking status was available in the majority of cases, however missing data occurred significantly more frequently in individuals with MMI without hypertension (4.5%) compared to individuals with MMI and hypertension (0.7%) and individuals with hypertension without MMI (0.4%) (Table 5-15).

	MMI No Hypertension (n=10,246)		Hypertension & MMI (n=2,013)		Hypertension No MMI (n=232,221)	
Smoking recorded	**9,789**	**(95.5)**	1,999	(99.3)	231,329	(99.6)
Missing	**457**	**(4.5)**	14	(0.7)	892	(0.4)

Table 5-15   Rates of recording of smoking status in individuals with MMI with/without hypertension
Bold if significant (p<0.001) compared to hypertension

Mean age of individuals with hypertension who had their smoking status recorded was higher than the mean age of individuals with MMI without hypertension (66.9 vs. 49.6 years, p<0.001) and MMI and hypertension (66.9 vs. 65.8 years, p<0.001). Rate of additional multimorbidity was common. Having three or more additional physical health comorbidities was most common in individuals with MMI and hypertension (54.1%) (Table 5-16).

All	MMI No Hypertension (n=9,789)		p value	MMI & Hypertension (n=1,999)		p value	Hypertension No MMI (n=231,329)	
Male n, %	**4,929**	**(50.4)**	**<0.001**	**746**	**(37.3)**	**<0.001**	102,312	(44.2)
Mean Age, sd	**49.6**	**(0.16)**	**<0.001**	**65.8**	**(0.29)**	**<0.001**	66.9	(0.03)
Mean Carstairs Score, sd	**0.42**	**(0.04)**	**<0.001**	0.003	(0.07)	0.003	-0.22	(0.01)
Deprivation Status								
Least deprived-1	**1,380**	**(14.1)**	**<0.001**	331	(16.6)	0.073	41,889	(18.1)
2	**1,810**	**(18.5)**	**<0.001**	383	(19.2)	0.002	51,067	(22.1)
3	2,241	(22.9)	0.098	509	(25.5)	0.053	54,634	(23.6)
4	**2,163**	**(22.1)**	**<0.001**	428	(21.4)	0.008	44,109	(19.1)
Most deprived 5	**2,195**	**(22.4)**	**<0.001**	348	(17.4)	0.743	39,630	(17.1)
Additional Multimorbidities								
0	2,084	(21.3)	0.115	**181**	**(9.1)**	**<0.001**	50,803	(22.0)
1	**2,683**	**(27.4)**	**<0.001**	**367**	**(18.4)**	**<0.001**	55,509	(24.0)
2	**2,045**	**(20.9)**	**<0.001**	370	(18.5)	0.376	44,634	(19.3)
3+	**2,977**	**(30.4)**	**<0.001**	**1,081**	**(54.1)**	**<0.001**	80,383	(34.7)

Table 5-16   Demographics of individuals with/without MMI with/without hypertension who have had their smoking status recorded
Bold if significant (p<0.001) compared to hypertension No MMI

5.4.4.1 Rate of Smoking in MMI vs. Hypertension:

When smoking status was recorded there were higher rates of smoking in individuals with MMI without hypertension (51.5%) and in individuals with MMI and hypertension (28.3%) compared to individuals with hypertension without MMI (17.2%) (Table 5-19). There were higher rates of ex-smoking in individuals with hypertension without MMI

(33.3%) and in individuals with MMI and hypertension (28.4%) compared to individuals with MMI without hypertension (16.8%). Rate of non-smoking was highest in individuals with hypertension without MMI (49.5%) (Table 5-17).

The odds ratio of smoking was highest in individuals with MMI without hypertension (2.91 95% CI 2.78-3.04) and was particularly high in men (3.50 95% CI 3.30-3.73) (Table 5-19). Odds ratio of ex-smoking was lower in individuals with MMI without hypertension (0.52 95% CI 0.49-0.55) and was particularly low in men (0.49 95% CI 0.45-0.53). Odds ratio of non-smoking was also lower in individuals with MMI without hypertension (0.46 95% CI 0.44-0.48) (Table 5-17).

	MMI without Hypertension (n=9,789)	Hypertension & MMI (n=1,999)	Hypertension No MMI (n=231,329)	Odd Ratio MMI no Hypertension vs. Hypertension No MMI	Odds ratio MMI & Hypertension vs. Hypertension No MMI
Smoking	5,038 (51.5)	566 (28.3)	39,775 (17.2)	All[1] 2.91 (2.78-3.04) Males[2] 3.50 (3.30-3.73) Females[2] 2.47 (2.32-2.63)	All[1] 1.85 (1.67-2.05) Males[2] 2.11 (1.81-2.47) Females[2] 1.72 (1.50-1.96)
Ex-Smoker	1,645 (16.8)	568 (28.4)	77,118 (33.3)	All[1] 0.52 (0.49-0.55) Males[2] 0.49 (0.45-0.53) Females[2] 0.62 (0.57-0.67)	All[1] 0.85 (0.77-0.94) Males[2] 0.75 (0.64-0.88) Females[2] 0.95 (0.83-1.07)
Non Smoker	3,106 (31.7)	865 (43.3)	114,436 (49.5)	All[1] 0.46 (0.44-0.48) Males[2] 0.34 (0.31-0.36) Females[2] 0.54 (0.51-0.57)	All[1] 0.74 (0.68-0.81) Males[2] 0.71 (0.61-0.82) Females[2] 0.73 (0.66-0.82)

Table 5-17   Odds Ratio of smoking, ex-smoking and non-smoking in individuals with/without MMI with/without hypertension
Bold if significant (p<0.001) compared to hypertension No MMI [1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

Of the individuals with hypertension without MMI identified as smokers, 47.1% were male, compared to 56.7% of individuals with MMI without hypertension who smoked and 44.9% of individuals with MMI and hypertension who smoked. Mean age of individuals with hypertension without MMI who smoked was 62.9 years (sd 0.60), which was significantly older than individuals with MMI without hypertension (46.3 years, p<0.001) and individuals with MMI and hypertension (61.0 years, p<0.001). Deprivation distribution of all three groups was similar. Rates of comorbidity were high in all three cohorts; rate of three or more additional physical health comorbidities was highest in MMI and hypertension (53.2%) (Table 5-18).

Smokers	MMI No Hypertension (n=5,038)		p value	MMI & Hypertension (n=566)		p value	Hypertension No MMI (n=39,775)	
Male n, %	**2,858**	**(56.7)**	**<0.001**	**254**	**(44.9)**	**<0.001**	18,747	(47.1)
Mean Age, sd	**46.3**	**(0.19)**	**<0.001**	**61.0**	**(0.51)**	**<0.001**	62.9	(0.60)
Age Group								
<25	**173**	**(3.4)**	**<0.001**	0	(0)	0.372	56	(0.1)
25-34	**833**	**(16.5)**	**<0.001**	10	(1.8)	0.111	425	(1.1)
35-44	**1,422**	**(28.2)**	**<0.001**	47	(8.3)	0.002	2,139	(5.4)
45-54	**1,289**	**(25.6)**	**<0.001**	103	(18.2)	0.405	6,709	(16.9)
55-64	**811**	**(16.1)**	**<0.001**	195	(34.5)	0.148	12,564	(31.6)
65+	**510**	**(10.1)**	**<0.001**	211	(37.3)	**<0.001**	17,881	(45.0)
Mean Carstairs Score, sd	**1.01**	**(0.05)**	**<0.001**	0.61	(0.15)	0.467	0.71	(0.02)
Deprivation Status								
Least deprived-1	**496**	**(9.9)**	**<0.001**	77	(13.6)	0.106	4,542	(11.4)
2	835	(16.6)	0.002	89	(15.7)	0.112	7,285	(18.3)
3	1,137	(22.6)	0.484	137	(24.2)	0.502	9,147	(23.0)
4	1,192	(23.7)	0.027	131	(23.1)	0.624	8,858	(22.3)
Most deprived 5	1,378	(27.4)	**<0.001**	132	(28.3)	0.357	9,943	(25.0)
Additional Multimorbidities								
0	1,007	(20.0)	0.016	**57**	**(10.1)**	**<0.001**	8,533	(21.5)
1	**1,386**	**(27.5)**	**<0.001**	96	(17.0)	**<0.001**	9,260	(23.3)
2	**1,107**	**(22.0)**	**<0.001**	112	(19.8)	0.782	7,683	(19.3)
3+	**1,538**	**(30.5)**	**<0.001**	301	(53.2)	**<0.001**	14,299	(35.9)

Table 5-18   Demographics of smokers with/without MMI with/without hypertension
Bold if significant (p<0.001) compared to hypertension No MMI

5.4.4.2 Rates of recording of smoking cessation advice in smokers in MMI vs. Hypertension:

Rates of recording of smoking cessation advice were significantly lower in smokers with MMI without hypertension (88.3%) compared to smokers with hypertension without MMI (98.5%) and smokers with comorbid hypertension and MMI (98.6%). Although OR of recording of smoking cessation advice in smokers with MMI without hypertension was lower than for smokers with hypertension without MMI (0.15 95% CI 0.13-0.18), it was similar for smokers with comorbid MMI and hypertension (OR 1.08 95% CI 0.53-2.18, p=0.830) (Table 5-19).

	MMI no Hypertension (n=5,038)	Hypertension & MMI (n=566)	Hypertension No MMI (n=39,775)	Odd Ratio MMI no Hypertension vs. Hypertension No MMI	Odds ratio MMI & Hypertension vs. Hypertension No MMI
Offered Smoking Cessation	**4,449** **(88.3)**	558 (98.6)	39,186 (98.5)	**All[1]0.15 (0.13-0.18)** **Males[2]0.18 (0.15-0.22)** **Females[2] 0.13 (0.10-0.16)**	All[1]1.08 (0.53-2.18) Males[2]0.99 (0.41-2.43) Females[2]1.33 (0.42-4.18)
Not offered Smoking Cessation	**589** **(11.7)**	8 (1.4)	589 (1.5)		

Table 5-19   Rates of recording of smoking cessation advice in individuals with/without MMI with/without Hypertension
 Bold if significant (p<0.001) compared to Hypertension No MMI [1]**Adjusted for age, sex and deprivation status** [2]**Adjusted for age and deprivation status**

5.4.4.3 Rates of NRT Prescription in smokers in MMI vs. Hypertension:

There was no difference in rate of NRT prescription in smokers with MMI (25.4%) compared to smokers with hypertension without MMI (26.4%) and smokers with comorbid MMI and hypertension (27.4%) (Table 5-20).

When adjusted for age, sex and deprivation, the OR of NRT prescription in smokers with MMI without hypertension was significantly lower compared to smokers with hypertension without MMI (OR 0.71 95% CI 0.66-0.76) (Table 5-20). However there was no difference in OR of NRT prescription in smokers with comorbid MMI and hypertension compared to smokers with hypertension without MMI (OR 1.01 95%CI 0.84-1.22) (Table 5-20).

	MMI no Hypertension (n=5,038)	Hypertension & MMI (n=566)	Hypertension No MMI (n=39,775)	Odd Ratio MMI no Hypertension vs. Hypertension No MMI	Odds ratio MMI & Hypertension vs. Hypertension No MMI
Prescribed NRT	1,278 (25.4)	155 (27.4)	10,495 (26.4)	**All[1]0.71 (0.66-0.76)** **Males[2]0.67 (0.37-0.71)** **Females[2] 0.80 (0.72-0.89)**	All[1]1.01 (0.84-1.22) Males[2]0.85 (0.63-1.15) Females[2]1.15 (0.90-1.46)
Not Prescribed NRT	3,760 (74.6)	411 (72.6)	29,280 (73.6)		

Table 5-20   Rates of Nicotine Replacement Therapy (NRT) in smokers with/without MMI with/without Hypertension
 Bold if significant (p<0.001) compared to Hypertension No MMI [1]**Adjusted for age, sex and deprivation status** [2]**Adjusted for age and deprivation status**

5.4.5 Comparison of Schizophrenia with bipolar disorder:

From 1,426,670 individuals aged over 18, 9,677 individuals with schizophrenia (0.7%) and 2,582 individuals with bipolar disorder (0.2%) were identified.

Recording of smoking status was available in the majority of cases. There was no difference in the rate of missing data between individuals with schizophrenia and individuals with bipolar disorder (4.1% vs. 2.8%; p=0.002) (Table 5-21).

	Schizophrenia (n=9,677)		Bipolar Disorder (n=2,582)		p value
Missing data on smoking	399	(4.1)	72	(2.8)	0.002
Smoking recorded	9,278	(95.9)	2,510	(97.2)	

Table 5-21   Rates of recording of smoking status in individuals with Schizophrenia vs. Bipolar Disorder

There was also no significant difference in rates of diabetes, CHD and hypertension between both groups (Table 5-22).

	Schizophrenia (n=9,677)		Bipolar Disorder (n=2,582)		p value
Diabetes	870	(9.0)	218	(8.4)	0.386
CHD	579	(6.0)	170	(6.6)	0.257
Hypertension	1,551	(16.0)	462	(17.9)	0.023

Table 5-22   Rates of comorbid diabetes, CHD and hypertension in individuals with Schizophrenia vs. Bipolar Disorder

When smoking was recorded, rates of smoking were higher in individuals with schizophrenia (48.8%) compared to individuals with bipolar disorder (42.8%, p<0.001). Rates of ex-smoking were higher in the bipolar disorder group compared to the schizophrenia group (21.2% vs. 48.8%, p<0.001). Rates of non-smoking were similar (33.1% vs. 36.0%). There was no difference in rates of smoking, ex-smoking and non-smoking between the two groups when adjusted for age, sex and deprivation (Table 5-23).

	Schizophrenia (n=9,278)	Bipolar Disorder (n=2,510)	Odd Ratio All Schizophrenia vs. Bipolar Disorder
Smoking	**4,529 (48.8)**	**1,075 (42.8)**	All[1] 1.03 (0.94-1.13) Males[2] 1.19 (1.03-1.37) Females[2] 0.93 (0.82-1.05)
Ex-Smoker	**1,681 (18.1)**	**532 (21.2)**	All[1] 0.86 (0.77-0.96) Males[2] 0.83 (0.70-0.99) Females[3] 0.92 (0.80-1.07)
Non-Smoker	3,068 (33.1)	903 (36.0)	All[1] 1.01 (0.92-1.11) Males[2] 0.92 (0.79-1.07) Females[3] 1.06 (0.94-1.20)

Table 5-23   Odds Ratio of smoking, ex-smoking and non-smoking in individuals with schizophrenia vs. bipolar disorder
Bold if significant (p<0.001) difference between groups[1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

Of the individuals with schizophrenia identified as smokers, 58.6% were male, compared to 42.4% of individuals with bipolar disorder (p<0.001). Mean age of the schizophrenia cohort was 47.1 years (sd 0.21) which was significantly younger than the bipolar disorder group (50.7 years, p<0.001). There were some differences in distribution of deprivation of smokers with schizophrenia compared to smokers with bipolar disorder: whereby individuals with schizophrenia were more likely to come from the most deprived area and less likely to come from the least deprived area compared to smokers with bipolar disorder. Rates of comorbidity were similar in smokers with schizophrenia and bipolar disorder (Table 5-24).

	Schizophrenia (n=4,529)		Bipolar Disorder (n=1,075)		p value
Male n, %	**2,656**	**(58.6)**	**456**	**(42.4)**	**<0.001**
Mean Age, sd	**47.1**	**(0.21)**	**50.7**	**(0.42)**	**<0.001**
Age Group					
<25	**158**	**(3.5)**	**15**	**(1.4)**	**<0.001**
25-34	**723**	**(16.0)**	**120**	**(11.2)**	**<0.001**
35-44	1,231	(27.2)	238	(22.1)	0.001
45-54	1,091	(24.1)	301	(28.0)	0.008
55-64	785	(17.3)	221	(20.6)	0.013
65+	**541**	**(11.9)**	**180**	**(16.7)**	**<0.001**
Mean Carstairs Score, sd	**1.14**	**(0.53)**	**0.26**	**(0.11)**	**<0.001**
Deprivation Status					
Least deprived-1	**409**	**(9.0)**	**164**	**(15.3)**	**<0.001**
2	**711**	**(15.7)**	**213**	**(19.8)**	**0.001**
3	1,030	(22.7)	244	(22.7	0.975
4	1,083	(23.9**)**	240	(22.3)	0.271
Most deprived 5	**1,296**	**(28.6)**	**214**	**(19.9)**	**<0.001**
Additional Multimorbidities					
0	816	(18.0)	191	(17.8)	0.848
1	1,183	(26.1)	260	(24.2)	0.192
2	984	(21.7)	219	(20.4)	0.331
3+	1,546	(34.1)	405	(37.7)	0.029

Table 5-24 Demographics of smokers with schizophrenia and bipolar disorder
Bold if significant (p<0.001) difference between schizophrenia and bipolar disorder

5.4.5.1 Rates of recording of smoking cessation advice in smokers in schizophrenia vs. bipolar disorder:

There was no difference in rates of recording of smoking cessation advice in smokers with schizophrenia compared to smokers with bipolar disorder (89.2% vs. 90.1%, p=0.349) and

there was no difference in the odds ratio calculated when adjusted for age, sex and deprivation (OR 1.00 95% CI 0.80-1.26) (Table 5-25).

	Schizophrenia (n=4,529)	Bipolar Disorder (n=1,075)	Odd Ratio All Schizophrenia vs. Bipolar Disorder
Offered Smoking Cessation	4,038 (89.2)	969 (90.1)	All[1] 1.00 (0.80-1.26)
Not offered Smoking Cessation	491 (10.8)	106 (9.9)	Males[2] 1.10 (0.81-1.50) Females[2] 0.91 (0.65-1.27)

Table 5-25 Rates of recording of smoking cessation advice in individuals with schizophrenia vs. bipolar disorder.
Bold if significant (p<0.001) difference between groups[1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

5.4.5.2 Rates of NRT Prescribing in smokers in schizophrenia vs. bipolar disorder:

There was no difference in rates of NRT prescribing in smokers with schizophrenia compared to smokers with bipolar disorder (25.2% vs. 27.4%, p=0.137) and no difference in the odds ratio when adjusted for age, sex and deprivation (OR 0.95 95% CI 0.82-1.11) (Table 5-26).

	Schizophrenia (n=4,529)	Bipolar Disorder (n=1,075)	Odd Ratio All Schizophrenia vs. Bipolar Disorder
Prescribed NRT	1,139 (25.2)	294 (27.4)	All[1] 0.95 (0.82-1.11)
Not Prescribed NRT	3,390 (74.8)	781 (72.6)	Males[2] 1.10 (0.85-1.42) Females[2] 0.87 (0.72-1.06)

Table 5-26 Rates of Nicotine Replacement Therapy (NRT) in smokers with schizophrenia and bipolar disorder
Bold if significant (p<0.001) difference between groups[1]Adjusted for age, sex and deprivation status [2]Adjusted for age and deprivation status

5.5 Discussion:

5.5.1 Increased smoking rates in individuals with MMI:

Rates of smoking were significantly higher in individuals with a record of MMI compared to individuals without MMI who had diabetes, CHD or hypertension. Rates of smoking were also significantly higher in individuals with MMI and comorbid diabetes, CHD and hypertension compared to individuals who had diabetes, CHD and hypertension without MMI. Males with MMI had particularly elevated odd ratios of smoking compared to females, across most of the comparator groups.

The high rates of smoking seen in our cohort are in keeping with other studies, with one meta-analysis reporting that individuals with schizophrenia have more than five times the odds of current smoking than the general population (Tsoi et al., 2013). While other studies have reported higher rates of smoking in men with MMI compared to women (Ma et al., 2009), to date, there have been no studies calculating odds ratios by sex, for rates of smoking, ex-smoking and non-smoking in MMI compared to other chronic diseases. These findings are therefore novel and of clinical note.

In this cohort odds ratios (adjusted for age, sex and deprivation status) for non-smoking and ex-smoking were lower in individuals with MMI compared to individuals with diabetes and hypertension without MMI. This was an expected finding, given the evidence for the impact of smoking cessation on vascular risk (Price et al., 1999) and the high priority level given to smoking cessation promotion for individuals with a diagnosis of diabetes or hypertension. However in this cohort the odds ratio of non-smoking was higher in individuals with MMI without CHD compared to individuals with CHD without MMI. This unexpected finding may be explained by the differences in age profile of the groups (individuals with CHD without MMI were significantly older compared to individuals with MMI without CHD).

5.5.2 Smoking rates in individuals with schizophrenia and bipolar disorder:

Although absolute rates of smoking were higher and absolute rates of ex-smoking were lower in individuals with schizophrenia compared to bipolar disorder there was no difference in adjusted odds ratios for smoking, ex-smoking and non-smoking in individuals with schizophrenia compared to individuals with bipolar disorder. This was a surprising finding as other studies have reported higher rates of smoking in schizophrenia compared to bipolar disorder (Myles et al., 2012). This finding may in part, be explained by the smaller than expected cohort of individuals with bipolar disorder.

5.5.3 Reduced rates of smoking cessation advice and reduced NRT prescription rates in individuals with MMI:

We found that recorded rates of smoking cessation advice in smokers with MMI were significantly lower than the recorded rates of smoking cessation advice in smokers with diabetes (88.7% vs. 98.0%, p<0.001), smokers with CHD (88.9% vs. 98.7%, p<0.001) and smokers with hypertension (88.3% vs. 98.5%, p<0.001). This is similar to de Leon and

colleagues (2005) who found lower rates of smoking cessation advice in smokers with schizophrenia compared to controls who smoked (ORs 0.19 CI, 0.14–0.24) (de Leon and Diaz, 2005) and similar to the findings of Szatkowski and McNeill, (2013), who reported lower rates of smoking cessation advice per consultation in individuals with a mental illness or prescription of a psychoactive medication, compared to individuals without mental illness or psychoactive medication prescription.

Individuals who smoked with comorbid MMI and diabetes, comorbid MMI and CHD and comorbid MMI and hypertension had comparable recorded rates of smoking cessation advice compared to smokers without MMI and the comparator chronic disease. To date, there have been no similar comparisons between recorded rates of smoking cessation advice in individuals with comorbid MMI and physical health problems with recorded rates of smoking cessation advice in individuals with chronic physical health problems without MMI. These findings are therefore novel.

Although the recording of smoking cessation advice for certain chronic diseases is incentivised through the Quality and Outcome Framework (QOF), prescribing of NRT is not incentivised for any chronic disease. The impact of the QOF on rates of recording of smoking cessation in primary care has been investigated. For example Taggar and colleagues reported that since the introduction of the QOF in 2004, there had been a substantial increase in the recording of smoking status and cessation advice in primary care, which was sustained over time (Taggar et al., 2012). They also reported that factors such as: greater social deprivation, being female and having a chronic medical condition, were associated with an increased likelihood of having a recent recording of smoking status or have smoking cessation advice recorded. They also found that since the introduction of the QOF, the strongest characteristic associated with recording of smoking status and cessation advice was the presence of comorbidity. The findings in this cohort appear to echo this: as the presence of comorbidity (MMI and diabetes, MMI and CHD and MMI and hypertension) was associated with an increased likelihood of smoking cessation advice being recorded.

In this study, the odds ratio of prescription of NRT in smokers with MMI without a comorbid chronic physical disease (diabetes, CHD or hypertension) was lower than NRT prescription rates in smokers without MMI with the comparable comorbid chronic physical disease (diabetes, CHD and hypertension). This finding is in keeping with that of Szatkowski and McNeill, (2013), who reported lower rates of NRT prescription per

consultation in individuals with a mental illness or prescription of a psychoactive medication, compared to individuals without mental illness or psychoactive medication prescription.

In this cohort when NRT prescription rates for smokers with MMI and a comorbid chronic physical disease (diabetes, CHD and hypertension) were compared to individuals who smoked with a chronic physical disease (diabetes, CHD and hypertension) without MMI, there was no significant difference in NRT prescription rates. To my knowledge studies comparing rates of NRT prescription in individuals with comorbid MMI and a physical health disorder with rates of NRT prescription in individuals with a physical health disorder without MMI have not been done. This finding again suggests that physical health comorbidity is associated with higher rates of NRT prescription in individuals with MMI.

5.5.4 Rates of smoking cessation advice and NRT prescription in individuals with schizophrenia compared to bipolar disorder:

In this cohort, there was no difference in recorded rates of smoking cessation advice or prescription of NRT in smokers with schizophrenia compared to smokers with bipolar disorder. While there have been studies comparing rates of NRT use in individuals with severe mental illness and "general mental illness" (Bowden et al., 2011), NRT use was self-reported retrospectively in a small sample size. Therefore this study is novel in its comparison of recording of rates of cessation advice and NRT prescription in a large epidemiological cohort of individuals with major mental illness within primary care.

5.5.5 Possible Reasons for the study findings:

Heavy smoking in individuals with schizophrenia has been associated with increased positive symptoms and it is hypothesised that individuals may self-medicate with tobacco and nicotine in an attempt to alleviate distressing and troubling symptoms (Goff et al., 1992). Nicotine is known to act on various neurotransmitters and may be associated with increased positive reinforcement in individuals with MMI (Picciotto and Corrigall, 2002). Smoking is also known to increase the metabolism of some antipsychotic drugs (Desai et al., 2001) and some individuals may smoke heavily to reduce the adverse effects of antipsychotic medication.

It is also recognised that individuals with schizophrenia often have difficulty in filtering out unnecessary information, thought to be secondary to abnormalities in sensorimotor gating (Kumari and Sharma, 2002), and it has been reported that cigarette smoking can improve sensory gating in individuals with schizophrenia (Adler et al., 1998). This may potentially partly explain the increased smoking rates in individuals with schizophrenia. Additionally, many individuals with MMI who consume tobacco, may spend time in settings that tolerate smoking and so may experience less stigma associated with smoking and less pressure to quit than the general population (Bayer and Stuber, 2006). As highlighted in Chapter 1, smoking has been seen as part of psychiatry's culture, and so these factors in combination, may in part explain the high smoking rates seen in this cohort of individuals.

While it is recognised that successful smoking cessation in all individuals is challenging, a number of factors which predict success in the general population are the same as those which predict success in individuals with MMI. These factors include; pharmacotherapy for nicotine dependence, confidence in ability to quit and age at initiation of smoking (Culhane et al., 2008). Therefore it is clear that in order to reduce the high smoking rates in individuals with MMI, appropriate access to NRT is essential. Reasons as to why in this cohort, rates of recording of smoking cessation advice and NRT prescription were less in individuals with MMI are multifactorial and likely include patient and clinician factors.

It has been hypothesised that the cognitive deficits in frontal executive function in particular in attention among individuals with schizophrenia, may contribute to the low success rates of smoking cessation (Moss et al., 2009). There is also some evidence to suggest that the perceived health risks associated with smoking may be lower in individuals with schizophrenia (Kelly et al., 2012). Individuals with MMI may also be ambivalent to stopping smoking due to the absence of positive role models of ex-smokers, tolerance of smoking in mental health environments despite smoking bans in the wider society (The Scottish Government, 2008) and previous experience of cigarettes being used as positive reinforcement in token economies (Gustafson, 1992). These factors may contribute to lower rates of individuals with MMI seeking out opportunities to stop smoking.

Possible clinician factors leading to reduced smoking cessation advice recording and NRT prescription may include: clinician smoking status, clinician attitude to smoking (Stead et al., 2009), stigma, lack of specific information regarding prescribing of smoking cessation

therapies in individuals with MMI and potentially perceived hopelessness in achieving abstinence by the clinician (Williams and Ziedonis, 2006).

However despite the combination of high smoking rates, potential perceived beneficial effects of smoking (in terms of positive symptoms, medication side effect management and cognitive improvement) and possible ambivalence to smoking cessation, there is evidence that individuals with severe mental illness (SMI) are able to successfully quit smoking, despite extensive histories of heavy smoking. Dickerson and colleagues, (2011) interviewed 78 individuals with SMI who had successfully quit smoking for an average of 7.4 years (± 8.6) after smoking for a mean of 25.3 years (± 11.4). In their cohort, the primary reasons for quitting smoking were health concerns and cost of cigarettes and the main contributing factors to achieving abstinence were; social support from friends/family, direction from a doctor, use of NRT and the advice of friends who had previously quit. This study therefore reinforces the importance of providing adequate smoking cessation advice and appropriate prescription of NRT for smokers with MMI. With the implementation of changes to smoking laws within mental health institutions later this year, acute admission units, may present a route to discussing smoking cessation and indeed NRT prescription.

5.6 Strengths and limitations:

Strengths of this study include the large sample size (almost 1.8 million individuals) and so it is likely to be representative of the wider Scottish population. The rate of a recorded diagnosis of diabetes of 5.2% is similar to the Scottish estimate of 4.3% (Diabetes.org, 2012) and the rate of a recorded diagnosis of CHD of 5.7% is also similar to the British Heart Foundation (BHF) estimates of male prevalence of CHD of 7.5% and female prevalence of 5.2% (Coronary Heart Disease Statistics, 2012). Although the rate of a recorded diagnosis of hypertension in this cohort was 16.3%, which is lower than the Scottish estimates of around one third (ScotPHO High Blood Pressure Prevalence, 2012). It is well recognised that under-diagnosis and under-treatment of hypertension is a major problem- with estimates of between 11-14% of individuals with hypertension receiving no treatment (HSCIS Hypertension 2012). The estimated prevalence in this cohort is similar to the OQF hypertension prevalence rate of 12.5% for the same contract year (QOF Scotland 2006/2007).

The rate of a recorded diagnosis of MMI (namely bipolar disorder and schizophrenia combined) in this cohort of 0.9% is lower than population estimates of 2% (when the disorders are combined) (Saha et al., 2008; Ferrari et al., 2011). This may reflect both under-diagnosis compared to epidemiological estimates and under-recording of MMI in primary care. In particular there is considerable debate and variation in the definitions and prevalence of bipolar disorder and this has likely impacted on the estimated prevalence rates in this cohort. Other possible reasons for the lower than expected recorded prevalence rate of MMI, is that although individuals with MMI are known to secondary care services they may not be recorded within primary care. Additionally some individuals may not be in contact with either primary or secondary care and so would be missing from this study population. These factors represent limitations of these data.

The data used in this study is from 314 primary care practices and is routine clinical data. As such there may be variability of diagnostic coding for all the conditions included in this study. This is a limitation of the design of this analysis whereby Read Codes without confirmatory interviews were used to define diagnoses. A further limitation is the potential for smoking status to be noted and where appropriate smoking cessation advice given, but for this advice not to be recorded on the primary care clinical record. It was also impossible to determine from our data if there had been previous attempts at smoking cessation and if there was historical NRT prescription use. This is again a limitation of the design of this study and could only be overcome by detailed review of individual electronic records and where appropriate paper case notes.

A further limitation of this study is with regard the exclusion of individuals with missing data. Missing data occurred more frequently in individuals with MMI. Although reasons for this are unclear. Missing data may be: missing completely at random (MCAR), missing at random (MAR) or not missing at random (NMAR) and possible reasons for missing data need to be considered. It is possible that in the SPICE dataset the presence of MMI may have impacted on the likelihood of data on smoking status being missing, although this was impossible to determine. As the data was cross-sectional, individuals with missing data were excluded from the analysis. Although this in itself has limitations and consequences for data interpretation it was felt that given the large sample size, this was the most suitable action.

The impact of the Quality and Outcome Framework (QOF) incentivising the recording of smoking status and the recording of smoking cessation advice in certain chronic diseases

also has to be considered. Since the introduction of the QOF in 2004, recording of smoking status in individuals aged 15-75 with a physical comorbidity has been incentivised. From 2004 until 2008, individuals with a chronic disease (namely diabetes, CHD, hypertension, asthma, COPD, TIA or stroke) had both smoking status and smoking cessation advice incentivised. For the smoking status indicator target to be achieved, it was required that for any individual with one or any combination of the aforementioned chronic diseases, smoking status should be recorded in the past 15 months. For those who smoked, smoking cessation advice or referral to a specialist service, where available, within the previous 15 months was also incentivised. In 2008 the list of chronic diseases incentivised was expanded to include CKD, schizophrenia, bipolar disorder and related psychoses. Therefore smoking cessation advice for individuals with MMI was not specifically incentivised by the QOF until 2008. As this data was captured in March 2007 this may partly explain the differences in smoking cessation advice in those with MMI. Of note however is that NRT prescription is not (and indeed has never been) incentivised in the QOF.

5.7 Conclusions:

Smoking rates were significantly higher in individuals with a record of MMI compared to individuals in the primary care cohort without MMI and with the other chronic diseases investigated: diabetes, CHD and hypertension. Despite this, rate of recording of smoking cessation advice was significantly lower in individuals with MMI compared to the rate in individuals with a chronic disease without MMI and individuals with MMI and comorbid diabetes, CHD and hypertension. NRT prescribing also occurred less frequently in smokers with MMI compared to smokers with comorbid diabetes and MMI and smokers with diabetes without MMI. These findings are suggestive of inequalities in access to health care advice and prescribing in individuals with MMI compared to individuals without MMI within primary care.

Cigarette smoking remains a major modifiable risk factor for many chronic diseases and as such smoking cessation is recognised as being one of the most cost effective methods for improving an individual's health and wellbeing. Given the particularly high rates of smoking and evidence of higher levels of nicotine dependence in individuals with MMI, smoking cessation represents an important and essential public health intervention for this cohort of patients. Given the effectiveness of smoking cessation advice and NRT prescribing in achieving abstinence from smoking and the evidence to suggest that

individuals with MMI are motivated to stop smoking, more needs to be done to promote these interventions for individuals with MMI.

Chapter 6 Possible mechanisms for inequality: Data from the Quality and Outcomes Framework (QOF) across the UK.

Chapter Overview:

This chapter describes in detail data from the primary care Quality and Outcomes Framework (QOF). Here access to healthcare is measured by comparing payment, population achievement and exception rates of two specific Mental Health (MH) indicators with two similar indicators for Diabetes and Chronic Kidney Disease (CKD). A comparison of these indicators across the whole of the United Kingdom (UK), with data from England, Scotland, Northern Ireland and Wales is used and a cross jurisdiction analysis is undertaken. Differences in rates of payment, population achievement and exception between indicators are described and possible reasons for the findings are explored. These measures are used as a proxy indicator of access to healthcare within primary care.

6.1 Background to the Quality and Outcomes Framework (QOF):

The General Medical Services' Quality and Outcomes Framework (QOF), which was introduced into the UK in 2004, is an annual contract for the provision of care delivered by General Practices. It was introduced to standardise the improvement in the delivery of primary care and largely forms the basis of supplementary payment for General Practioners (GPs). Since Healthcare devolution in 1998 which gave the Scottish Parliament, the Northern Ireland Assembly and the National Assembly for Wales, greater power over health services and public health matters, the NHS, in terms of its management, structure and trajectory have continued to diverge (Greer, 2004). Although some QOF indicators differ between Scotland, England, Northern Ireland and Wales, many are consistent across the four countries and so QOF data analysis allows a unique opportunity for a cross jurisdiction comparison of health care and quality.

The QOF is dynamic in nature and so in Scotland, England, Northern Ireland and Wales many indicators have changed since their inception in 2004. From 2006 onwards, any

changes made to the QOF occur after consensus decision by an expert panel, made up of a consortium of academic bodies, who review new evidence. Any changes suggested by this panel are then discussed, negotiated and a joint decision is made involving coordination between NHS Employers and the General Practitioners Committee (GPC) which are part of the British Medical Association (BMA). The National Institute for Health and Clinical Excellence (NICE) also provide independent expertise surrounding developing further clinical and health improvement indicators and this has been ongoing since April 2009. The QOF Advisory Board along with NHS Employers and the General Practitioners Committee (GPC) have developed a number of principles which are enshrined within the QOF. These principles include-

- Indicators should, where possible, be based on the best available evidence,

- The number of indicators in each clinical condition should be kept to the minimum number compatible with an accurate assessment of patient care,

- Data should never be collected purely for audit purposes,

- Only data which is useful in patient care should be collected. The basis of the consultation should not be distorted by an over emphasis on data collection. An appropriate balance has to be struck between excess data collection and inadequate sampling and

- Data should never be collected twice for example data required for audit purposes should be data routinely collected for patient care and obtained from existing practice clinical systems.

In the 2012/2013 Scottish, English, Northern Irish and Welsh QOF there were four main components, known as domains. The four domains; clinical, organisation, patient experience and additional services, contain indicators against which the primary care practice scores points according to their level of achievement. In 2012/2013 practices could score up to a maximum of 1,000 points across 148 indicators.

6.2 Clinical Domains:

These are clinical indicators which exist across a wide variety of clinical conditions which are largely managed within primary care. The clinical conditions which are included in the QOF are common, associated with significant morbidity and are diagnostically unambiguous. The indicators that are set are evidence based, achievable by the primary care team, clearly defined and are able to be consistently extracted from the computerised

records of the general practices which participate in the QOF. Since the inception of the QOF the clinical indicators have evolved and developed over time; for example in Scotland in 2004/2005 there were 76 indicators from 10 clinical domains however in 2012/2013 there were 96 indicators from 22 clinical domains (Table 6-1). Similar changes to the QOF have occurred throughout the UK.

Clinical indicator area	2004/05 - 2005/06		2006/07 - 2007/08		2008/09		2009/10 - 2010/11		2011/12		2012/13	
	Number of indicators	Total points available	Number of indicators	Total points available	Number of indicators	Total points available	Number of indicators	Total points Available	Number of indicators	Total points Available	Number of indicators	Total points Available
Asthma	7	72	4	45	4	45	4	45	4	45	4	45
Atrial Fibrillation	-	-	3	30	3	30	3	27	3	27	4	27
Cancer	2	12	2	11	2	11	2	11	2	11	2	11
CHD (Coronary Heart Disease)	15	121	10	89	10	89	8	76	10	87	7	69
CKD (Chronic Kidney Disease)	-	-	4	27	4	27	5	38	5	38	5	36
COPD	8	45	5	33	5	28	5	30	5	30	5	30
Cardiovascular Disease - Primary Prevention	-	-	-	-	-	-	2	13	2	13	2	13
Dementia	-	-	2	20	2	20	3	26	2	20	3	26
Depression	-	-	2	33	2	33	3	31	3	53	3	31
Diabetes Mellitus	18	99	16	93	16	93	15	92	17	100	15	88
Epilepsy	4	16	4	15	4	15	4	14	4	15	4	14
Heart Failure	-	-	3	20	3	20	4	29	4	29	4	29
Hypertension	5	105	3	83	3	83	3	79	3	81	3	69
Hypothyroidism	2	8	2	7	2	7	2	7	2	7	2	7
Learning Disabilities	-	-	1	4	1	4	2	7	1	4	2	7
Mental Health	5	41	6	39	6	39	10	40	6	39	10	40
Obesity	-	-	1	8	1	8	1	8	1	8	1	8
Osteoporosis	-	-	-	-	-	-	-	-	-	-	3	9
(PAD) Peripheral Artery Disease	-	-	-	-	-	-	-	-	-	-	4	9
Palliative Care	-	-	2	6	2	6	2	6	2	6	2	6
Conditions assessed for smoking	-	-	2	68	2	68	2	60	2	60	4	73
Stroke & Transient Ischaemic Attack	10	31	8	24	8	24	7	22	8	24	7	22
Totals	76	550	80	655	80	650	87	661	86	697	96	669

Table 6-1   Clinical domains and indicators included in the Scottish QOF by year 2004/2005 to 2012/2013

6.3 Health care system changes since devolution:

Since health care devolution, the NHS, in Scotland, England, Northern Ireland and Wales, has undergone significant change. In Scotland, integration of healthcare occurred, with the formation of fourteen geographical health boards and a "flat" organisational structure where the power previously associated with trusts was reduced (McLean et al., 2007). In England, the NHS took a "top down" approach to management and became focused on meeting targets- especially focusing on waiting times. This led to the formation of independent sector treatment centres, foundation trusts and private polyclinics (Bevan and Hood, 2006). However of late, focus has shifted towards providing a healthcare service based on patient choice resulting in more healthcare providers and increased privatisation especially within primary care. In Wales, after devolution, a relatively radical change to the NHS occurred. A strong public health focus resulted in local health boards working in partnership with local commissioning authorities (National Assembly for Wales, 2001). While in Northern Ireland difficulties in the peace process meant that changes to healthcare policy have been limited with periods of "direct rule" from UK ministers even after devolution (Greer, 2004).

Given these changes, comparing quality of care across the UK has been challenging. However some QOF indicators are consistent across the UK and given the high uptake of the QOF amongst UK GPs, analysis of QOF data allows a unique opportunity for the comparison of the quality of care between the four countries to occur. This cross-jurisdiction comparison is helpful to determine possible trends, potential areas of concern and possible patterns in performance that occur within primary care.

6.3.1 QOF in Scotland:

In 2012/2013, 988 practices out of 996 practices participated in the QOF (99.2%). The average number of points obtained by the GP practices was 979 out of a possible 1000 (QOF Scotland, 2013). Ten Mental Health (MH) indicators for individuals with schizophrenia, bipolar disorder and other psychoses contributed a maximum of 40 points from the available 1,000 points in 2012/2013. QOF data is published by ISD Scotland and is readily available on their website.

6.3.2 **QOF in England:**

As was seen in Scotland, the English QOF had a high uptake amongst GP practices, with 8,020 practices covering over 99% of registered patients participating in the 2012/2013 QOF. The average number of points achieved was 960.8 (QOF England, 2013). As with the Scottish 2012/2013 QOF, there were 148 indicators across four domains, making up a possible 1,000 points. In parallel with Scotland there were ten Mental Health indicators contributing to a maximum of 40 points. English QOF data is published by the Health and Social Care Information Centre (HSCIC) and again is readily available.

6.3.3 **QOF in Northern Ireland:**

In Northern Ireland in 2012/2013, every single GP practice (353) participated in the QOF. The average total number of points achieved was 981 (QOF Northern Ireland, 2013). As with Scotland and England, 148 indicators were measured across the four domains contributing to a maximum of 1,000 points. QOF data is published by the Department of Health, Social Service and Public Safety (DHSSPSNI) and is readily available on their website. In parallel with Scotland and England, in the 2012/2013 QOF there were ten Mental Health indicators contributing to a maximum of 40 points.

6.3.4 **QOF in Wales:**

In Wales in 2012/2013, every single GP practice (471) participated in the QOF. Again 148 indicators were measured across the four domains contributing to a maximum of 1,000 points. The average number of points achieved was 970 (QOF Wales, 2013). QOF data is published by the Welsh Government and is readily available on their website. In the 2012/2013 Welsh QOF there were ten Mental Health indicators contributing to a maximum of 40 points.

6.4 Concerns about the QOF:

Although the QOF was introduced as a way of incentivising practices and improving the delivery of care, it has been recognised that it has a number of limitations. Despite the high rates of GP participation and high level of point attainment over a number of years (Sutton and McLean, 2006; Doran et al., 2008; Fischbacher et al., 2009; Kiran et al., 2010), the evidence for improvement in patient outcome has been inconsistent. For example Sermuga and colleagues, (2011) found that "good quality of care for hypertension was stable or

improving before pay for performance was introduced" and "(pay for performance) had no discernible effects on processes of care or on hypertension related clinical outcomes" (Sermuga et al., 2011). Similar findings have been found by Purdy and colleagues, (2011) who investigated emergency respiratory admissions and by Bottle and colleagues, (2008) who reported on rates of hospitalisation for coronary heart disease. These reports have all led to concerns about the effectiveness of the QOF in improving patient care.

There is also recognition that the use of individual measures of care delivery (such as a single QOF indicator) as a marker of quality of clinical care is limited and that composite models (Holmboe et al., 2010) may be more helpful. It is thought that composite models highlight opportunities for further improvement in care provision even when the individual measures already indicate that care quality is high. Additionally there have been concerns, that the maximum payment thresholds for QOF indicators are too low- which may lead to some high performing practices wrongly assuming that their quality of care does not require further improvement (Fleetcroft et al., 2008; Ashworth and Kordowicz, 2010) and so further compromising patient care. The use of multiple QOF indicators within a composite model, as an alternative method of describing the quality of clinical care processes and outcome may be helpful in the future when evaluating quality of care delivered and is an area of recent interest. In a provisional study, de Wet and colleagues (2012), combined QOF indicators to generate a care bundle to measure the quality of evidence based care provision in nine practices in Scotland. They found that while compliance with individual QOF-based care bundle components was high, overall ('all or nothing') compliance with QOF-based care bundles was substantially lower. They therefore concluded that "care bundles may provide a more informed measure of care quality than existing methods" (de Wet et al., 2012). Their work has highlighted some further limitations of measuring and interpreting single indicator QOF rates.

It has also been recognised that by financially rewarding practices for meeting a range of clinical, organisational and patient experience indicators a number of unintended adverse consequences may arise. The risks to the quality of care delivered, if payment is linked to delivery of care have long been recognised. A systematic review by Choix- Couturier and colleagues, (2000) identified a number of risks including:

- Limited continuity of care,

- Reduced range of services available, especially preventative and psychological support,

- Under use or improper use of emergency services resulting in delayed treatment,

- Reduced confidence of patients,

- Risk of ethical conflicts,

- Reduced time for teaching and research,

- Multiplicity of guidelines from different sources and

- Conflicts of interest between physicians and patients.

In particular there have also been concerns that patients may be coerced or refused care if they are non-compliant with the indicator QOF (Casalino and Elster, 2007; McDonald and Roland, 2009). In order to protect against this, a number of mechanisms have been built into the QOF system. In particular the setting of the target of the upper payment thresholds for indicators at under 100% and the facility to "except" patients from QOF indicator targets, if felt to be clinically appropriate.

6.5 Exception Codes:

Exception codes can be applied to individuals within certain indicators included in the QOF if felt to be clinically appropriate. These individuals are then excepted from the indicator denominator and therefore the payment calculation. Reasons for exception coding include:

- patient refusal to attend; for this to occur, patients have to be recorded as refusing to attend for review after being invited to attend on at least three occasions during the financial year to which achievement payments relate (except in the case of indicator CS002(S), where the patient should have received the nationally agreed invitations from the recall system),

- patients for whom it is not appropriate to review the chronic disease parameters due to particular circumstances, for example, a patient who has a terminal illness or is extremely frail,

- patients newly diagnosed or who have recently registered with the contractor who should have measurements made within three months and delivery of clinical standards within nine months e.g. blood pressure or cholesterol measurements within target levels,

- patients who are on maximum tolerated doses of medication whose levels remain sub-optimal,

- patients for whom prescribing a medication is not clinically appropriate e.g. those who have an allergy, contraindication or have experienced an adverse reaction,

- where a patient has not tolerated medication,

- where a patient does not agree to investigation or treatment (informed dissent) and this has been recorded in their patient record following a discussion with the patient,

- where the patient has a supervening condition which makes treatment of their condition inappropriate e.g. cholesterol reduction where the patient has liver disease or

- where an investigative service or secondary care service is unavailable.

Although an individual may meet more than one reason for exception, only one exception code is recorded. The exact reason for exception coding is often not recorded by the GP surgery and data regarding exception rate by exception type is extremely limited.

Since 2011/2012 there have been three clinical indicator groups where exception reporting is not applicable- Obesity, Learning Difficulties and Palliative Care. In obesity and learning difficulties the QOF indicator refers only to a register- with no numerator or denominator and so no exceptions are possible. In Palliative Care, the indicators are structured in such a way that neither a numerator nor denominator exists, therefore exception reporting does not apply.

6.5.1 Exception coding across Scotland, England, Northern Ireland and Wales

Reasons for exception reporting are fairly consistent across all four countries, except in Scotland, where failure to attend for a review after three invitations is classified as informed dissent (along with patient choice to not engage with a treatment and/or investigation). However this failure to attend after three invitations is considered as a separate exception code in England, Northern Ireland and Wales.

6.5.2 Exception coding in MMI

For individuals on the Mental Health register, exception reporting may additionally occur if the individual has an exception code for a similar indicator for another chronic disease - for example if an individual with diabetes and schizophrenia is excepted from the HbA1c diabetes target indicator, then they too will be excepted from the mental health blood glucose indicator. This does not occur across other comorbid chronic diseases (for example diabetes and coronary heart disease) even if the indicators are similar.

6.5.3 **Concerns about exception reporting:**

Although exception reporting was introduced as a way of safe guarding patient care, it has been recognised that it has potential drawbacks. Exception reporting allows practices to receive the maximum renumeration without necessarily providing the required care for all eligible patients and so it is recognised that if exception rules are applied too readily or indeed inappropriately, high achievement scores may mask suboptimal care (Roland 2004). There are also concerns that exception coding can be used for financial exploitation-whereby patients in whom the target has been missed are falsely excluded, a practice known as "gaming". In the UK however, there is little evidence of this practice occurring.

Since the introduction of the QOF in 2004, there have also been concerns expressed by the Royal College of General Practioners (RCGP) that exception reporting may be disproportionately elevated in certain cohorts of the population- namely individuals with multiple chronic physical health problems, individuals living in more deprived areas and individuals with mental illness (NHS Alliance, 2004). These individuals are often the most vulnerable and most in need of high quality clinical care. This has led to concerns that individuals who are excepted may paradoxically experience a lower standard of treatment and care, due to increased focus on target attainment. Given the profile of individuals at most risk of being excepted, clinicians and academics have argued that this may contribute to a worsening of health inequalities (NHS Alliance, 2004).

Exception rates are generally low (less than 6%) (Doran et al., 2008), with little evidence of widespread fraud or gaming (Simpson et al., 2007), but there are concerns about some practices achieving high scores by excepting or excluding unusually large numbers of patients (Doran et al., 2008; Gravelle et al., 2010). There is also wide variation in exception rates by clinical indicator, potentially indicating variation in prioritisation of care and subsequent inequality in level of care and delivery of treatment provided for certain QOF indicators.

Despite there being concerns about the inappropriate use of exception reporting with subsequent calls for changes to be made (Audit Commission, 2011), General Practitioners perceive exception reporting as an important and defensible safeguard against inappropriate or over treatment of patients (Campbell et al., 2011). To date little work has been done, comparing rates of exception coding by QOF indicator over time, exploring the

characteristics of low achievement indicators and exploring the characteristics of practices with high exception rates.

6.6 Exclusion Criteria:

Given the range of clinical indicators within a clinical domain, not all individuals on a clinical domain register, will be suitable for every indicator. Some individuals will therefore require to be excluded from a certain indicator for definitional reasons. For example for attainment of mental health indicator 16 at least 40% of patients aged 20 to 60 in Scotland with schizophrenia, bipolar affective disorder and other psychoses should have a cervical screening test performed in the preceding 5 years, all males of any age and all females aged <20 and >60 require to be excluded from the QOF denominator as they are unable to participate in cervical screening.

Similarly other indicators (and therefore the indicator denominator) may refer only to patients of a specific age group (e.g. 14 to 19 years old), patients with a specific status (e.g. those who smoke), or patients with a specific length of diagnosis (e.g. greater than 1 year). A further example of reasons for exclusion would be for the 2011/2012 QOF Asthma 3 indicator (40% of patients with asthma between the ages of 14 and 19 should have a record of smoking status in the previous 15 months). Asthma patients who do not fit into this age bracket (i.e. individuals who are <14 and >19) are excluded from the denominator on the basis of the indicator definition. Exclusions are important considerations when calculating target attainment rates and in the generation of supplementary payment for GPs.

6.7 QOF Data Collection and analysis:

Although the QOF data that is collected is not primarily a research data set, the information gathered can be utilised for clinical audit purposes. Due to the level of detail obtained from each practice it can be used to help gauge healthcare equality. Information regarding exception reporting across many clinical domains can also be obtained and comparisons of exception rates within countries and between indicators can be reported.

Given the consistency of some QOF indicators between Scotland, England, Northern Ireland and Wales, QOF data analysis allows a unique opportunity to compare health care data and aspects of quality of care across the four countries. In particular the ten Mental Health indicators were consistent across all four countries until 2013/2014.

6.8 Exception Rate Reporting Work to date:

Studies on QOF data and in particular QOF exception reporting are infrequent and much of the literature surrounding exception reporting arise from English General Practices and as such are not directly comparable to the Scottish, Welsh and Northern Irish populations. While there have been studies investigating the relationship between remoteness and quality of care (McLean et al., 2007), practice size and QOF attainment (Wany et al., 2006) and the relationship between choice of clinical computing system and QOF attainment (Kontopantelis et al., 2013) studies investigating exception rates are infrequent.

One recent paper, focused on rates of informed dissent as a particular reason for exception coding across clinical indicators (including three Mental Health Indicators). It found that higher rates of informed dissent were associated with: higher numbers of registered patients, higher levels of local area deprivation, and failure of the practice to secure maximum remuneration in the previous year (Doran et al., 2012). The relationship of higher exception coding rates and deprivation has been reported elsewhere; where one study found that "practices with a more deprived patient population were more likely to report 'exceptions' for Diabetes indicators." Interestingly no such relationship was reported with the achievement of QOF targets (Sigfrid et al., 2006). However clearly more work regarding exception rates could be undertaken, especially within a Scottish primary care setting.

6.9 Cross Jurisdiction QOF Work to Date:

Studies comparing QOF data between the four UK countries are extremely limited. One study by Saxena and colleagues, (2007) investigated the relationship between practice size, caseload, deprivation and quality of care of patients with coronary heart disease, hypertension and stroke using primary care data from Scotland and England- however this study did not compare data between the countries during their analysis. To date only one study has directly compared indicator achievement rates, across Scotland, England, Northern Ireland and Wales. McLean and colleagues, (2007) compared achievement rate data across a number of indictors in coronary heart disease (CHD), hypertension, stroke and diabetes. They found that the quality of care in CHD, stroke, hypertension and diabetes in Wales was significantly lower than elsewhere in the UK particularly for the complex care process, intermediate outcomes and treatment QOF indicators (McLean et al., 2007).

There has also been one qualitative study investigating GPs attitudes to exception reporting across all four UK countries (Campbell et al., 2011). This qualitative analysis of practice staffs' views on exception reporting in 27 practices recruited from Scotland (2), England (21), Northern Ireland (2) and Wales (2) found that practice staff viewed exception reporting as "an important and clinically necessary part of the QOF." They justified exceptions on the basis of "practicing patient-centred care within a framework of population-based health measures", or "because of the poor face validity of the indicators themselves for individual patients". Practices generally reported that excepting patients was the "exception to the rule" and that it was an important and defensible safeguard against inappropriate treatment or over-treatment of patients. When directly questioned about inappropriate excepting they stated that this may occur in "other practices". However some participants did acknowledge that exception reporting was used, particularly at the end of the financial year, to help meet unmet targets and to prevent the practice being penalised financially. Nonetheless the authors concluded that "most practices value and use exception reporting as a clinical safeguard to quality individual patient care within an evidence-based but largely population-level and inflexible framework" (Campbell et al., 2011). Unfortunately in the study, no comment in potential differences in attitudes between the four countries was made. This would likely have been limited by the small numbers of non-English practices included in the study.

To date little work has specifically focused on rates of payment, rates of population achievement and exception rates of Mental Health indicators compared to other physical health indicators. There have also been no studies which have specifically explored exception and achievement rates for Mental Health indicators as a potential marker of inequalities in health care provision across all four UK countries.

6.10 Aims:

1. To describe and compare indicator payment, population achievement and exception rates for Body Mass Index (BMI) and Blood Pressure (BP) recording for individuals with Major Mental Illness (schizophrenia, bipolar disorder and other psychoses) relative to Diabetes and Chronic Kidney Disease (CKD) across the UK in 2011/2012 and 2012/2013.

2. To compare population achievement rates of these indicators across Scotland, England, Northern Ireland and Wales for 2011/2012 and 2012/2013.

6.11 Scientific rationale:

The QOF incentivises Body Mass Index (BMI) and Blood Pressure (BP) recording for individuals with Major Mental Illness (schizophrenia, bipolar disorder and other psychoses). It also incentivises BMI recording in Diabetes and BP recording in Chronic Kidney Disease (CKD). As these indicators were defined in the same way and were consistent across the four UK countries, they were chosen for further study and comparison.

6.12 Methodology:

To explore the potential inequality in access to care, a detailed comparison of payment, population achievement and exception rates for two of the ten Mental Health (MH) indicators was undertaken for the two most recent QOF years (2011/2012 and 2012/2013). The indicators (Blood Pressure (BP) recording and Body Mass Index (BMI) recording in MMI) were chosen as both are clinically important and are consistent across the whole of the UK.

For comparison, BP recording in Chronic Kidney Disease (CKD) and BMI recording in diabetes were chosen as proxy comparator indicators. Again both indicators are clinically important and were consistent across the whole of the UK.

High blood pressure is an important cardiovascular risk factor. The health benefits gained from successful BP control (defined as systolic BP<140mmHg) are marked- with a predicted reduction in 28-44% of strokes and 20-35% of ischaemic heart disease (He and MacGregor, 2003). Frequent, accurate recording and monitoring of BP is also associated with reductions in systolic and diastolic BP (Glynn et al., 2010) and so is recognised as an important intervention. BP recording in individuals with CKD and MMI has been included in the QOF since 2006 and 2011 respectively and given its consistency across the four countries within the UK, it was chosen for more detailed study.

While it is recognised that poor diet and sedentary lifestyle has contributed to increased rates of obesity (Healthy Lives, Healthy People, 2011), Scotland in particular has one of the highest prevalence's of obesity in Europe (28.2% of all adults have a BMI > 30kg/m^2) (Grieve et al., 2013). In individuals with MMI, obesity occurs at an even higher rate (Ratliff et al., 2013; Allison et al., 1999) and there is evidence to suggest that obesity in

individuals with schizophrenia, has a profound influence on cardiometabolic risk compared to age, gender, race and BMI matched controls without MMI (Bailey et al., 2012). Reasons for the increased risk are unclear but may be partly explained by poor diet, physical inactivity and psychotropic medications. Across Europe a drive towards increased screening and preventative interventions, particularly for cardiovascular disease (European Guidelines on CVD Prevention, 2012) has led to a subsequent reduction in mortality (The Scottish Government Better Heart Disease and Stroke Care Action Plan, 2009). It is recognised that BMI recording in individuals with diabetes and MMI is an important public health issue. As such it has been included in the QOF since 2004 and 2011. Given its importance and its consistency across the UK it was chosen for more detailed study.

These two pairs of indicators were the only directly comparable, consistent indicators which occurred across the UK in the QOF.

Exception rate and payment rate data for recording of Body Mass Index (BMI) in individuals with Major Mental Illness (MMI) and Diabetes and BP recording in individuals with MMI and Chronic Kidney Disease (CKD) for 2012/2013 and 2011/2012 was obtained, from the Health and Social Care Information Service in England (HSCIS), Information Services Division (ISD) in Scotland, the Department of Health, Social Service and Public Safety in Northern Ireland (DHSSPSNI) and the Welsh Government Website.

Practice performance and payment was calculated based on indicator achievement rate; whereby achievement rate equalled the number of individuals who had successfully met the indicator criteria (numerator) divided by the total number of individuals who could have achieved that indicator target (denominator) once exclusions and exceptions had been removed. However given that high exception rates may artificially inflate achievement (payment) rate and mask suboptimal care, population achievement rate can be calculated for individual practices by dividing the number of patients who achieved the target by the number of patients who were eligible for the target with exceptions included back into the denominator (Figure 6-1). This is felt to be a more useful measurement of quality of care.

$$\text{Practice Payment/Indicator achievement rate} = \frac{\text{number of individuals who have successfully met the indicator criteria (numerator)}}{\text{number of individuals who could have achieved that indicator target (denominator)}}$$

once exclusions and exceptions have been removed.

$$\text{Population achievement rate} = \frac{\text{number of patients who achieved the target (numerator)}}{\text{number of patients who were eligible for the target}}$$

with exceptions included (denominator + exceptions)

Figure 6-1   Practice Payment and Population Achievement Rate Calculations

For some practices exception rate data was not available. This was due to either inconsistencies with the exception and achievement rate data or due to the exception data not being definitive (ISD Scotland). Only practices with an indicator denominator >5 were included in this study.

For both blood pressure and BMI, the Mental Health (MH) indicator was compared with the non-MH indicator within the same year and geographical location (i.e. within Scotland, England, Northern Ireland and Wales and also for the UK as a whole). As data were non-parametric and paired (within countries by GP practice identifier), differences in rates within the same country were compared using a sign test. Median population achievement rate, payment rate and exception rate were calculated along with inter quartile range (IQR). For the UK wide figures, differences in rates were compared using a non-parametric equality of medians test. Differences in median population achievement rate between countries were compared to England using a quantile regression analysis weighted for practice denominator. Results are reported as percentage point difference with 99% confidence intervals (CI).

6.13 Results:

6.13.1 2012/2013:

In Scotland, indicator payment and exception rate data were available for a maximum of 97.3% GP practices (n=969). In England data was available for 99% of practices (n=7,938) and in Northern Ireland and Wales, QOF data was available for all (100%) GP practices (Northern Ireland n=353 and Wales n= 471).

The percentage of the practice population on each disease register differed across the four countries to a significant extent; with higher prevalence found for Mental Health in Scotland and Wales (0.87% and 0.86%), for diabetes in England (4.83%) and for CKD in Wales (3.58%) (Table 6-2).

	England	Scotland	Northern Ireland	Wales
Mental Health				
Raw proportion (%)	0.84	**0.87**	0.84	**0.86**
Ratio to England	1	**1.04**	1	**1.02**
Diabetes				
Raw proportion (%)	4.83	**4.62**	**4.14**	**5.44**
Ratio to England	1	**0.96**	**0.86**	**1.13**
Chronic Kidney Disease				
Raw proportion (%)	3.36	**3.25**	**3.52**	**3.58**
Ratio to England	1	**0.97**	**1.05**	**1.07**

Table 6-2   Raw prevalence rate of QOF Registers, with comparison to England 2012/2013
All significant difference in prevalence rate from England are shown in bold

6.13.2 Body Mass Index (BMI) recording in Mental Health versus Diabetes:

Unweighted indicator payment and population achievement rate for BMI recording in Major Mental Illness was significantly lower than the payment and population achievement rates for BMI recording in diabetes throughout the whole of the UK combined; payment rate 92.7% vs. 95.5%, $p < 0.001$, population achievement rate: 84.0% vs. 92.5%, $p < 0.001$ and for each country individually; payment rate 92.4% vs. 95.4%, $p < 0.001$ and population achievement rate: 84.0% vs. 92.5%, $p < 0.001$ in England; payment rate 94.0% vs. 96.3%, $p < 0.001$ and population achievement rate: 82.2% vs. 92.1%, $p < 0.001$ in Scotland; payment rate 93.3% vs. 95.2%, $p < 0.001$ and population achievement rate 88.0% vs. 93.1%, $p < 0.001$ in Northern Ireland and payment rate 92.2% vs. 95.6%, $p < 0.001$ and population achievement rate: 82.1% vs. 91.8%, $p < 0.001$ in Wales (Table 6-3).

Although payment rates were consistently higher in Scotland for each of the indicators studied, higher exception rates led to the lower population achievement rates reported.

Exception rate, for BMI recording in MMI was significantly higher than the exception rate for BMI recording in diabetes; for the UK combined; 7.4% vs. 2.3%, $p < 0.001$ and for each country individually; 6.5% vs. 2.2%, $p < 0.001$ in England; 11.8% vs. 3.5%, $p < 0.001$ in Scotland; 4.3% vs. 1.6%, $p < 0.001$ in Northern Ireland and 9.5% vs. 3.4%, $p < 0.001$ in Wales. (Table 6-3)

		Payment Rate Median (IQR)		Exception Rate Median (IQR)		Population Achievement Rate Median (IQR)	
UK (n=9645)	MMI	92.7	(89.3-95.8)	7.4	(3.3-15.9)	84.0	(76.3-90.0)
	Diabetes	95.5	(93.3-97.2)	2.3	(0.9-4.7)	92.5	(89.7-94.9)
England (n=7856)	MMI	92.4	(88.5-95.5)	6.5	(2.2-13.0)	84.0	(76.4-90.0)
	Diabetes	95.4	(93.2-97.1)	2.2	(1.0-4.0)	92.5	(89.8-94.9)
Scotland (n=965)	MMI	94.0	(91.4-97.2)	11.8	(5.4 - 19.3)	82.2	(74.4 – 88.9)
	Diabetes	96.3	(94.3-97.8)	3.5	(1.9 -6.1)	92.1	(89.4-94.6)
Northern Ireland (n=353)	MMI	93.3	(90.9-95.7)	4.3	(0.0-8.1)	88.0	(84.1-92.7)
	Diabetes	95.2	(93.3 – 97.1)	1.6	(0.5-3.4)	93.1	(91.2-95.0)
Wales (n=471)	MMI	92.2	(89.8-94.7)	9.5	(4.2-15.4)	82.1	(75.0-88.5)
	Diabetes	95.6	(93.4-97.3)	3.4	(1.8-5.7)	91.8	(88.9-94.0)

Table 6-3   Payment, exception and population achievement rates for recording of BMI in MMI and diabetes across the UK 2012/2013
Unweighted results All differences between payment, exception and population achievement rates for MMI vs. CKD for all countries individually and UK combined, **bold if statistically significant p<0.001**

6.13.3 Blood Pressure (BP) recording in Mental Health versus Chronic Kidney Disease:

Unweighted indicator payment and population achievement rates for Blood Pressure (BP) recording in Major Mental Illness were also significantly lower than payment and population achievement rates for Chronic Kidney Disease (CKD) across the whole of the UK combined; payment rate: 94.1% vs.97.8%, p<0.001 and population achievement rate: 87.0% vs. 97.1%, p<0.001; and for each country individually; payment rate: 93.8% vs. 97.7%, p<0.001 and population achievement rate: 87.0% vs. 97.2%, p<0.001 in England; payment rate: 95.9% vs. 98.4%, p<0.001 and population achievement rate: 85.7% vs. 97.2%, p<0.001 in Scotland; payment rate 94.9% vs. 97.9% and population achievement rate: 91.1% vs. 97.4%, p<0.001 in Northern Ireland and payment rate 94.0% vs. 97.8%, p<0.001 and population achievement rate 85.5% vs. 97.0%, p<0.001 in Wales (Table 6-4).

Although payment rates were consistently higher in Scotland for each of the indicators studied, higher exception rates led to the lower population achievement rates reported.

Exception rate was also significantly higher in MMI compared to CKD; 6.4% vs. 0.3%, p<0.001 for the UK combined, 5.6% vs. 0.0%, p<0.001 in England, 9.7% vs. 0.6%,

p<0.001 in Scotland, 3.4% vs. 1.6%, p<0.001 in Northern Ireland and 7.7% vs. 0.4%, p<0.001 in Wales (Table 6-4).

		Payment Rate Median (IQR)		Exception Rate Median (IQR)		Population Achievement Rate Median (IQR)	
UK (n=9725)	MMI	**94.1**	**(90.9-97.1)**	**6.4**	**(3.0-13.1)**	**87.0**	**(81.3-91.7)**
	CKD	**97.8**	**(96.3-98.9)**	**0.3**	**(0.0-1.0)**	**97.1**	**(95.5-98.4)**
England (n=7942)	MMI	**93.8**	**(90.5-96.8)**	**5.6**	**(1.7-10.6)**	**87.0**	**(81.3-91.7)**
	CKD	**97.7**	**(96.2-98.9)**	**0.0**	**(0.0-0.8)**	**97.2**	**(95.5 – 98.4)**
Scotland (n=962)	MMI	**95.9**	**(93.1-100.0)**	**9.7**	**(4.4- 15.7)**	**85.7**	**(80.0 - 91.2)**
	CKD	**98.4**	**(97.0-99.5)**	**0.6**	**(0.0-1.7)**	**97.2**	**(95.6 - 98.6)**
Northern Ireland (n=353)	MMI	**94.9**	**(92.4-97.5)**	**3.4**	**(0.0-6.9)**	**91.1**	**(86.7-94.3)**
	CKD	**97.9**	**(96.5-99.0)**	**1.6**	**(0.5-3.4)**	**97.4**	**(96.2-98.9)**
Wales (n=468)	MMI	**94.0**	**(91.1-97.2)**	**7.7**	**(3.5-13.2)**	**85.5**	**(80.4-90.0)**
	CKD	**97.8**	**(96.3-98.8)**	**0.4**	**(0.0-1.2)**	**97.0**	**(95.4-98.2)**

Table 6-4   Payment, exception and population achievement rates for recording of BP in MMI and CKD across the UK 2012/2013
Unweighted results All differences between payment, exception and population achievement rates for MMI vs. CKD for all countries individually and UK combined, **bold if statistically significant p<0.001**

6.13.4 Differences between countries:

The weighted median population achievement rates for BMI and BP recording in MMI were significantly lower in Scotland compared to England (BMI:-1.5% 99% CI -2.7 to -0.3%, p<0.001 and BP: -1.8% 99% CI -2.7 to -0.9%, p<0.001). Population achievement rates were also lower in Wales compared to England (Table 6-5). Rates in Northern Ireland for both Mental Health indicators were significantly higher compared to England (BMI: 2.1% 99%CI 1.1 to 3.0, p<0.001 and BP: 2.1% 99% CI 1.4-2.8%, p<0.001) (Table 6-5).

Differences in weighted median population achievement rates for BMI recording in Diabetes and BP recording in CKD in Scotland, Northern Ireland and Wales were less marked compared to weighted median population achievement rates in England (Table 6-5).

		England	Scotland	Northern Ireland	Wales
BMI Recording	Mental Health (MH12) % point difference (99% CI)	82.9 (76.0-88.5)	**-1.5 (-2.7 to -0.3) p<0.001**	**2.1 (1.1 to 3.0) p<0.001**	**-0.5 (-1.0 to -0.01) p=0.025**
	Diabetes (DM02) % point difference (99% CI)	92.2 (89.6-94.5)	**-0.5 (-1.0 to -0.05) p=0.004**	0.3 (-0.1 to 0.7) p=0.028	**-0.2 (-0.4 to -0.04) p=0.002**
BP Recording	Mental Health (MH13) % point difference (99% CI)	86.1 (81.0-90.3)	**-1.8 (-2.7 to - 0.9) p<0.001**	**2.1 (1.4 to 2.8) p<0.001**	-0.4 (-0.7 to 0.01) p = 0.013
	CKD (CKD02) % point difference (99% CI)	97.0 (95.4-98.1)	0.02 (-0.2 to 0.3) p=0.797	0.2 (0.01 to 0.4) p= 0.012	-0.07 (-0.17 to 0.03) p=0.058

Table 6-5 **Weighted Median Population Achievement Rate Percentage Point Difference from England by indicator for 2012/2013 with 99% Confidence Intervals weighted by practice denominator. All significant differences in percentage point from England are shown in bold**

6.13.5 **2011/2012**

In Scotland, indicator achievement and exception rate data were available for a maximum of 97.3% of GP practices (n=969). In England data was available for 99% of practices (n=7,938) and in Northern Ireland and Wales, QOF data was available for all (100%) GP practices (Northern Ireland n=353 and Wales n= 471).

Prevalence rates for the Mental Health, Diabetes and Chronic Kidney Disease (CKD) registers differed across the four countries to a significant extent; with higher prevalence rates for Mental Health found in Scotland and Wales (0.85% and 0.84%) for diabetes in England and Wales (4.62% and 5.26%) and for Chronic Kidney Disease in Wales (3.45%) (Table 6-6).

	England	Scotland	Northern Ireland	Wales
Mental Health				
Raw prevalence rate (%)	0.82	**0.85**	0.83	**0.84**
Ratio to England	1	**1.04**	1.01	**1.02**
Diabetes				
Raw prevalence rate (%)	4.62	**4.43**	**4.00**	**5.26**
Ratio to England	1	**0.96**	**0.87**	**1.14**
Chronic Kidney Disease				
Raw prevalence rate (%)	3.37	**3.27**	**3.28**	**3.45**
Ratio to England	1	**0.97**	**0.97**	**1.02**

Table 6-6   Raw prevalence rate of QOF Registers, with comparison to England 2011/2012
All significant difference in prevalence rate from England are shown in bold

6.13.6 Body Mass Index (BMI) recording in Mental Health versus Diabetes:

Unweighted indicator payment and population achievement rate for BMI recording in Major Mental Illness was significantly lower than the payment and population achievement rates for BMI recording in diabetes throughout the whole of the UK combined: payment rate 92.3% vs. 95.7%, p<0.001 and population achievement rate: 82.4% vs. 92.8%, p<0.001 and for each country individually; payment rate 92.2% vs. 95.7%, p<0.001 and population achievement rate: 82.6% vs. 92.9%, p<0.001 in England; payment rate 93.5% vs. 96.0%, p<0.001 and population achievement rate 78.1% vs. 92.1%, p<0.001 in Scotland; payment rate 92.5% vs. 95.5%, p<0.001 and population achievement rate: 86.7% vs. 93.2%, p<0.001 in Northern Ireland and payment rate 92.5% vs. 95.8%, p<0.001 and population achievement rate 80.0% vs. 91.9%, p<0.001 in Wales (Table 6-7).

Although payment rates were consistently higher in Scotland for each of the indicators studied, higher exception rates led to the lower population achievement rates reported.

Exception rate, for BMI recording in MMI was significantly higher than the exception rate for BMI recording in diabetes; for the UK combined; 8.9% vs. 2.8%, p<0.001 and for each country individually; 7.5% vs. 2.1%, p<0.001 in England; 14.3% vs. 3.5%, p<0.001 in Scotland; 4.8% vs. 1.7%, p<0.001 in Northern Ireland and 10.5% vs. 3.4%, p<0.001 in Wales. (Table 6-7)

		Payment Rate Median (IQR)		Exception Rate Median (IQR)		Population Achievement Rate Median (IQR)	
UK (n=9645)	MMI	92.3	(87.5-95.7)	8.9	(3.0-17.8)	82.4	(74.2-89.0)
	Diabetes	95.7	(93.6-97.4)	2.8	(1.1-6.8)	92.8	(90.0-95.1)
England (n=7998)	MMI	92.2	(86.7-95.7)	7.5	(2.5-14.3)	82.6	(74.5-89.2)
	Diabetes	95.7	(93.5-97.4)	2.1	(0.9-4.0)	92.9	(90.2-95.2)
Scotland (n=942)	MMI	93.5	(90.7-96.8)	14.3	(7.1 - 22.6)	78.1	(70.1-86.4)
	Diabetes	96.0	(94.0-97.7)	3.5	(1.8-6.0)	92.1	(88.8-94.6)
Northern Ireland (n=349)	MMI	92.5	(90.0-95.2)	4.8	(0.0-9.1)	86.7	(80.6-91.5)
	Diabetes	95.5	(93.5-97.1)	1.7	(0.6-3.1)	93.2	(91.0-95.3)
Wales (n=469)	MMI	92.5	(88.2-95.5)	10.5	(5.1-17.7)	80.0	(72.7-87.3)
	Diabetes	95.8	(93.6-97.5)	3.4	(1.8-5.2)	91.9	(89.2-94.4)

Table 6-7   Payment, exception and population achievement rates for recording of BMI in MMI and diabetes across the UK 2011/2012
Unweighted results Differences between payment, exception and population achievement rates for MMI vs. CKD for all countries individually and UK combined, **bold if statistically significant p<0.001**

6.13.7 Blood Pressure (BP) recording in Mental Health versus Chronic Kidney Disease:

Unweighted indicator payment and population achievement rates for Blood Pressure (BP) recording in Major Mental Illness were also significantly lower than payment and population achievement rates for Chronic Kidney Disease (CKD) across the whole of the UK combined; payment rate 94.1% vs. 97.8%, p<0.001 and population achievement rate: 86.3% vs. 97.2%, p<0.001; and for each country individually; payment rate 93.9% vs. 97.7%, p<0.001 and population achievement rate 86.4% vs. 97.2%, p<0.001 in England; payment rate 95.9% vs. 98.3% and population achievement rate: 84.1% vs. 97.5%, p<0.001 in Scotland; payment rate 94.7% vs. 98.0%, p<0.001 and population achievement rate: 90.0% vs. 97.5%, p<0.001 in Northern Ireland and payment rate 94.4% vs. 97.8%, p<0.001 and population achievement rate: 84.8% vs. 97.1%, p<0.001 in Wales (Table 6-8).

Although payment rates were consistently higher in Scotland for each of the indicators studied, higher exception rates led to the lower population achievement rates reported.

Exception rate was also significantly higher in MMI compared to CKD; 6.4% vs. 0.3%, p<0.001 for the UK combined, 5.9% vs. 0.0%, p<0.001 in England, 10.9% vs. 0.6%,

p<0.001 in Scotland, 3.7% vs. 0.0%, p<0.001 in Northern Ireland and 8.3% vs. 0.3%, p<0.001 in Wales (Table 6-8).

		Payment Rate Median (IQR)		Exception Rate Median (IQR)		Population Achievement Rate Median (IQR)	
UK (n=9725)	MMI	94.1	(90.6-97.4)	7.4	(2.5-17.8)	86.3	(80.0-91.3)
	CKD	97.8	(96.3-99.1)	0.3	(0.0-1.8)	97.2	(95.5-98.6)
England (n=8019)	MMI	93.9	(90.3-97.2)	5.9	(1.9-11.4)	86.4	(80.4-91.4)
	CKD	97.7	(96.2-99.0)	0.0	(0.0-0.7)	97.2	(95.5-98.5)
Scotland (n=902)	MMI	95.9	(92.9-100.0)	10.9	(5.6 -17.2)	84.1	(77.4 – 89.8)
	CKD	98.3	(97.0-99.5)	0.6	(0.0-1.6)	97.5	(95.5-98.7)
Northern Ireland (n=349)	MMI	94.7	(91.7-97.3)	3.7	(0.0-7.7)	90.0	(84.5-93.8)
	CKD	98.0	(96.8-99.0)	0.0	(0.0-0.6)	97.5	(96.0-98.8)
Wales (n=471)	MMI	94.4	(91.2-97.7)	8.3	(3.9-14.1)	84.8	(77.6-90.0)
	CKD	97.8	(96.2-99.0)	0.3	(0.0-1.0)	97.1	(95.2-98.4)

Table 6-8   Payment, exception and population achievement rates for recording of BP in MMI and CKD across the UK 2011/2012
Unweighted results Differences between payment, exception and population achievement rates for MMI vs. CKD for all countries individually and UK combined, **bold if statistically significant p<0.001**

6.13.8 Differences between countries:

Weighted median population achievement rates for BMI and BP recording in MMI were significantly lower in Scotland compared to England (BMI:-3.6% 99% CI -4.8 to -2.5%, p<0.001 and BP: -2.1% 99% CI -3.0 to -1.3%, p<0.001). Rates were also lower in Wales compared to England (Table 6-9). Rates in Northern Ireland for both Mental Health indicators were significantly higher compared to England (BMI: 2.5% 99%CI 1.6 to 3.4, p<0.001 and BP: 2.0% 99% CI 1.4 to 2.6%, p<0.001) (Table 6-9).

Differences in weighted median population achievement rates for BMI recording in Diabetes and BP recording in CKD in Scotland, Northern Ireland and Wales were less marked compared to weighted median population achievement rates in England (Table 6-9).

		England	Scotland	Northern Ireland	Wales
BMI Recording	Mental Health (MH12) % point difference (99% CI)	82.6 (74.5-89.2)	**-3.6 (-4.8 to -2.5) p<0.001**	**2.5 (1.6 to 3.4) p<0.001**	-0.4 (-0.9 to -0.1) p=0.025
	Diabetes (DM02) % point difference (99% CI)	92.9 (90.2-95.2)	**-0.8 (-1.2 to -0.3) p<0.001**	0.3 (0.04 to 0.7) p=0.025	**-0.3 (-0.4 to -0.9) p<0.001**
BP Recording	Mental Health (MH13) % point difference (99% CI)	86.4 (80.4-91.4)	**-2.1 (-3.0 to -1.3) p<0.001**	**2.0 (1.4 to 2.6) p<0.001**	**-0.4 (-0.8 to -0.1) p=0.002**
	CKD (CKD02) % point difference (99% CI)	97.2 (95.5-98.5)	0.002 (-0.2 to 0.2) p=0.979	**0.2(0.01 to 0.4) p=0.006**	-0.009 (-0.11 to 0.09) p=0.803

Table 6-9   Weighted Median Population Achievement Rate Percentage Point Difference from England by indicator for 2011/2012
99% Confidence Intervals weighted by practice denominator. **All significant differences in percentage point from England are shown in bold**

6.13.9 Summary of Main Findings:

Throughout the UK, population achievement and payment rates for recording of BMI and Blood Pressure in MMI were significantly lower than population achievement and payment rates for recording of BMI and Blood Pressure in diabetes and CKD. In general mental health population achievement rates were lower in Scotland and Wales compared to England but were higher in Northern Ireland compared to England. When directly comparing indicators which were of the same type, higher exception rates and lower population achievement and payment rates in MMI compared to diabetes and CKD were found across the whole of the UK. This is the first study to directly compare similar measurement indicator population achievement rates for different chronic diseases across Scotland, England, Northern Ireland and Wales. While the full reasons for these findings are unclear, the clinical, societal and financial implications of undetected, raised BMI and Blood Pressure would be significant.

6.14 Discussion:

6.14.1 Comparison with existing literature:

Almost ten years after the introduction of the QOF, there have been few studies comparing indicator achievement rates across the different countries. Changes in healthcare policy since devolution, with increased integration in Scotland (McLean et al., 2007), a "top

down," "target meeting" approach in England (Bevan and Hood, 2006), a strong public health focus in Wales (National Assembly for Wales, 2001) and limited change in Northern Ireland due to a protracted peace process (Greer, 2004) has led to difficulties in cross-national comparisons of healthcare systems and outcomes. However the consistency across the UK of the QOF indicators included in this study, has allowed a comparison of the quality of care between the four countries. This cross- jurisdiction comparison is helpful to determine trends, potential areas of concern and possible patterns in performance that occur within primary care. The finding of lower population achievement rates and higher exception rates for both mental health indicators across all four countries improves not only the generalisability of these results but also suggests that this is a UK wide pattern.

Difference in prevalence rates of the registers included in this study across the four countries is of note. In particular the finding of the relatively high prevalence rate of the diabetes register in England compared to Scotland and Northern Ireland. This finding was unexpected, and represents a marked increase in the English estimated prevalence of diabetes from the 2004/2005 QOF data. This finding may in part be explained by differences in disease prioritisation since devolution within the four countries.

The finding of higher population achievement rates in Northern Ireland, and lower population achievement rates in Scotland and Wales compared to England has been reported elsewhere, although for intermediate outcome and treatment indicators for CHD, stroke, hypertension and diabetes (McLean et al., 2007). Potential reasons for the higher population achievement rates in Northern Ireland may include better health, improved population stability or a younger population compared to the rest of the UK. There is evidence from England that practices with a higher proportions of patients over the age of 65 have lower achievement rates (Doran et al., 2006).

6.14.2 Differences between BMI Recording in Mental Health versus Diabetes:

The findings of significantly lower population achievement rates for BMI recording in MMI compared to Diabetes, is of clinical concern. Given the move towards primary prevention, a population achievement rate of 78%, for recording of BMI in MMI in Scotland suggests that although the majority are receiving QOF level care, there is room for improvement as the remaining proportion may be missing out on opportunities for

screening and subsequent intervention to address cardiometabolic risk. Whether this improvement is possible, given that the onus is on individuals to attend their practice, would be best explored through subsequent studies.

Reasons for the lower achievement rates observed in the MMI indicators may be best considered in relation to the patient, the practice and the indicator itself. The QOF does not incentivise home visits and so, if individuals do not attend, they are more likely to be excepted: this may account for higher levels of exceptions in individuals with MMI, who at times can be difficult to engage with. It is also recognised that individuals who are housebound (which is a reason for exception) have higher rates of mental illness (Joan et al., 2011). While obesity is recognised as a major public health problem, there are many barriers to its management including- lack of motivation on the patient's part (Mercer and Tessier, 2001). These reasons may contribute to the lower population achievement rates and higher exception rates reported in this study.

Practice factors contributing to lower achievement rates may include GPs or practice nurses perceiving a lack of training, inadequate facilities and poor success rates within obesity management (Mercer and Tessier, 2001). The primary care clinician may also perceive that obesity should be addressed within secondary care and so they may focus their consultation on adherence to antipsychotic medications and assessing suicide risk (which are not QOF incentive outcomes). However given the high rates of obesity within the UK and the planned retirement of the BMI indicator for the 2014/2015 QOF in England this finding is of concern (QOF England, 2015), as it may lead to further losses in opportunity to intervene and improve the physical health of this group of individuals.

6.14.3 Differences in BP Recording in Mental Health versus Chronic Kidney Disease:

The findings of significantly lower population achievement rates for BP recording in MMI is also of clinical concern. While it is unclear from this data what proportion of those with a recorded BP had normal or elevated BP, it is recognised that frequent, accurate recording and monitoring of BP is associated with reductions in systolic and diastolic BP and therefore better control. BP monitoring for individuals with schizophrenia on antipsychotic medication, has also been recommended in the NICE guideline for schizophrenia since 2009 (NICE Clinical Guideline 82, 2009). Although the drive towards a more integrated approach to the management of the physical health of individuals with MMI, has been

relatively recent (London School of Economics, 2012: Schizophrenia Commission, 2012), the evidence for poor cardiometabolic health in this cohort of patients has been apparent since the late 1990s and early 2000s (Harris and Barraclough, 1998; Brown et al., 2000) and has been reflected within clinical guidelines over the past 5 years. This disparity in recording of BP in individuals with MMI compared to individuals with CKD is of concern and highlights possible inequalities in access to incentivised healthcare.

6.14.4 Other possible reasons for the differences observed:

While it is recognised that individuals with MMI experience many barriers to care, one possible reason for the lower population achievement and payment rates observed may include the stigma associated with mental illness, as well as the perceived separation of physical and mental healthcare by the patient, their carer, GPs and psychiatrists. Although individuals with MMI have more physical health problems than the general population, inequalities such as those outlined in Chapter 1 are persistently reported for both the access to and the quality of a range of physical healthcare services (Lambert and Newcomer, 2009; de Hert 2011a).

However, there are likely to be several other factors which interact to contribute to the lower population achievement and payment rates observed in the MMI indicators. Firstly, the Mental Health BMI and BP indicators were introduced into the QOF in 2011/2012, while the BMI measurement indicator for Diabetes has been part of the QOF since its inception in 2004/2005 and, similarly, the BP measurement indicator QOF for CKD was introduced in 2006/2007. It is recognised that indicator payment rates improve with time and then plateau (Reeves et al., 2010) and so the disparity in length of time that the indicators have existed may contribute to the differences in population achievement and payment rate observed.

Another possible explanation may be that while Blood Pressure recording and BMI calculation have long been recognised as important aspects of the management of CKD and Diabetes - as evidenced by guidelines dating back many years - this aspect of monitoring and treatment for individuals with MMI has been highlighted only relatively recently. A further important factor that may contribute to the lower population achievement and payment rates observed in the MMI indicators is that of multimorbidity and the inadequacy of a single-disease focused practice and organisation that currently dominates clinical work in the NHS. This often leads not only to the separation of the

physical and mental health needs of patients, but also the separation of the multiple physical health needs of a complex multimorbid patient into single organ or single disease focused specialists.

6.15 Strengths and Limitations:

This is the first study to directly compare population achievement, payment and exception rates for individual mental health indicators with other individual chronic disease indicators across the whole of the UK. These results may act as a starting point for a more detailed examination of the possible reasons for these findings. The national scope of this study, with data from England, Scotland, Wales and Northern Ireland and the high level of uptake of the QOF within UK practices represents strengths of this study, but some limitations are acknowledged.

The QOF data used is a payment rather than quality monitoring system and was obtained at a practice rather than a patient level basis- this meant that patient level case mix adjustment was not possible. Given that individuals with a chronic disease are likely to have more than one (Barnett et al., 2012), it was not possible to assess the effect of multimorbidity on achievement and exception rates and is a limitation to this work. As individual patients can appear in more than one chronic disease indicator denominator, the level of patient overlap between the three chronic diseases (MMI, CKD and diabetes) investigated was not ascertained.

A further limitation is that due to exception reporting being under individual practice control, there may be some variation in practice policy, both locally and between countries. For example some practices in certain parts of the country may not directly record all rates of exception if they have exceeded the upper payment threshold for the indicator however this may not be the case in other parts of the country. Differences in practice performance are also associated with choice of clinical computing system (Kontopantelis et al., 2013) and given that data were obtained from the whole of the UK, variation in clinical computing software likely occurred and may be a confounder. While data from two contractual years has been reviewed, further longitudinal work is required to determine if these differences are sustained over a prolonged time frame.

6.16 Conclusions:

Although rates of population achievement, payment and exception reporting vary across clinical indicators, this study has found evidence of: lower population achievement rates, lower payment rates and higher rates of exception reporting for BMI and BP recording in MMI compared to Diabetes and CKD, throughout the whole of the UK. Variation in population achievement rate of the mental health indicators across the UK, with generally lower rates in Scotland and Wales relative to England and higher rates in Northern Ireland was also found. Explanations for these findings are multifactorial and include patient, clinician and wider organisational factors. However, they may represent an element of inequality in access to healthcare for individuals with MMI compared to individuals without MMI. Given these findings, further investigation, for example through detailed auditing of patient level data, and monitoring of patterns of exception coding, along with continued monitoring of population achievement rate data, is required to ensure that the QOF indicators and indeed exception reporting is appropriately used within primary care. Continued efforts must also be made to reduce barriers and improve integration of primary and secondary care to provide higher quality healthcare for individuals with Major Mental Illness.

Chapter 7 Possible mechanisms for inequality: longitudinal data from the Scottish Quality and Outcomes Framework (QOF)

Chapter Overview:

Further to the findings in Chapter 6, this chapter focuses on the QOF in Scotland and compares access to health care for individuals with MMI to a number of other chronic physical diseases using data from 2005/2006 until 2012/2013. Access to health care and potential inequalities are assessed using exception reporting data. Individual mental health indicators, single chronic disease indicators and composite indicator exception rates are compared to measure access to care and to determine possible inequalities in healthcare.

7.1 Aims:

1. To describe rates of exception reporting across different Mental Health indicators in Scotland compared to rates of exception reporting for other chronic physical health conditions.

2. To determine if specific mental health indicators in Scotland have significantly different rates of exception reporting compared to specific indicators for asthma, epilepsy, diabetes, dementia, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD) and hypertension.

3. To determine if composite Mental Health indicators have significantly different rates of exception reporting compared to other composite clinical indicators, for the two most recent QOF years (2012/2013 and 20112/2012).

4. To describe patterns of exception rates for each of the mental health indicators and their proxy comparator indicators over time (i.e. 2005/2006 to 2012/2013) within Scotland.

7.2 Methodology:

A retrospective survey of exception rate data available on the Quality and Outcome Frameworks (QOF) Information Services Division (ISD) of NHS Scotland, website for 2005/2006 until 2012/2013 for all the Mental Health indicators was carried out. This data

is freely available and contains information on nearly all the 988 GP practices in Scotland which utilise the QOF scheme.

Median rate of exception reporting for each Mental Health indicator and comparator physical health indicator, along with the 95% confidence interval (CI) and the inter-quartile range (IQR) were calculated. Median rates were charted over time to determine trends in exception rate reporting.

A number of proxy indicators for other chronic physical health conditions, deemed comparable to the Mental Health (MH) indicators were identified. As data was non-parametric medians across different indicators over different years were calculated using a non-parametric equality of medians test. All statistical analysis were carried out in STATA version 12.

7.2.1 Mental Health Indicators in the Scottish QOF over time:

Mental health (MH) has been represented in the QOF since its inception in 2004/2005. Initially there were 5 indicators (Table 7-1).

Short QOF Code	Descriptor of Code	No of points	Minimum Threshold attainment	Maximum Threshold attainment
MH01	The practice can produce a register of people with severe long term-mental health problems who require and have agreed to regular follow-up	7		
MH02	The percentage of patients with severe long-term mental health problems with a review recorded in the preceding 15 months. This review includes a check on the accuracy of prescribed medication, a review of physical health and a review of co-ordination arrangements with secondary care	23	25	90
MH03	The percentage of patients on lithium therapy with a record of lithium levels checked within the previous 6 months	3	25	90
MH04	The percentage of patients on lithium therapy with a record of serum creatinine and TSH in the previous 15 months	3	25	90
MH05	The percentage of patients on lithium therapy with a record of lithium levels in a therapeutic range within the previous 6 months	3	25	90

Table 7-1   Mental Health (MH) Indicators 2004/2005

However in the 2006/2007 QOF a number of changes occurred; MH01 was reworded from "severe long term mental health problems" to specifically mentioning mental health disorders- namely schizophrenia, bipolar affective disorder and other psychoses; MH03

was removed; MH06 and MH07 were added and MH02 was reworded and recoded as MH09. These remained in place until 2010/2011 (Table 7-2).

Short QOF Code	Descriptor of Code	No of points	Minimum Threshold attainment	Maximum Threshold attainment
MH04	The percentage of patients on lithium therapy with a record of serum creatinine and TSH in the previous 15 months	1	40	90
MH05	The percentage of patients on lithium therapy with a record of lithium levels in a therapeutic range within the previous 6 months	2	40	90
MH06	The percentage of patients on the register who have a comprehensive care plan documented in the records agreed between individuals, their family and/or carers as appropriate	6	25	50
MH07	The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who do not attend the practice for their annual review who are identified and followed up by practice team within 14 days of non-attendance	3	40	90
MH08	The practice can produce a register of people with schizophrenia, bipolar affective disorder and other psychoses	4		
MH09	The percentage of patients with schizophrenia and bipolar affective disorder and other psychoses with a review recorded in the previous 15 months. In the review there is evidence that the patient has participated in routine health promotion and prevention advice appropriate to their age and health status	23	40	90

Table -7-2   Mental Health (MH) Indicators 2006/2007 until 2010/2011

In 2011/2012 the mental health QOF underwent further substantial revision; MH04 and MH05 were reworded and recoded to MH17 and MH18; MH06 was re-coded as MH10; MH09 was expanded with specific targeting of alcohol consumption (MH11), body mass index (BMI) (MH12), blood pressure (BP) (MH13), cholesterol:hdl ratio (MH14) and blood glucose (MH15). Finally MH16 was added to incentivise cervical screening for women with MMI (Table 7-3).

Short QOF Code	Descriptor of Code	No of points	Minimum Threshold attainment	Maximum Threshold attainment
MH08	The practice can produce a register of people with schizophrenia, bipolar affective disorder and other psychoses	4		
MH10	The percentage of patients on the register who have a comprehensive care plan documented in the records agreed between individuals, their family and/or carers as appropriate	6	25	50
MH11	The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of alcohol consumption in the preceding 15 months	4	40	90
MH12	The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of BMI in the preceding 15 months	4	40	90
MH13	The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of blood pressure in the preceding 15 months	4	40	90
MH14	The percentage of patients aged 40 years and over with schizophrenia, bipolar affective disorder and other psychoses who have a record of total cholesterol:hdl ratio in the preceding 15 months	5	40	80
MH15	The percentage of patients aged 40 years and over with schizophrenia, bipolar affective disorder and other psychoses who have a record of blood glucose level in the preceding 15 months	5	40	80
MH16	The percentage of patients (aged from 25 to 64 in England and Northern Ireland, from 20 to 60 in Scotland and from 20 to 64 in Wales) with schizophrenia, bipolar affective disorder and other psychoses whose notes record that a cervical screening test has been performed in the preceding 5 years	5	40	80
MH17	The percentage of patients on lithium therapy with a record of serum creatinine and TSH in the preceding 9 months	1	40	90
MH18	The percentage of patients on lithium therapy with a record of lithium levels in the therapeutic range within the preceding 4 months	2	40	90

Table 7-3   Mental Health (MH) Indicators 2011/2012

In 2012/2013 the mental health indicators underwent further revision. MH14 was renumbered as MH19 (due to changes in the minimum threshold for attainment) and MH15 was replaced by MH20 (whereby HbA1c was added as an alternative to blood glucose level obtainment for individuals aged 40 years and over with schizophrenia, bipolar affective disorder and other psychoses). MH08, MH10, MH11, MH12, MH13, MH16, MH17 and MH18 remained unchanged from the previous year (Table 7-4).

Short QOF Code	Descriptor of Code	No of points	Minimum Threshold attainment	Maximum Threshold attainment
MH08	The practice can produce a register of people with schizophrenia, bipolar affective disorder and other psychoses	4		
MH10	The percentage of patients on the register who have a comprehensive care plan documented in the records agreed between individuals their family and/or carers as appropriate	6	30	55
MH11	The percentage of patients with schizophrenia bipolar affective disorder and other psychoses who have a record of alcohol consumption in the preceding 15 months	4	50	90
MH12	The percentage of patients with schizophrenia bipolar affective disorder and other psychoses who have a record of BMI in the preceding 15 months	4	50	90
MH13	The percentage of patients with schizophrenia bipolar affective disorder and other psychoses who have a record of blood pressure in the preceding 15 months	4	50	90
MH16	The percentage of patients (aged from 25 to 64 in England and Northern Ireland from 20 to 60 in Scotland and from 20 to 64 in Wales) with schizophrenia bipolar affective disorder and other psychoses whose notes record that a cervical screening test has been performed in the preceding 5 years	5	45	80
MH17	The percentage of patients on lithium therapy with a record of serum creatinine and TSH in the preceding 9 months	1	50	90
MH18	The percentage of patients on lithium therapy with a record of lithium levels in the therapeutic range within the preceding 4 months	2	50	90
MH19	The percentage of patients aged 40 years and over with schizophrenia; bipolar affective disorder and other psychoses who have a record of total cholesterol:hdl ratio in the preceding 15 months	5	45	80
MH20	The percentage of patients aged 40 years and over with schizophrenia; bipolar affective disorder and other psychoses who have a record of blood glucose or HbA1c in the preceding 15 months	5	45	80

Table 7-4   Mental Health (MH) Indicators 2012/2013

For each indicator, information technology systems hold the number of patients in each practice on every single clinical register. For the indicator target to be met and for payment to occur, each indicator has a minimum threshold for attainment. For example in 2012/2013, for MH10, a minimum of 30% of individuals on the mental health register should have a comprehensive care plan documented in their records in order for the practice to receive any payment for this indicator. Provided the minimum attainment figure is met, payment will occur.

7.2.2 **Identification of Comparator Indicators:**

As detailed in Table 6-1 in Chapter 6, many chronic physical diseases such as asthma, diabetes, epilepsy, COPD, chronic kidney disease (CKD) and dementia are included within the QOF. If there is equal access to care across all chronic diseases (both physical and mental illnesses), rates of exception should be similar across QOF indicators. Therefore indicators across a range of chronic physical health conditions deemed similar to the Mental Health Indicators were identified for each year of interest and exception rates were compared. Given the dynamic nature of the QOF, care was taken to ensure that indicators matched on a year to year basis.

Unfortunately an exact comparator for all mental health indicators across all years was not possible. Therefore comparable indicators from other chronic physical health conditions were selected as proxy comparators to the mental health indicators. These proxy indicators were also dynamic over time, with some being phased out and replaced by others.

For MH04: The percentage of patients on lithium therapy with a record of serum creatinine and TSH in the previous 15 months, DM22: The percentage of patients with diabetes who have a record of estimated glomerular filtration rate (eGFR) or serum creatinine testing in the previous 15 months was the best comparator indicator identified for years 2006/2007 until 2010/2011. MH04 was superseded by MH17, (the percentage of patients on lithium therapy with a record of serum creatinine and TSH in the preceding 9 months) in 2011/2012 and due to the change in timeframe for recording of estimated glomerular filtration rate (eGFR) or serum creatinine from 15 months to 9 months, no indicator from 2011/2012 onwards was deemed suitable as a comparator.

For MH05: The percentage of patients on lithium therapy with a record of lithium levels in a therapeutic range within the previous 6 months. No indicator was deemed suitable for comparison- as there is no other indicator for therapeutic drug level monitoring.

For MH06: The percentage of patients on the mental health register who have a comprehensive care plan documented in the records agreed between individuals, their family and/or carers as appropriate, it was deemed that EPILEPSY07: The percentage of patients aged 18 years and over on drug treatment for epilepsy who have a record of medication review involving the patient or carer in the previous 15 months, DEMENTIA02: The percentage of patients diagnosed with dementia whose care has been

reviewed in the previous 15 months, COPD13: The percentage of patients with COPD who have had a review, undertaken by a healthcare professional, including an assessment of breathlessness using the Medical Resource Council (MRC) dyspnoea score in the preceding 15 months and ASTHMA06: The percentage of patients with asthma who have had an asthma review in the previous 15 months were the best indicators to use for comparison.

The indicators EPILEPSY07, DEMENTIA02 and ASTHMA06 were available for comparison for 2006/2007 until 2010/2011 while the COPD13 indicator was available for comparison after its introduction in 2009/2010. EPILEPSY07 was withdrawn in 2010/2011 and so data for comparison after this time was not available. In 2011/2012 MH06 was recoded as MH10 and so in 2011/2012 MH10 was compared to DEMENTIA02, ASTHMA06 and COPD13. In 2012/2013 ASTHMA06 was replaced by ASTHMA09 (The percentage of patients with asthma who have had an asthma review in the preceding 15 months that includes an assessment of asthma control using the 3 Royal College of Physicians (RCP) questions). This was still deemed a comparable indicator to MH10. Therefore in 2012/2013 MH10 was compared to DEMENTIA02, ASTHMA09 and COPD13.

For MH07: The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who do not attend the practice for their annual review who are identified and followed up by practice team within 14 days of non-attendance, no comparable indicators for any of the years reviewed was identified.

For MH09: The percentage of patients with schizophrenia and bipolar affective disorder and other psychoses with a review (namely routine health promotion and prevention advice appropriate to their age and health status) recorded in the previous 15 months, indicator CVD02: The percentage of people diagnosed with hypertension who are given lifestyle advice in the last 15 months for: increasing physical activity, smoking cessation, safe alcohol consumption and healthy diet exception rate was deemed suitable as a comparator indicator. Exception rates for the indicator CVD02 was available for 2010/2011, allowing comparison for this year only. MH09 was then superseded and expanded in 2011/2012 and so data for comparison is available for 1 year only (2010/2011).

For MH11: The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of alcohol consumption in the preceding 15 months, no direct comparator indicator was identified.

For MH12: The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of BMI in the preceding 15 months which was introduced in 2011/2012, DM02: The percentage of patients with diabetes whose notes record BMI in the previous 15 months was identified as a comparator indicator and available from 2011/2012 onwards.

For MH13: The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of blood pressure in the preceding 15 months which was introduced in 2011/2012, CKD02: The percentage of patients on the CKD register whose notes have a record of blood pressure in the previous 15 months was identified as a comparator indicator and available from 2011/2012 onwards.

For MH14: The percentage of patients aged 40 years and over with schizophrenia, bipolar affective disorder and other psychoses who have a record of total cholesterol: High Density Lipoprotein (HDL) ratio in the preceding 15 months, no comparator indicator was identified. Although indicators in other chronic physical health conditions, involve the recording of cholesterol: HDL ratio, they all state that the ratio of cholesterol: HDL should be below a certain target in the preceding 15 months. Given this difference, no comparator proxy indicator was identified.

For MH15: The percentage of patients aged 40 years and over with schizophrenia, bipolar affective disorder and other psychoses who have a record of blood glucose level in the preceding 15 months, no comparator indicator was found.

For MH16: The percentage of patients aged 20 to 60 in Scotland with schizophrenia, bipolar affective disorder and other psychoses whose notes record that a cervical screening (CS) test has been performed in the preceding five years no comparator indicator exception data were available. Although indicator CS01: (the percentage of patients aged from 21 to 60 whose notes record that a cervical smear has been performed in the last five years) exists, no exception rate data were available.

For MH17: The percentage of patients on lithium therapy with a record of serum creatinine and (Thyroid Stimulating Hormone) (TSH) in the preceding 9 months introduced in 2011/2012, no comparator indicator was identified.

For MH18: The percentage of patients on lithium therapy with a record of lithium levels in the therapeutic range within the preceding 4 months, no comparator indicator was identified.

For MH19: The percentage of patients aged 40 years and over with schizophrenia; bipolar affective disorder and other psychoses who have a record of total cholesterol: HDL ratio in the preceding 15 months no comparator indicator was identified.

For MH20: The percentage of patients aged 40 years and over with schizophrenia; bipolar affective disorder and other psychoses that have a record of blood glucose or HbA1c recording in the preceding 15 months, no comparator indicator was identified.

Table 7-5 describes the years for which exception rate data and comparator indicator data were available.

	2004/2005	2005/2006	2006/2007	2007/2008	2008/2009	2009/2010	2010/2011	2011/2012	2012/2013
MH01	√Exception data	√√Exception data							
MH02	√Exception data	√Exception data							
MH03	√Exception data	√Exception data							
MH04 *MH17 **	√Exception data	√Exception data	√Exception data √DIABETES22	√Exception data √DIABETES22	√Exception data √DIABETES22	√Exception data √DIABETES22	√Exception data √DIABETES22	* *√Exception data*	* *√Exception data*
MH05 *MH18 **	√Exception data	√Exception data	√Exception data	√Exception data	√Exception data	√Exception data	√Exception data	* *√Exception data*	* *√Exception data*
MH06 *MH10 **			√ Exception data √EPILEPSY07 √ASTHMA06 √DEMENTIA02	√ Exception data √EPILEPSY07 √ASTHMA06 √DEMENTIA02	√ Exception data √EPILEPSY07 √ASTHMA06 √DEMENTIA02	√ Exception data √EPILEPSY07 √ASTHMA06 √DEMENTIA02 √COPD13	√ Exception data √EPILEPSY07 √ASTHMA06 √DEMENTIA02 √COPD13	* *√ Exception data* *√ASTHMA06* *√DEMENTIA02* *√COPD13*	* *√ Exception data* *√ASTHMA09* *√DEMENTIA02* *√COPD13*
MH07			√Exception data	√Exception data	√Exception data	√Exception data	√Exception data	√Exception data	√Exception data
MH08			√Exception data	√Exception data	√Exception data	√Exception data	√Exception data	√Exception data	√Exception data
MH09			√Exception data	√Exception data	√Exception data	√Exception data	√Exception data √ CVD02		
MH11								√Exception data	√Exception data
MH12								√Exception data √ DM02	√Exception data √DM02
MH13								√Exception data √CKD02	√Exception data √CKD02
MH14 *MH19 **								√Exception data	* *√Exception data*
MH15 *MH20**								√Exception data	* *√Exception data*
MH16								√Exception data	√Exception data

Table 7-5   Mental Health (MH) Indicator and Physical Health Indicator Comparators over time

7.2.3 **Generation of Composite Indicators:**

Exception rate data for sixteen clinical indicator areas (in addition to the mental health indicators) were obtained from ISD Scotland for 2011/2012 and 2012/2013. These indicator areas comprised: atrial fibrillation (AF); asthma; coronary heart disease (CHD); cancer; chronic kidney disease (CKD); chronic obstructive pulmonary disease (COPD); epilepsy, heart failure (HF); diabetes; hypertension; hypothyroidism; osteoporosis; peripheral artery disease (PAD); stroke; dementia and depression. Composite indicators were generated by combining exception rates for all indicators within a clinical area; for example the mental health composite indicator contained exception rates for nine individual indicators, while the composite indicator for diabetes contained exception rates for fourteen individual indicators.

Composite indicators for the two most recent QOF years only were generated (2011/2012 and 2012/2013); this was due to the significant changes in the Mental Health indicators which were introduced in 2011/2012 (Tables 7-3 & 7-4).

7.3 Results:

7.3.1 **2012/2013 Median Exception Rates:**

Median rate of exception varied widely by clinical indicator (Table 7-6); MH17 (creatinine and TSH monitoring for lithium prescription) and MH18 (lithium level being within the therapeutic range) had the lowest rates of exception (both 0.0%) while MH20 (blood glucose/HbA1c recording) and MH16 (cervical smears) had the highest rate of exception reporting (25.5% and 17.8% respectively) (Table 7-6).

Of the comparator indicators: COPD13 (COPD review) and ASTHMA09 (asthma review) had the highest rate of exception reporting (11.9% and 11.6% respectively) while CKD02 (BP recording in Chronic Kidney Disease) had the lowest exception rate (0.6%) (Table 7-6).

QOF Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH10 Comprehensive Care Plan (n=966)	6.3	5.7- 6.9	2.0-12.2
MH11 Recording of alcohol consumption (n=965)	11.1	10.2- 11.9	5.0-19.3
MH12 BMI recording (n=965)	11.8	11.0-12.5	5.0-19.6
MH13 BP recording (n=965)	9.5	8.7- 10.3	4.0-15.8
MH16 Cervical Smears (n=948)	17.8	16.7- 20.0	7.3-28.6
MH17 Creatinine & TSH monitoring on lithium (n=905)	0.0	0.0-0.0	0.0-5.9
MH18 Therapeutic lithium level (n=901)	0.0	0.0- 6.0	0.0-18.2
MH19 Cholesterol:HDL ratio recording (n=959)	16.0	14.3 -17.6	6.7-27.3
MH20 blood glucose/HbA1c recording (n=965)	25.5	23.1- 24.1	16.7-31.6
ASTHMA09 Asthma review (n=968)	11.6	9.9- 12.9	2.7-23.4
DEM02 Dementia Review (n=963)	5.9	5.4- 6.3	2.1-11.0
COPD13 COPD Review (n=967)	11.9	11.3- 12.7	6.4-19.0
CKD02 BP recording in Chronic Kidney Disease (n=969)	0.6	0.5-0.7	1.9-6.1
DM02 BMI recording in Diabetes (n=968)	3.5	3.2- 3.6	0.0-1.7

Table 7-6   Indicator Exception Rates 2012/2013
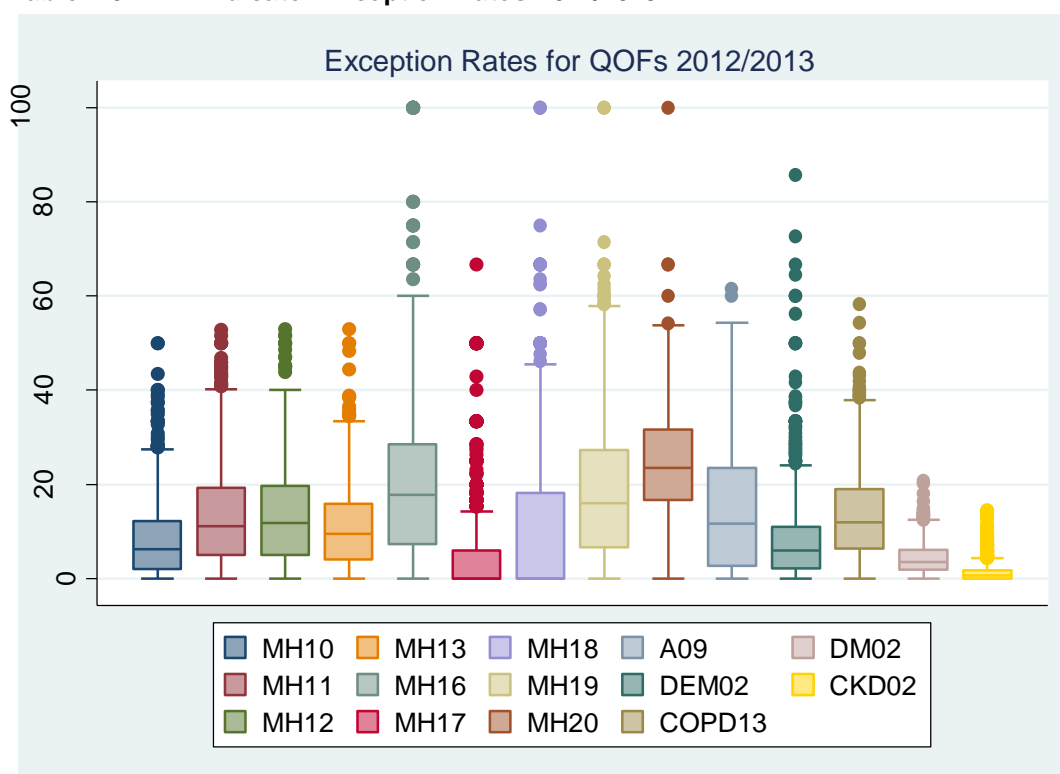
Figure 7-1   Indicator Exception Rates 2012/2013
Where line is median, box is the interquartile range (25th to 75th centile) and whiskers show the upper and lower adjacent values (furthest observation within 1.5 times the interquartile range of the upper and lower

7.3.1.1 Comprehensive Care Plan (MH10):

Median exception rate of documentation of a comprehensive care plan in MMI, was compared with rate of documentation of a care plan in dementia, (MH10 vs. DEM02), there was no significant difference in exception rate identified (6.3% vs. 5.9%, p=0.194). When median exception rates of documentation of a comprehensive care plan in MMI, were compared directly with the rates of a review for Asthma and COPD, (MH10 vs. ASTHMA09 and MH10 vs. COPD13), exception rates were significantly lower for comprehensive care plan reviews in MMI (6.3% vs. 11.6%, p<0.001 and 6.3% vs. 11.9%, p<0.001) (Table 7-7).

7.3.1.2 Blood Pressure (MH12) and Body Mass Index Recording (MH13):

Median exception rate of BMI recording in MMI, was compared directly with rate of BMI recording in diabetes, (MH12 vs. DM02): exception rate was found to be significantly higher in MMI compared to diabetes (11.8% vs. 3.5%, p<0.001) (Table 7-7).

Median exception rate of Blood Pressure recording in MMI, was compared with BP recording in Chronic Kidney Disease (CKD), (MH13 vs. CKD02), exception rate was found to be significantly higher in MMI (9.5% vs. 0.6%, p<0.001) (Table 7-7).

	Median Exception Rate (%)			p value
MH10 Comprehensive Care Plan vs. ASTHMA09 asthma review	*6.3*	*vs.*	*11.6*	*<0.001*
MH10 Comprehensive Care Plan vs. DEM02 Dementia review	6.3	vs.	5.9	0.194
MH10 Comprehensive Care Plan vs. COPD13 COPD review	*6.3*	*vs.*	*11.9*	*<0.001*
MH12 BMI recording vs. DM02 BMI recording in Diabetes	**11.8**	**vs.**	**3.5**	**<0.001**
MH13 BP recording vs. CKD02 BP recording in Chronic Kidney Disease	**9.5**	**vs.**	**0.6**	**<0.001**

Table 7-7 **Comparison of Indicator Exception rates 2012/2013 Bold if significantly higher,** *italic if significantly lower*

7.3.1.3 Composite Indicators:

In 2012/2013 sixteen composite physical health indicators were identified. The median exception rate for the Mental Health composite indicator was 11.1% (IQR 0.0-21.4%). This was significantly higher than the median exception rate for thirteen of the composite chronic disease indicators; atrial fibrillation (AF) (3.5% IQR 0.0-16.7%, p<0.001);

hypertension (3.4% IQR 1.4-6.6%, p<0.001); asthma (5.9% IQR 1.1-14.3%, p<0.001); coronary heart disease (CHD) (9.9% IQR 3.6-18.4%, p<0.001); cancer (0.0% IQR 0.0-0.0%, p<0.001); chronic kidney disease (CKD) (4.3% IQR 0.3-12.0%, p<0.001); diabetes (8.4% IQR 4.3-14.0%, p<0.001); depression (7.7% IQR 1.8-20.0%, p<0.001); dementia (10.0% IQR 2.6-25.0%, p=0.022); hypothyroidism (0.5% IQR 0.0-1.6%, p<0.001); osteoporosis (0.0% IQR 0.0-28.6%, p<0.001); peripheral artery disease (PAD) (7.3% IQR 2.6-15.0%, p<0.001) and stroke (6.6% IQR 2.8-12.5%, p<0.001) (Figure 7-2).

The Mental Health composite median exception rate was significantly lower than that of the epilepsy composite indicator (17.4% IQR 4.5-37.1%, p<0.001) and the COPD composite indicator (12.8% IQR 7.1-19.34%, p<0.001). No difference in exception rate was found compared to the composite heart failure indicator (11.1% IQR 3.0-26.5%, p=0.890) (Figure 7-2).

Figure 7-2   Median Exception Rates for Composite Indicators 2012/2013

7.3.2 **2011/2012 Median Exception Rates:**

In 2011/2012 median rate of exception varied widely by clinical indicator (Table 7-8); MH17 (creatinine and TSH monitoring in lithium prescription) and MH18 (lithium level being within the therapeutic range) had the lowest rates of exception (both 0.0%) while MH14 (cholesterol: HDL recording) and MH15 (blood glucose recording) had the highest median rate of exception reporting (16.0% and 25.0% respectively) (Table 7-8).

Of the comparator indicators COPD13 (COPD review) and ASTHMA06 (Asthma review) had the highest median rate of exception reporting (12.6% and 6.7% respectively) while CKD02 (BP recording in Chronic Kidney Disease) had the lowest median exception rate (0.6%) (Table 7-8 and Figure 7-3).

QOF Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH10 Comprehensive Care Plan (n=942)	7.8	7.1 - 8.3	2.9-14.3
MH11 recording of alcohol consumption (n=941)	13.7	12.8-14.7	6.7-22.4
MH12 BMI recording (n=941)	14.3	13.5-15.0	7.0-22.6
MH13 BP recording (n=942)	10.7	10.0- 11.7	5.1-17.2
MH14 Cholesterol:HDL ratio recording (n=942)	16.0	15.0-16.7	7.9-25.0
MH15 blood glucose recording (n=942)	25.0	23.7- 25.6	16.7-33.3
MH16 Cervical Smears (n=923)	17.8	16.7- 19.1	6.3-28.6
MH17 Creatinine & TSH monitoring on lithium (n=890)	0.0	0.0- 0.0	0.0-5.6
MH18 Therapeutic lithium level (n=887)	0.0	0.0- 0.0	0.0-16.7
ASTHMA09 Asthma review (n=943)	6.7	5.8- 8.1	2.2-18.4
DEM02 Dementia Review (n=938)	5.0	4.6- 5.6	0.0-10.2
COPD13 COPD Review (n=942)	12.6	11.8- 13.3	6.8-19.8
CKD02 BP recording in Chronic Kidney Disease(n=941)	0.6	0.5-0 .7	0.0-1.6
DM02 BMI recording In Diabetes (n=943)	3.5	3.3-3.7	1.6-6.0

Table 7-8 **Indicator exception Rates 2011/2012**
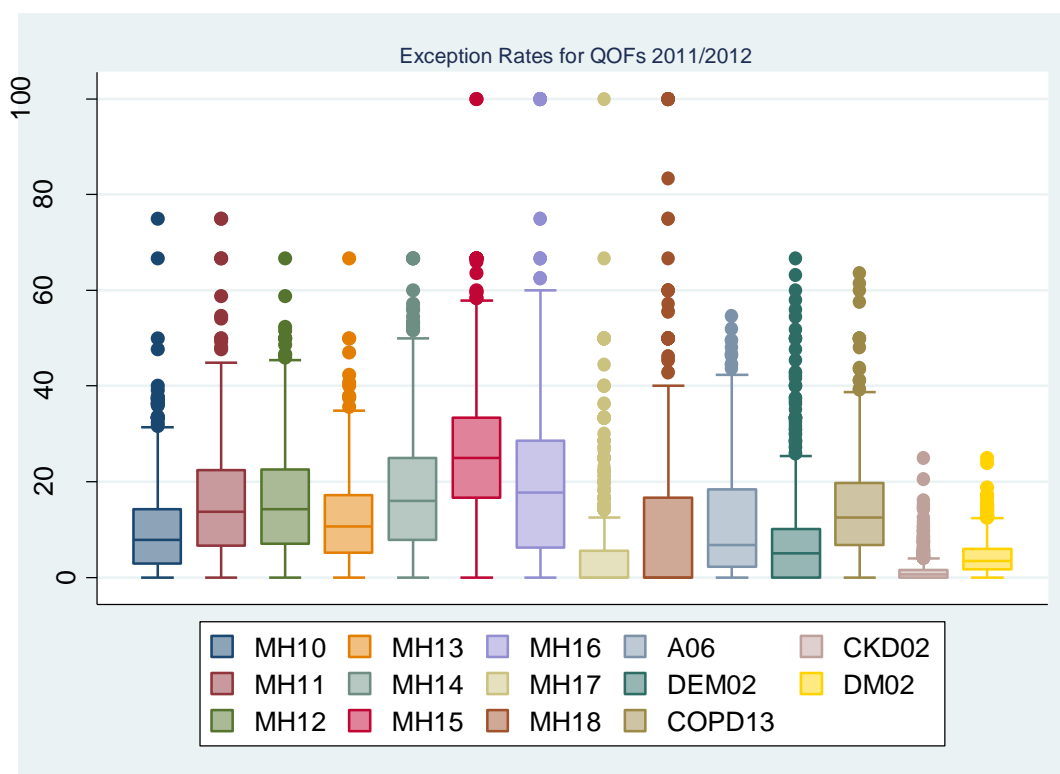
Figure 7-3   Indicator Exception Rates 2011/2012

7.3.2.1 **Comprehensive Care Plan (MH10):**

When median exception rate of documentation of a comprehensive care plan in MMI, was compared with the rate of documentation of a care plan in dementia (MH10 vs. DEM02), median exception rate in MMI was found to be significantly higher (7.8% vs. 5.0%, $p<0.001$) (Table 7-9).

Median exception rate of documentation of a comprehensive care plan in MMI, was compared with the exception rate for Asthma Review, (MH10 vs. ASTHMA06). No significant difference in exception rates was found (7.8% vs. 6.7%, $p=0.160$). Rate of exception for COPD review (COPD13) was significantly higher than for the comprehensive care plan review in MMI (12.6% vs. 7.8%, $p<0.001$) (Table 7-9).

7.3.2.2 **Blood Pressure (MH12) and Body Mass Index Recording (MH13):**

Median exception rate of recording of BMI in MMI (MH12), was significantly higher compared with median exception rate of BMI recording in diabetes (DM02), (14.3% vs. 3.5%, $p<0.001$) (Table 7-9).

Median exception rate of Blood Pressure recording in MMI (MH13) was also significantly higher than median exception rate for BP recording in Chronic Kidney Disease (CKD02), (10.7% vs. 0.6%, $p<0.001$) (Table 7-9).

	Median Exception Rate (%)			p value
MH10 Comprehensive Care Plan vs. ASTHMA09 asthma review	7.8	vs.	6.7	0.160
MH10 Comprehensive Care Plan vs. DEM02 Dementia review	**7.8**	**vs.**	**5.0**	**<0.001**
MH10 Comprehensive Care Plan vs. COPD13 COPD review	*7.8*	*vs.*	*12.6*	*<0.001*
MH12 (BMI recording) vs. DM02 (BMI recording)	**14.3**	**vs.**	**3.5**	**<0.001**
MH13 (BP recording) vs. CKD02 (BP recording)	**10.7**	**vs.**	**0.6**	**<0.001**

Table 7-9   Comparisons of Median Exception Rates 2011/2012 Bold if significantly higher, *italic if significantly lower*

7.3.2.3 Composite Indicators:

In 2011/2012 fourteen composite physical health indicators were identified. The median exception rate for the Mental Health composite indicator was 12.5% (IQR 2.4-22.2%), this was significantly higher than ten composite chronic disease indicators; atrial fibrillation (AF) (2.8% IQR 0.0-6.1%, p<0.001); hypertension (3.0% IQR 1.3-5.9%, p<0.001); asthma (4.7% IQR 0.59-11.3%, p<0.001); coronary heart disease (CHD) (4.2% IQR 0.9-11.2%, p<0.001); cancer (0.0% IQR 0.0-0.0%, p<0.001); chronic kidney disease (CKD) (4.2% IQR 0.9-11.2%, p<0.001); diabetes (8.1%, IQR 4.1-13.6% p<0.001); depression (8.7% IQR 2.2-23.1%, p<0.001); hypothyroidism (0.5% IQR 0.0-1.5%, p<0.001) and stroke (6.9% IQR 3.0-12.9%, p<0.001) (Figure 7-4).

As with 2012/2013 the Mental Health composite median exception rate was significantly lower than the epilepsy composite indicator (16.7% IQR 4.1-37.2%, p<0.001) and the COPD composite indicator (14.3% IQR 8.2-22.2%, p<0.001). No difference was found for the composite heart failure indicator (12.1% IQR 3.0-27.3%, p=0.330) and the dementia indicator (12.1% IQR 2.6-42.8%, p=0.853) (Figure 7-4).

Exception Rates for Composite Indicators 2011/2012
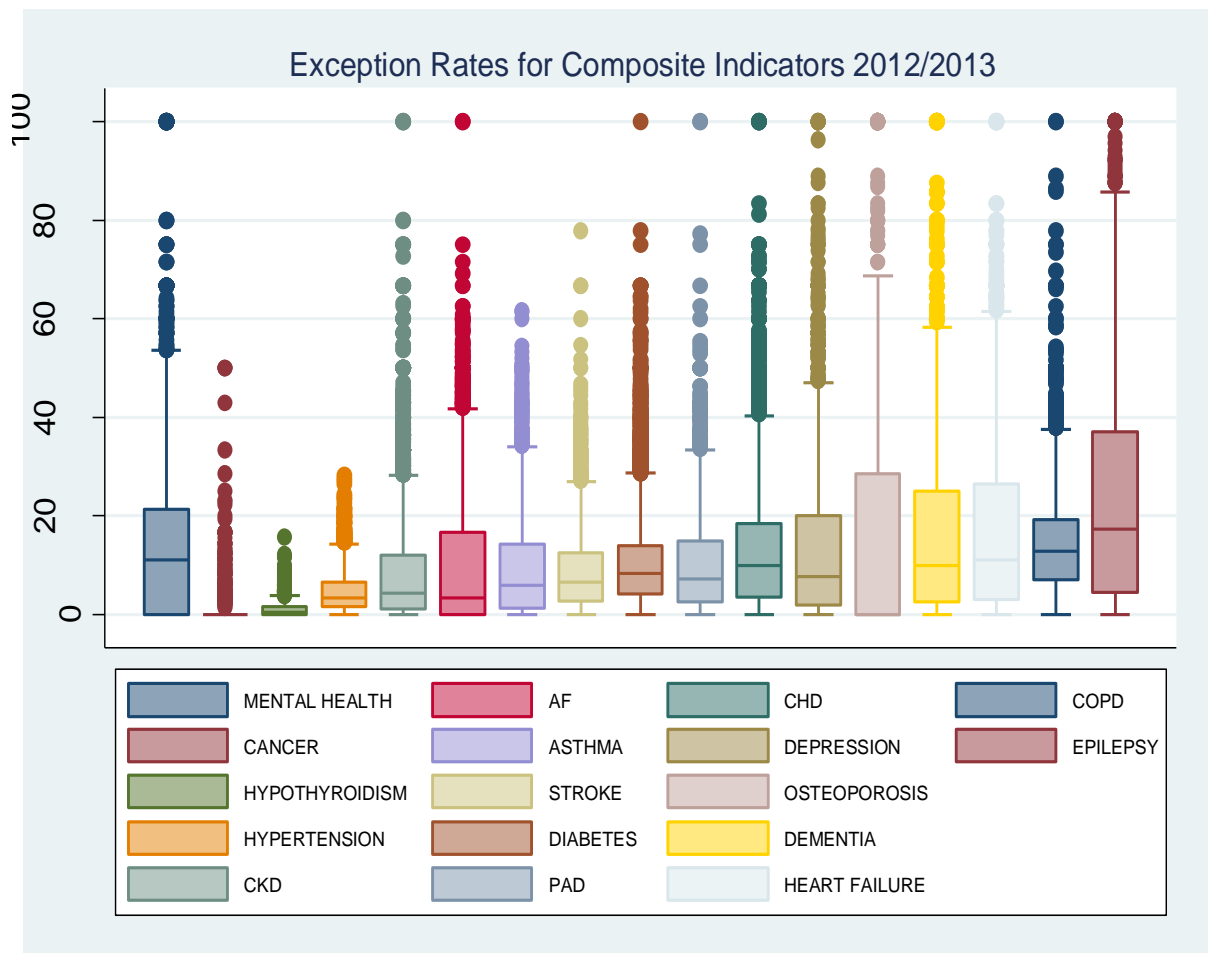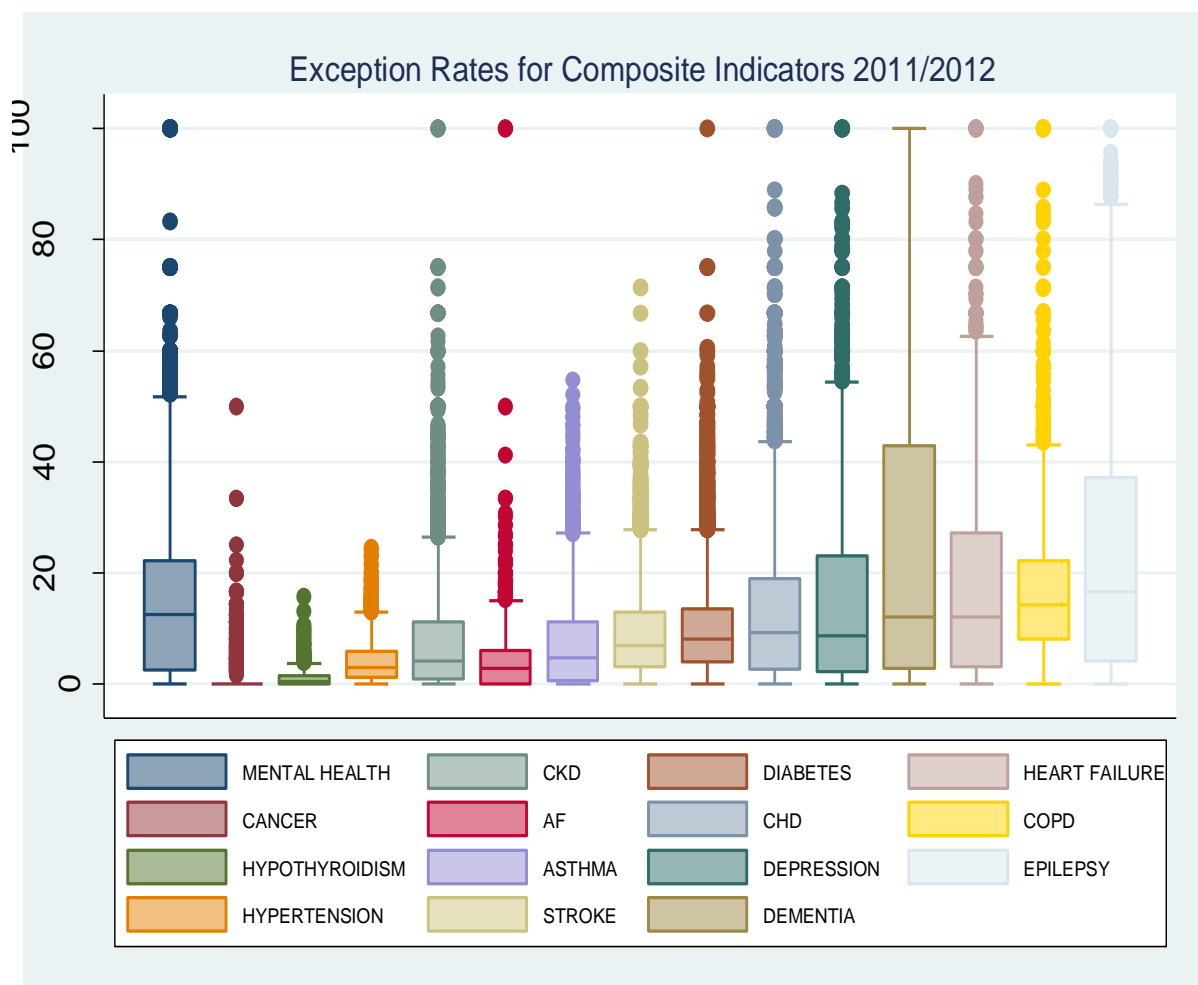
Figure 7-4   Median Exception Rates for Composite Indicators 2011/2012

7.3.3 **2010/2011 Median Exception Rates:**

In 2010/2011 median rate of exception varied widely by clinical indicator (Table 7-10); MH04 (Creatinine and TSH monitoring in lithium prescription), MH05 (Therapeutic lithium level) and MH07 (Mental Health Annual review) had the lowest rates of exception (all 0.0%) while MH06 (comprehensive care plan) and MH09 (routine health promotion) had the highest median rate of exception reporting (8.7% and 13.3% respectively) (Table 7-10) (Figure 7-5).

Of the comparator indicators; COPD13 (COPD Review) and ASTHMA06 (Asthma Review) had the highest median rate of exception reporting (11.7% and 6.7% respectively) while DM22 (estimated glomerular filtration rate (eGFR) or serum creatinine reported in Diabetes) had the lowest median exception rate (2.2%) (Table 7-10) (Figure 7-5).

Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH04 Creatinine & TSH monitoring on lithium (n=890)	0.0	0.0-0.0	0.0-0.0
MH05 Therapeutic lithium level (n=889)	0.0	0.0-0.0	0.0-16.7
MH06 Comprehensive Care Plan (n=950)	8.7	7.7- 9.5	2.6-15.9
MH07 Annual MH review (n=778)	0.0	0.0-0.0	0.0-0.0
MH09 Routine Health Promotion (n=949)	13.3	12.5- 14.3	5.7-23.8
ASTHMA06 Asthma review (n=955)	6.7	5.7-7.7	1.8-17.2
DEMENTIA02 Dementia review (n=946)	5.1	4.7- 5.8	0.0-10.2
DM22 eGFR or serum creatinine reported in Diabetes (n=954)	2.2	2.1-2.4	1.1-4.0
EPILEPSY07 Medication Review (n=947)	2.9	2.3 - 3.3	0.0-9.6
COPD13 COPD Review (n=953)	11.7	11.0-12.5	6.2-19.3
CVD02 Lifestyle Advice (n=952)	6.5	5.9- 7.1	2.5-11.8

Table 7-10   Indicator Exception rates2010/2011

Figure 7-5   **Indicator Exception Rates 2010/2011**

7.3.3.1 Renal Function Monitoring (MH04):

Median exception rate of creatinine and TSH monitoring in lithium prescription, was compared with the rate of eGFR/creatinine measurement in diabetes, (MH04 vs. DM22). Exception rate was significantly lower for creatinine and TSH monitoring in lithium prescription compared to diabetes (0.0% vs. 2.2%, p<0.001) (Table 7-11).

7.3.3.2 Comprehensive Care Plan (MH06):

Median exception rate of documentation of a comprehensive care plan in MMI was compared with the rate of documentation of a care plan in dementia and epilepsy, (MH10 vs. DEM02 and MH10 vs. EPILEPSY07). Median exception rates in MMI were significantly higher compared to dementia and epilepsy (8.7% vs. 5.1%, p<0.001 and 8.7% vs. 2.9%, p<0.001 respectively) (Table 7-11).

Median exception rate of documentation of a comprehensive care plan in MMI was also compared with the exception rate in Asthma Review. No difference in exception rate between asthma and MMI was found (6.7% vs. 8.7%, p=0.7757 respectively). Rate of exception for COPD Review was significantly higher than for comprehensive care plan reviews in MMI (11.7% vs. 8.7%, p<0.001) (Table 7-11).

7.3.3.3 Health Promotion (MH09):

Median exception rate of health promotion in MMI was compared with exception rate of lifestyle education in hypertension, (MH09 vs. CVD02). Median exception rate was significantly higher in MMI compared to hypertension (13.3% vs. 6.5%, p<0.001) (Table 7-11).

	Median Exception Rate (%)			p value
MH04 Creatinine & TSH monitoring on lithium vs. DM22 Creatinine or eGFR measurement in Diabetes	*0.0*	*vs.*	*2.2*	*<0.001*
MH06 Comprehensive Care Plan vs. EPILEPSY07 Medication review	**8.7**	**vs.**	**2.9**	**<0.001**
MH06 Comprehensive Care Plan vs. ASTHMA06 Asthma review	8.7	vs.	6.7	0.7757
MH06 Comprehensive Care Plan vs. COPD13 COPD review	*8.7*	*vs.*	*11.7*	*<0.001*
MH06 Comprehensive Care Plan vs. DEMENTIA02 Dementia Review	**8.7**	**vs.**	**5.3**	**<0.001**
MH09 Health Promotion vs. CVD02 Lifestyle Advice	**13.3**	**vs.**	**6.5**	**<0.001**

Table 7-11   Comparison of Median Exception rates 2010/2011 Bold if significantly higher, *italic if significantly lower*

7.3.4 2009/2010 Median exception rates:

In 2009/2010 median rate of exception varied widely by clinical indicator (Table 7-12); MH04 (Creatinine and TSH monitoring in lithium prescription), MH05 (Therapeutic lithium level) and MH07 (Mental Health Annual review) had the lowest median rates of exception (all 0.0%) while MH06 (comprehensive care plan) and MH09 (routine health

promotion) had the highest median rate of exception reporting (9.4% and 12.8% respectively) (Table 7-12 and Figure 7-6).

Of the comparator indicators COPD13 (COPD review) and ASTHMA06 (Asthma Review) had the highest median rate of exception reporting (12.8% and 6.1% respectively) while DM22 (eGFR or serum creatinine reported in Diabetes) had the lowest median exception rate (2.3%) (Table 7-12 and Figure 7-6).

Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH04 Creatinine & TSH monitoring on lithium (n=936)	0.0	0.0-0.0	0.0-0.0
MH05 Therapeutic lithium level (n=936)	0.0	0.0-0.0	0.0-14.3
MH06 Comprehensive Care Plan (n=993)	9.4	8.5- 1	3.6-18.4
MH07 Annual MH review (n=805)	0.0	0.0-0.0	0.0-0.0
MH09 Routine Health Promotion (n=991)	12.8	11.9- 13.8	5.1-23.8
ASTHMA06 Asthma review (n=995)	6.1	5.2-7.1	1.6-15.1
DEMENTIA02 Dementia review (n=985)	4.2	3.8- 4.8	0.0-9.3
DM22 eGFR or serum creatinine reported (n=997)	2.3	2.1- 2.5	1.0-4.0
EPILEPSY07 Medication Review (n=993)	2.9	2.4- 3.4	0.0-8.3
COPD13 COPD Review (n=993)	12.8	12.0- 13.6	6.7-20.0
CVD02 Lifestyle Advice (n=986)	9.8	8.7- 11.1	1.8-19.1

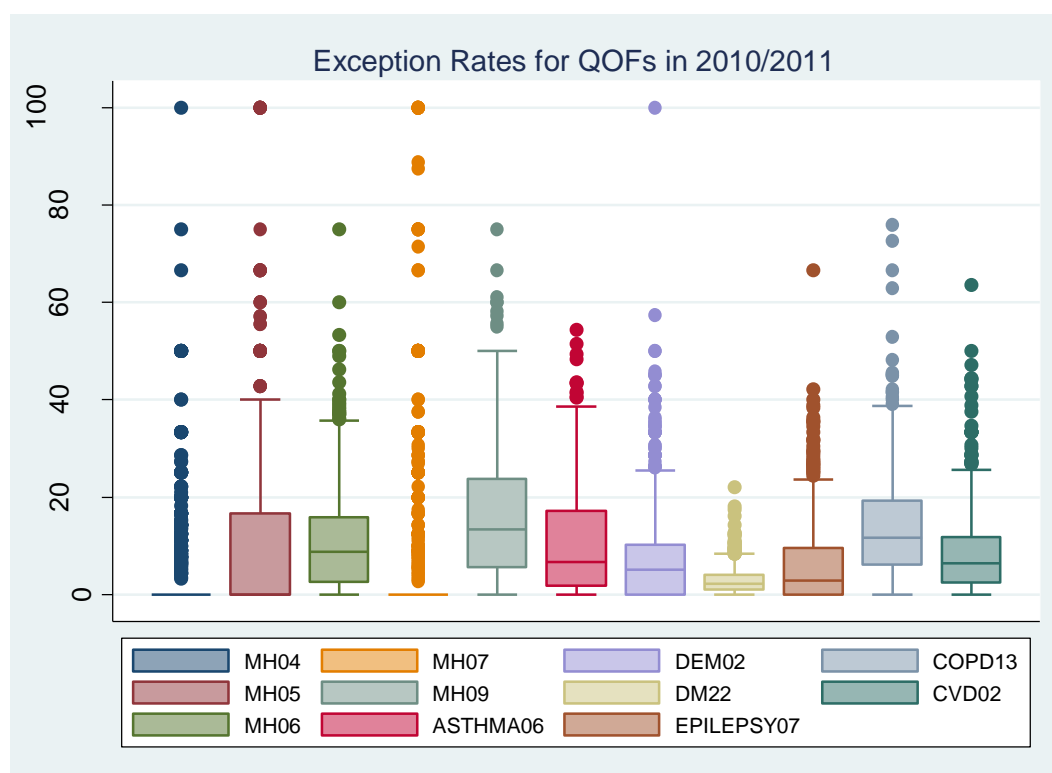**Table 7-12   Indicator Exception rates 2009/2010**

Figure 7-6　　**Indicator exception rates 2009/2010**

7.3.4.1 Renal Function Monitoring (MH04):

Median exception rate of creatinine and TSH monitoring in lithium prescription, was compared with the exception rate of creatinine or eGFR measurement in diabetes, (MH04 vs. DM22). Exception rate was significantly lower in lithium prescription monitoring compared to diabetes monitoring (0.0% vs. 2.3%, p<0.001) (Table 7-13).

7.3.4.2 Comprehensive Care Plan (MH06):

Median exception rate of documentation of a comprehensive care plan in MMI, was compared with the exception rate of documentation of a care plan in dementia, epilepsy and asthma, (MH10 vs. DEM02, MH10 vs. EPILEPSY07 and MH10 vs. ASTHMA06). Median exception rates in MMI were significantly higher compared to dementia, epilepsy and asthma (9.4% vs. 4.2%, p<0.001, 9.4% vs. 2.9%, p<0.001 and 9.4% vs. 6.1%, p<0.001 respectively) (Table 7-13).

Median exception rate of documentation of a comprehensive care plan in MMI, was compared with the exception rate of a COPD review, (COPD13 vs. ASTHMA06). Exception rate was significantly higher in COPD (12.8% vs. 9.4%, p<0.001) (Table 7-13).

	Median Exception Rates (%)	p value
MH04 Creatinine & TSH monitoring on lithium vs. DM22 Creatinine or eGFR measurement in Diabetes	*0.0 vs. 2.3*	*<0.001*
MH06 Comprehensive Care Plan vs. EPILEPSY07 Medication review	**9.4 vs. 2.9**	**<0.001**
MH06 Comprehensive Care Plan vs. ASTHMA06 Asthma review	**9.4 vs. 6.1**	**<0.001**
MH06 Comprehensive Care Plan vs. COPD13 COPD review	*9.4 vs. 12.8*	*<0.001*
MH06 Comprehensive Care Plan vs. DEMENTIA02 Dementia Review	**9.4 vs. 4.2**	**<0.001**

Table 7-13   Comparison of Median Exception Rates 2009/2010 Bold if significantly higher, *italic if significantly lower*

7.3.5 2008/2009 Median exception rates:

In 2008/2009, median rate of exception varied widely by clinical indicator (Table 7-14 and Figure 7-7); MH04 (Creatinine & TSH monitoring on lithium), MH05 (Therapeutic lithium level) and MH07 (Mental Health Annual review) had the lowest median rates of exception (all 0.0%) while MH06 (comprehensive care plan) and MH09 (routine health promotion) had the highest median rate of exception reporting (13.1% and 14.6% respectively) (Table 7-14 and Figure 7-7).

Of the comparator indicators ASTHMA06 (Asthma review) had the highest median rate of exception reporting (6.6%) while DM22 (eGFR or serum creatinine measurement in Diabetes) had the lowest median exception rate (2.2%) (Table 7-14 and Figure 7-7).

Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH04 Creatinine & TSH monitoring on lithium (n=942)	0.0	0.0-0.0	0.0-0.0
MH05 Therapeutic lithium level (n=935)	0.0	0.0-0.0	0.0-0.0
MH06 Comprehensive Care Plan (n=996)	13.1	12.0-14.1	5.7-22.8
MH07 Annual MH review (n=786)	0.0	0.0-0.0	0.0-0.0
MH09 Routine Health Promotion (n=987)	14.6	14.0-15.6	6.7-25.4
ASTHMA06 Asthma review (n=997)	6.6	5.8-7.5	1.6-15.7
DEMENTIA02 Dementia review (n=989)	5.0	4.4-5.6	1.3-5.0
DM22 eGFR or serum creatinine reported (n=998)	2.2	2.0-2.3	0.9-3.8
EPILEPSY07 Medication Review (n=994)	3.8	3.2-4.4	0.0-10.5

Table 7-14   Indicator Exception Rates 2008/2009
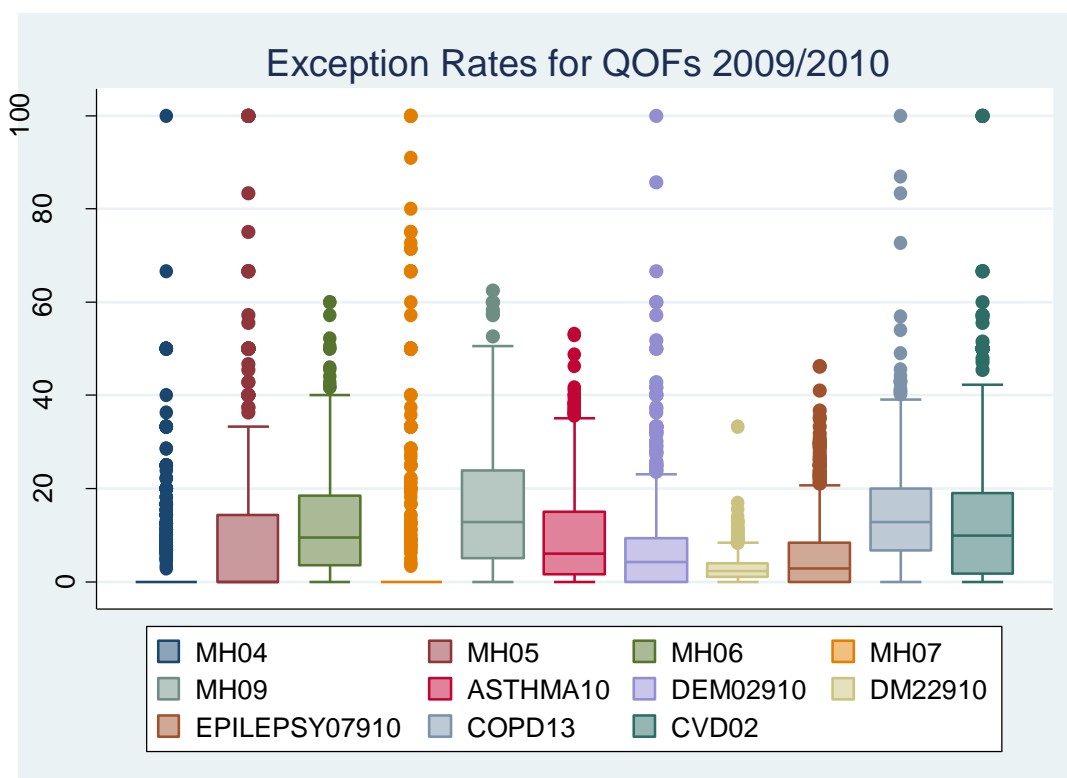
Figure 7-7   Indicator exception rates 2008/2009
7.3.5.1 Renal Function Monitoring (MH04):

Median exception rate of creatinine and TSH monitoring in lithium prescription, was compared with the exception rate of eGFR estimation and creatinine measurement in diabetes, (MH04 vs. DM22). Exception rate was significantly lower in lithium prescription compared to diabetes (0.0% vs. 2.2%, p<0.001) (Table 7-15).

7.3.5.2 Comprehensive Care Plan (MH10):

Median exception rate of documentation of a comprehensive care plan in MMI, was compared with the rate of documentation of a care plan in dementia, epilepsy and asthma, (MH10 vs. DEM02, MH10 vs. EPILEPSY07 and MH10 vs. ASTHMA06). Median exception rates in MMI were significantly higher compared to dementia, epilepsy and asthma (13.1% vs. 5.0%, p<0.001, 13.1% vs. 3.8%, p<0.001 and 13.1% vs. 6.6%, p<0.001) (Table 7-15).

	Median Exception Rates (%)			p value
MH04 Creatinine & TSH monitoring on lithium vs. DM22 Creatinine or eGFR measurement in Diabetes	*0.0*	*vs.*	*2.2*	*<0.001*
MH06 Comprehensive Care Plan vs. EPILEPSY07 Medication review	**13.1**	**vs.**	**3.8**	**<0.001**
MH06 Comprehensive Care Plan vs. ASTHMA06 Asthma review	**13.1**	**vs.**	**6.6**	**<0.001**
MH06 Comprehensive Care Plan vs. DEMENTIA02 Dementia Review	**13.1**	**vs.**	**5.0**	**<0.001**

Table 7-15   Comparison of Median Exception rates 2008/2009 Bold if significantly higher, *italic if significantly lower*

7.3.6 **2007/2008 Median exception rates:**

In 2007/2008 median rate of exception varied widely by clinical indicator (Table 7-16 and Figure 7-8); MH04 (Creatinine and TSH monitoring in lithium prescription), MH05 (Therapeutic lithium level) and MH07 (Mental Health Annual review) had the lowest median rates of exception (all 0.0%) while MH06 (comprehensive care plan) and MH09 (routine health promotion) had the highest median rate of exception reporting (16.7% and 15.0% respectively) (Table 7-16 and Figure 7-8).

Of the comparator indicators DEMENTIA02 (Dementia Review) had the highest median rate of exception reporting (5.7%) while DM22 (eGFR or serum creatinine recording in Diabetes) had the lowest median exception rate (2.2%) (Table 7-16 and Figure 7-8).

Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH04 Creatinine & TSH monitoring on lithium (n=947)	0.0	0.0-0.0	0.0-0.0
MH05 Therapeutic lithium level (n=944)	0.0	0.0 -5.6	0.0-20.0
MH06 Comprehensive Care Plan (n=993)	16.7	15.4 - 18.2	8.1-28.1
MH07 Annual MH review (n=761)	0.0	0.0-0.0	0.0-39.6
MH09 Routine Health Promotion (n=983)	15.0	14.3- 16.4	6.6-26.8
ASTHMA06 Asthma review (n=998)	3.4	5.5- 7.3	1.7-15.7
DEMENTIA02 Dementia review (n=991)	5.7	5.1- 6.2	0.0-11.1
DM22 eGFR or serum creatinine reported (n=999)	2.2	2.1- 2.4	0.9-3.8
EPILEPSY07 Medication Review (n=994)	3.7	3.1- 4.4	0.0-9.5

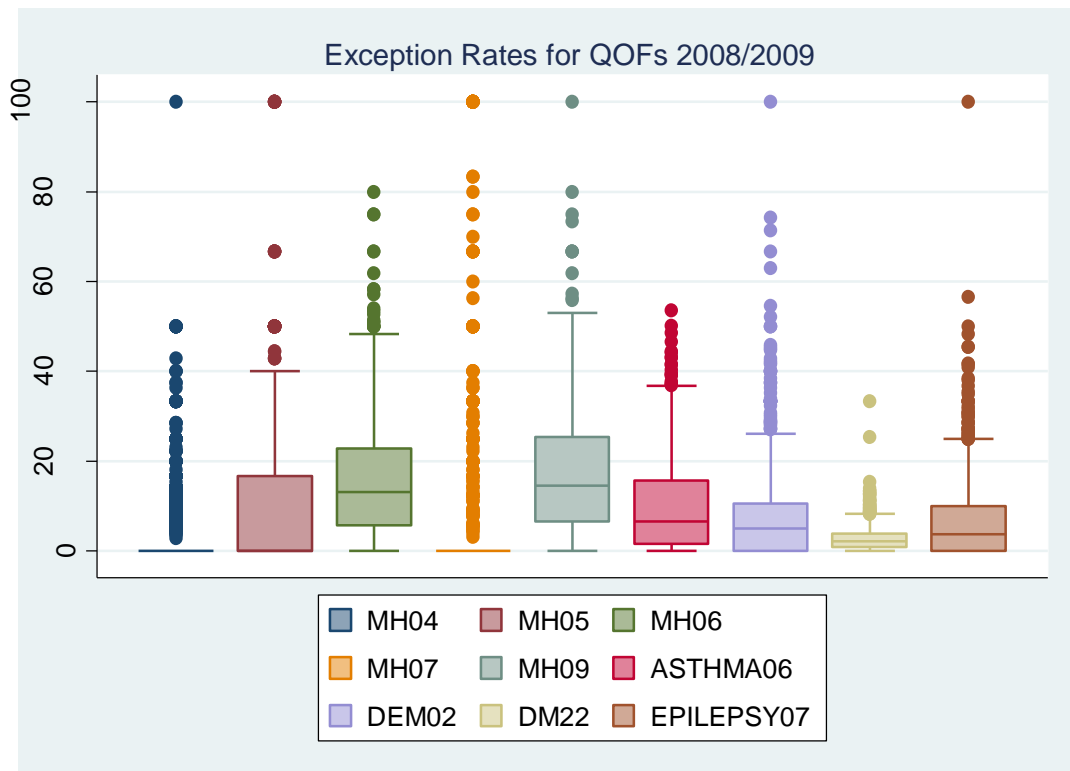**Table 7-16   Indicator Exception Rates 2007/2008**

Figure 7-8   Indicator exception rates 2007/2008:
7.3.6.1 **Renal Function Monitoring (MH04):**

Median exception rate of creatinine and TSH monitoring in lithium prescription, was compared with the rates of eGFR estimation or creatinine measurement in diabetes, (MH04 vs. DM22). Exception rate was lower in lithium prescription compared to diabetes (0.0% vs. 2.2%, p<0.001) (Table 7-17).

7.3.6.2 **Comprehensive Care Plan (MH06):**

Median exception rate of documentation of a comprehensive care plan in MMI was compared with the exception rate of documentation of a care plan in dementia, epilepsy and asthma, (MH10 vs. DEM02, MH10 vs. EPILEPSY07 and MH10 vs. ASTHMA06). Median exception rates in MMI were significantly higher compared to dementia, epilepsy and asthma (16.7% vs. 5.7%, p<0.001, 16.7% vs. 3.7%, p<0.001 and 16.7% vs. 3.4%, p<0.001 respectively) (Table 7-17).

	Median Exception Rates (%)			p value
MH04 Creatinine & TSH monitoring on lithium vs. DM22 Creatinine or eGFR measurement in Diabetes	*0.00*	*vs.*	*2.22*	*<0.001*
MH06 Comprehensive Care Plan vs. EPILEPSY07 Medication Review	**16.7**	**vs.**	**3.7**	**<0.001**
MH06 Comprehensive Care Plan vs. ASTHMA06 Asthma review	**16.7**	**vs.**	**3.4**	**<0.001**
MH06 Comprehensive Care Plan vs. DEMENTIA02 Dementia Review	**16.7**	**vs.**	**5.7**	**<0.001**

Table 7-17   Comparison of Median Exception Rates 2007/2008 Bold if significantly higher, *italic if significantly lower*

7.3.7 **2006/2007 Median exception rates:**

In 2006/2007, median rate of exception varied widely by clinical indicator (Table 7-18 and Figure 7-9); MH04 (Creatinine and TSH monitoring in lithium prescription), MH05 (Therapeutic lithium level) and MH07 (Mental Health Annual review) had the lowest median rates of exception (all 0.0%) while MH06 (comprehensive care plan) and MH09 (routine health promotion) had the highest median rate of exception reporting (18.9% and 14.8% respectively) (Table 7-18 and Figure 7-9).

Of the comparator indicators ASTHMA06 (Asthma Review) had the highest median rate of exception reporting (6.0%) while DM22 (eGFR or serum creatinine reported in Diabetes) had the lowest median exception rate (2.2%) (Table 7-18 and Figure 7-9).

Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH04 Creatinine & TSH monitoring on lithium (n=928)	0.0	0.0-0.0	0.0-4.9
MH05 Therapeutic lithium level (n=927)	0.0	0.0-0.0	0.0-15.0
MH06 Comprehensive Care Plan (n=984)	18.9	17.2- 20.4	8.3-33.3
MH07 Annual MH review (n=669)	0.0	0.0-0.0	0.0-0.0
MH09 Routine Health Promotion (n=982)	14.8	13.3-16.4	5.6-27.4
ASTHMA06 Asthma review (n=987)	6.0	5.2-6.8	1.8-15.2
DEMENTIA02 Dementia review (n=983)	5.5	4.9-5.9	0.0-11.1
DM22 eGFR or serum creatinine reported (n=990)	2.2	2.1-2.4	1.0-3.9
EPILEPSY07 Medication Review (n=981)	3.4	3.0-4.0	0.0-9.1

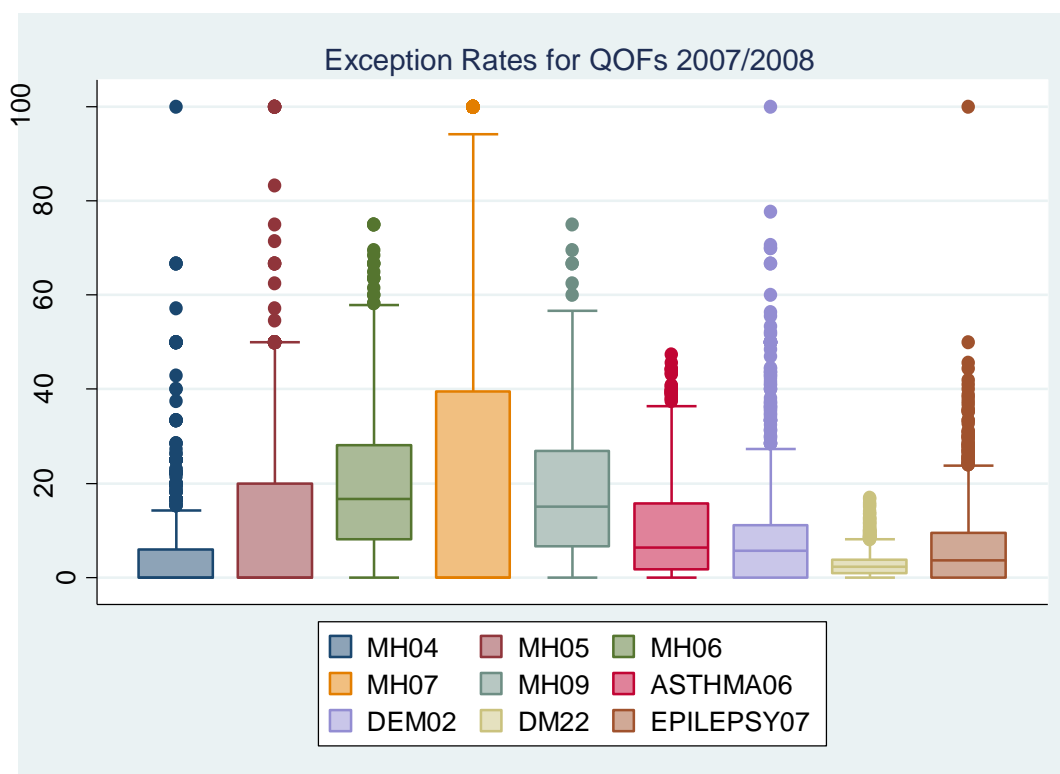**Table 7-18   Indicator Exception rates 2006/2007**
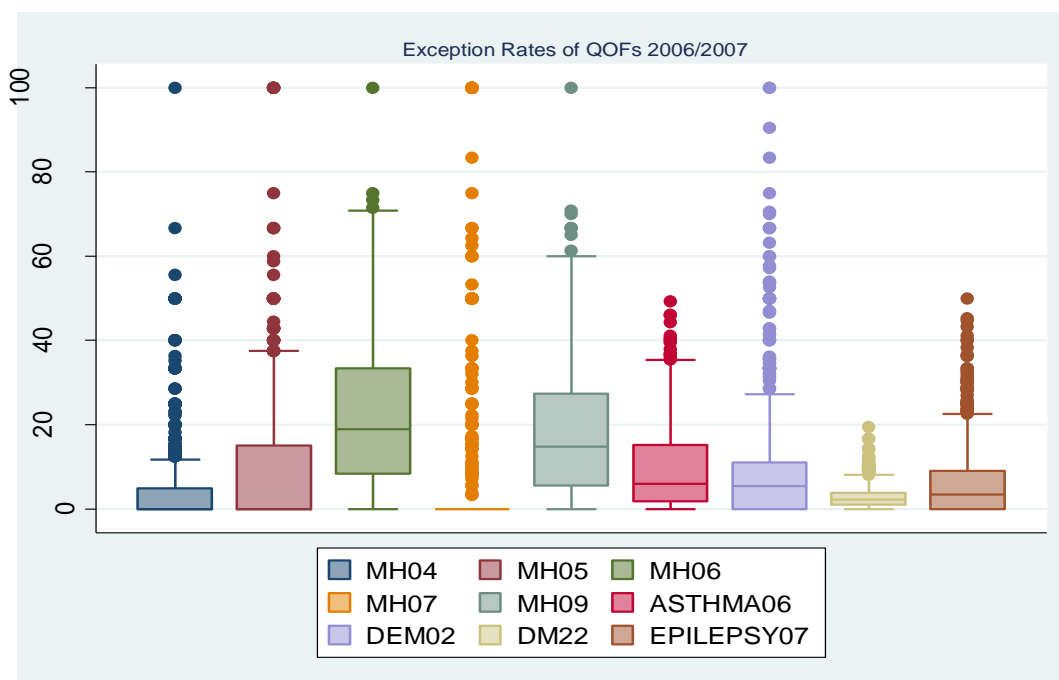
Figure 7-9   Indicator exception rates 2006/2007:
7.3.7.1 Renal Function Monitoring (MH04):

Median exception rate of creatinine and TSH monitoring in lithium prescription, was compared with the rates of eGFR estimation and creatinine measurement in diabetes, (MH04 vs. DM22). Exception rate was significantly lower in lithium prescription compared to diabetes (0.0% vs. 2.2%, p<0.001) (Table 7-19).

7.3.7.2 Comprehensive Care Plan (MH10):

Median exception rates of documentation of a comprehensive care plan in MMI were significantly higher compared to documentation of a care plan in dementia, epilepsy and asthma (18.9% vs. 6.0%, p<0.001, 18.9% vs. 3.4%, p<0.001 and 18.9% vs. 6.0%, p<0.001 respectively) (Table 7-19).

	Median Exception Rate (%)			p value
MH04 Creatinine & TSH monitoring on lithium vs.DM22 Creatinine or eGFR measurement in Diabetes	*0.0*	*vs.*	*2.2*	*<0.001*
MH06 Comprehensive Care Plan vs. EPILEPSY07 Medication review	**18.9**	**vs.**	**3.4**	**<0.001**
MH06 Comprehensive Care Plan vs. ASTHMA06 Asthma review	**18.9**	**vs.**	**6.0**	**<0.001**
MH06 Comprehensive Care Plan vs. DEMENTIA02 Dementia Review	**18.9**	**vs.**	**6.0**	**<0.001**

Table 7-19   Comparison of Median Exception rates 2006/2007 Bold if significantly higher, *italic if significantly lower*

7.3.8 **2005/2006 Median exception rates:**

In 2005/2006 median rate of exception for MH04 (Creatinine and TSH monitoring in lithium prescription) and MH05 (Therapeutic lithium level) were low (both 0.0%). ASTHMA06 (Asthma Review) had the highest median rate of exception reporting (4.5%) (Table 7-20 and Figure 7-10).

No direct comparison between proxy indicators was possible for this QOF year.

Variable	Median Exception Rate (%)	95% Confidence Interval	Inter-Quartile Range (IQR)
MH04 Creatinine & TSH monitoring on lithium (n=924)	0.0	0.0-0.0	0.0-4.8
MH05 Therapeutic lithium level (n=920)	0.0	0.0-0.0	0.0-14.3
ASTHMA06 Asthma review (n=973)	4.5	3.9-5.3	1.3-12.4

Table 7-20 **Indicator Exception rates 2005/2006 Bold if significantly higher,** *italic if significantly lower*
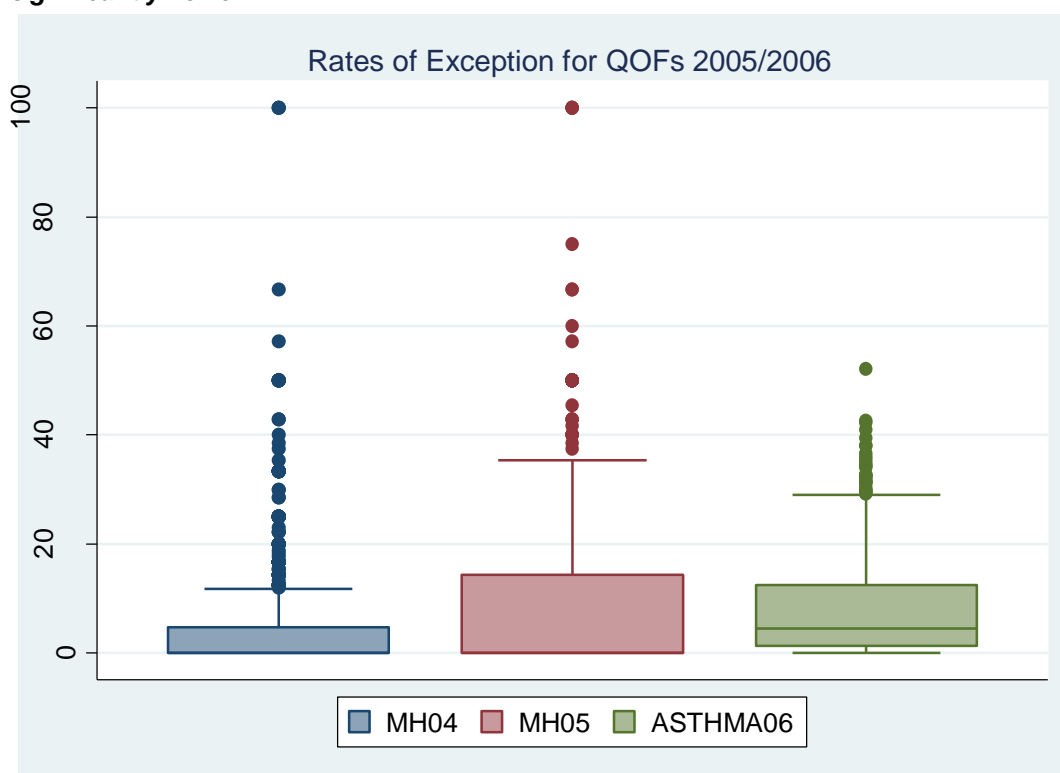
Figure 7-10 **Indicator exception rates 2005/2006:**

7.3.9 **Patterns of Mental Health Indicator median exception rates over time:**

For the Mental Health indicators related to lithium therapy (MH04/MH17 measurement of creatinine and TSH and MH05/MH18 therapeutic level of lithium) exception rates were low and remained static throughout the duration of the study (Table 7-21 and Figure 7-11).

Exception rate of non-attendance at a Mental Health annual review (MH07), was also low (0.0%). It too remained at this level, until it was removed as an indicator in 2010/2011 (Table 7-21 and Figure 7-11).

The median exception rate for the Comprehensive Care Plan Indicator (MH06/MH10) decreased over the study timeframe; from 18.9% IQR 9.3-32.7% in 2006/2007 to 8.8% IQR3.1-15.4% in 2010/2011, p<0.001 and then from 7.9% IQR 3.2–14.0% in 2011/2012 to 6.4% IQR 2.4-11.8% in 2012/2013, p<0.001 as MH10 (Table 7-21 and Figure 7-11).

For the health promotion indicator (MH09), median exception rates fell during the study timeframe: from 14.8% IQR 5.6-27.4% in 2006/2007 to 13.3% IQR 5.7-23.8% in 2010/2011, p<0.001. (Table 7-21 and Figure 7-11).

For the recording of alcohol consumption (MH11) median exception reporting rate also fell from 13.7% IQR 6.7-22.4% in 2011/2012 to 11.1% IQR 5.0-19.3% in 2012/2013, p<0.001. (Table 7-21 and Figure 7-11).

For BMI recording (MH12), median exception reporting rate fell from 14.3% IQR 7.0-22.6% in 2011/2012 to 11.8% IQR 5.0-19.6% in 2012/2013, p<0.001. (Table 7-21 and Figure 7-11).

For blood pressure recording (MH13) median exception reporting rate fell marginally from 10.7% IQR 5.1-17.2% in 2011/2012 to 9.5% IQR 4.0-15.8% in 2012/2013, p=0.005 (Table 7-21 and Figure 7-11).

For recording of total cholesterol:hdl ratio (MH14/MH19), blood glucose or HbA1c (MH15/MH20) and recording of cervical smear (MH16), median exception reporting rates were relatively stable over the study timeframe (Table 7-21 and Figure 7-11).

7.3.10 Patterns of Chronic Disease Comparator Indicator median exception rates over time:

There was a mixed pattern in exception rate reporting trends for the comparator chronic disease indicators during this study timeframe; with some rates falling, some increasing and others remaining relatively stable throughout.

There was a significant reduction in median exception rate from 9.8% IQR 1.8-19.1% in 2009/2010 to 6.5% IQR 2.5-11.8% in 2010/2011, p<0.001, for the lifestyle advice in hypertension indicator (CVD02). However median exception rate for the asthma review indicator (ASTHMA06) increased from 4.5% IQR 1.3-12.4% in 2005/2006 to 6.7% IQR 2.2-18.4% in 2011/2012, p<0.001 (Table 7-21 and Figure 7-12).

There was no significant change in median exception rate for the: epilepsy care plan indicator (EPILEPSY07), COPD review indicator (COPD13), dementia indicator (DEMENTIA02), monitoring of eGFR or creatinine in diabetes (DM 22), Blood Pressure monitoring in CKD (CKD02) and BMI recording in Diabetes (DM02) throughout the study timeframe (Table 7-21 and Figure 7-12).

Variable	2005/2006	2006/2007	2007/2008	2008/2009	2009/2010	2010/2011	2011/2012	2012/2013	P[1] value
MH04/MH17 Creatinine & TSH check on lithium	*0.0	0.0	0.0	0.00	0.0	0.0	0.0	*0.0	0.6947
MH05/MH18 Therapeutic lithium level	*0.0	0.0	0.0	0.00	0.0	0.0	0.0	*0.0	0.0025
MH06/MH10 Comprehensive Care Plan		***18.9**	**16.7**	**13.1**	**9.4**	**8.7**	**7.8**	***6.3**	**<0.001**
MH07 Annual MH review		0.0	0.0	0.0	0.0	0.0			
MH09 Routine Health promotion		***14.8**	**15.0**	**14.6**	**12.8**	***13.3**			**<0.001**
MH11 recording of alcohol consumption							***13.7**	***11.1**	**<0.001**
MH12 BMI recording							***14.3**	***11.8**	**<0.001**
MH13 BP recording							*10.7	*9.5	0.005
MH14/MH19 Cholesterol:HDL ratio recording							*16.0	*16.0	0.3886
MH15/MH20 Blood glucose (HbA1c) recording							*25.0	*25.5	0.0336
MH16 Cervical Screening							*17.8	*17.8	0.553
ASTHMA06 Asthma Review	*4.5*	*6.0*	*3.4*	*6.6*	*6.1*	*6.7*	*6.7*		*<0.001*
ASTHMA09 Asthma Review								11.6	
DEM02 Dementia Review		*5.5	5.7	5.0	4.2	5.1	5.0	*5.9	0.7653
DM22 Creatinine/eGFR check in diabetes		*2.2	2.2	2.2	2.3	*2.2			0.9010
EPILEPSY07 Epilepsy Review		*3.4	3.7	3.8	2.9	*2.9			0.6690
COPD13 COPD Review					*12.8	11.7	12.6	*11.9	0.0662
CVD02 Lifestyle Advice					***9.8**	***6.5**			**<0.001**
CKD02 BP recording							*0.6	*0.6	0.4157
DM02 BMI recording							*3.5	*3.5	0.5400

Table 7-21   Mental Health and Comparator Indicators changes over time 2005/2006 – 2012/2013 P[1] sign rank test between years marked with * Bold if significantly reduction in exception rate over time
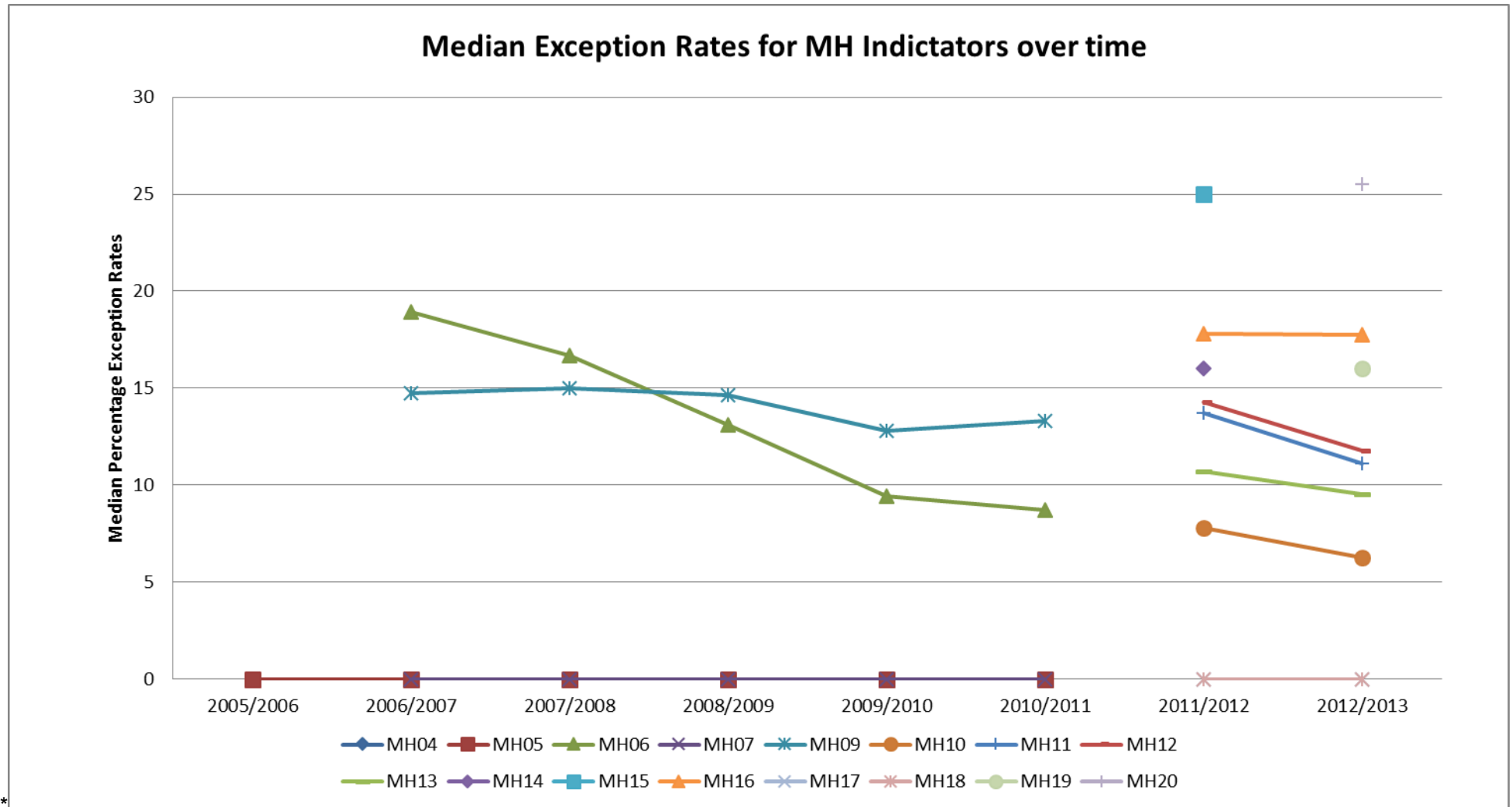
Figure 7-11   Mental Health Indicators over time 2005/2006 – 2012/2013
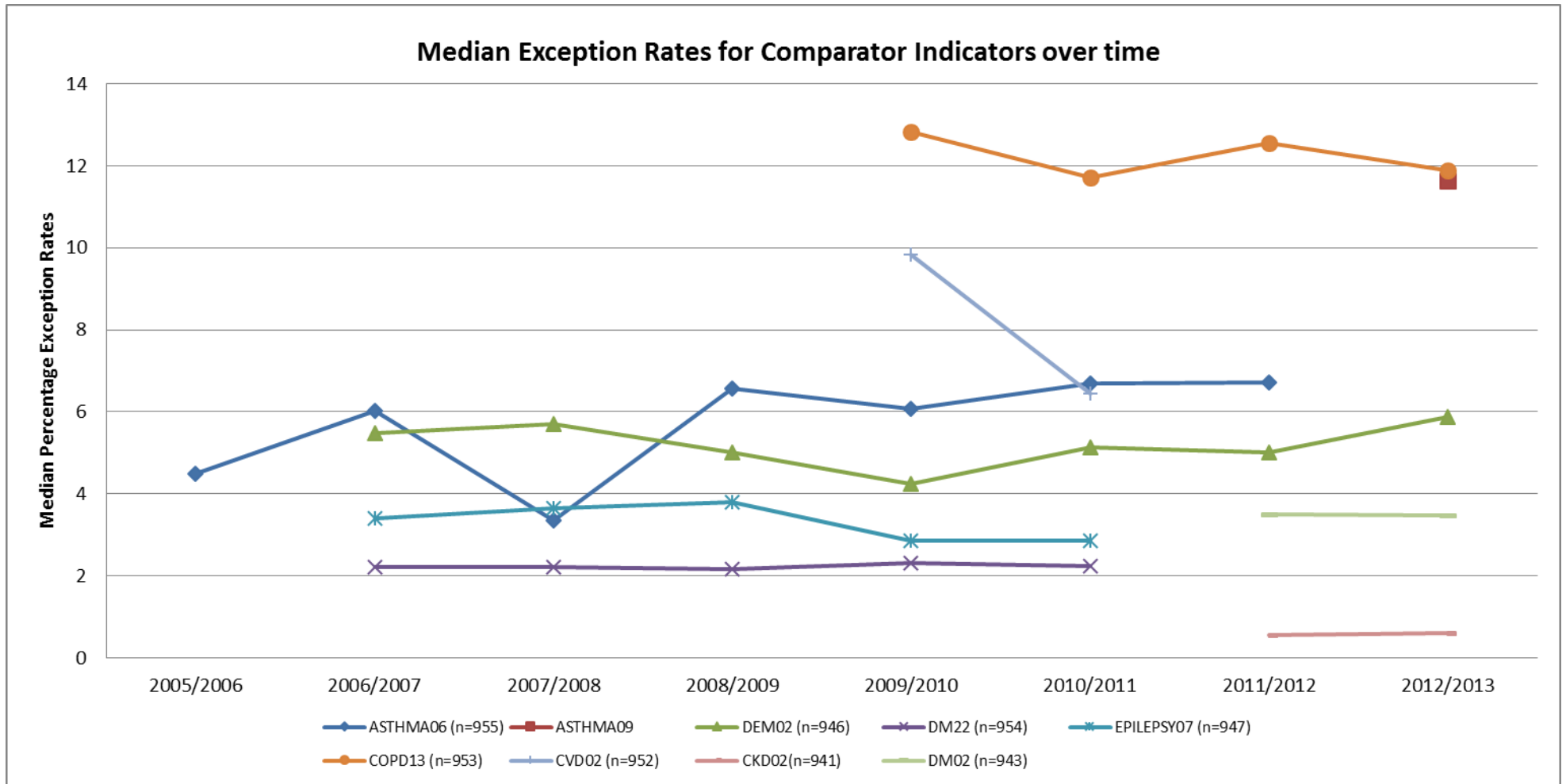
Figure 7-12   Comparators Indicators over time 2005/2006 – 2012/2013

7.3.11 **Summary of Main Findings:**

7.3.11.1 **Composite Indicators:**

Median rates of exception reporting for the composite mental health indicators were significantly higher in thirteen out of sixteen comparable composite chronic disease indicators for the 2012/2013 QOF year. For example median exception rate was for the composite MH indicator was 11.1% IQR 0.0-21.4% compared to 3.4% IQR 1.4-6.6%, $p<0.001$ for the hypertension composite indicator. A similar pattern was seen in 2011/2012; where exception reporting for the composite mental health indicators was significantly higher in ten out of fourteen of the comparable composite chronic disease indicators.

7.3.11.2 **Individual Indicators:**

7.3.11.2.1 Body Mass Index (BMI) recording (MH12):

There was a higher rate of median exception reporting for BMI recording in MMI compared to diabetes in 2012/2013 and 2011/2012.

7.3.11.2.2 Blood Pressure (BP) monitoring (MH13):

The median exception rate for BP recording in MMI was also significantly higher than the median exception rate for BP recording in chronic kidney disease in 2012/2013 and 2011/2012.

7.3.11.2.3 Routine health promotion & prevention advice (MH09):

The median exception rates for routine health promotion in MMI was significantly higher than the median exception rate for the documentation of lifestyle advice in hypertension in both 2010/2011 and 2009/2010.

7.3.11.2.4 Creatinine and TSH monitoring (MH04):

Lower rates of exception reporting for creatinine and TSH monitoring in lithium prescription compared to eGFR and creatinine monitoring in diabetes occurred throughout this study from 2006/2007 until 2011/2012.

7.3.11.2.5 Comparison of Comprehensive Care Plans (MH06/MH10) with similar reviews:

Exception reporting rates were significantly higher for the mental health care plan indicator compared to the dementia, asthma and epilepsy review indicators for each year from 2006/2007 until 2009/2010. In 2010/2011 there was no difference in exception rates between the mental health care plan indicator and the asthma review indicator but exception rates for the mental health indicator remained higher than that of the dementia and epilepsy reviews. By 2012/2013, there was no difference in exception rates between the mental health care plans and dementia reviews.

Notably median exception rates for the metal health care plan were significantly lower for all comparator years, than the median exception rates for COPD reviews.

7.4 Discussion:

7.4.1 Composite Indicator Exception Rates:

In Scotland rates of exception reporting for the composite mental health indicators were significantly higher compared to the majority of the other composite chronic disease indicators within the two most recent QOF years. This finding is in keeping with Doran and colleagues (Doran et al., 2006), who found overall median exception rates for mental health indicators to be higher than that for asthma and COPD in English practices (median exception rate 9.5% for mental health, 2.7% for asthma and 8.2% for COPD). While it is recognised that individuals with MMI experience many barriers to care, possible reasons underlying the higher exception rates observed in this study are likely to include; the stigma associated with mental illness, as well as the perceived separation of physical and mental healthcare. The latter issue may be of particular significance given that many of the indicators included in the mental health QOF are related to physical healthcare measures.

While it is recognised that exception rates may vary widely by indicator (Doran et al., 2008; Sigfrid et al., 2006) - often partly due to whether the indicator of interest is a measurement indicator (e.g. BP measurement), treatment indicator (e.g. prescribing ACE inhibitors in certain populations) or an outcome indicator (e.g. cholesterol level $<5mmoll^{-1}$) –this study has found that when directly comparing individual indicators which were of the same type, higher exception rates in MMI persisted across a range of indicators over a

number of years. This suggests possible inequalities in access to certain aspects of incentivised healthcare in Scotland which have persisted over at least 2 QOF years.

7.4.2 Lower Exception rates in the Lithium Indicators

However higher exception rates were not universally reported across all Mental Health indicators. For example exception rates for the creatinine and TSH monitoring in lithium prescription indicator were lower than exception rates for the comparable eGFR and creatinine monitoring indicator in diabetes. This was persistent across the duration of the study. Given the importance of lithium monitoring not only due to its narrow therapeutic window, its potential for side effects and its risk of toxicity, it would appear that in Scotland, there are extremely low levels of exception reporting for this indicator in primary care. Reasons may be due in part to a high level of awareness of the potential risks of lithium, along with clinically cautious prescribing by secondary care. Improved prescribing guidance along with possible high levels of patient involvement in their care, may in part explain this low exception rate. The need for adherence to therapeutic monitoring before the dispensing of medication may also occur (as is seen with clozapine) and this may also help explain the low exception rates observed for this indicator.

7.4.3 Comprehensive Care Plan Documentation Exception Rates:

Median rates of exception reporting for the comprehensive care plan documentation indicator (MH06/MH10) improved during this study timeframe. Although the median exception rates were significantly higher than that for dementia care plans, asthma reviews and medication reviews in epilepsy, at the start of this study, by 2012/2013 exception rates either showed no difference or were lower than comparator indicators, suggesting improvement with time. This finding of a decrease in exception rate over time for this Mental Health indicator may be in keeping with general trends of improved achievement rates and reduced exception rates which occur as the age of the indicator increases (Reeves et al., 2010). The finding of higher exception rate for the COPD indicator may be due in part to increased rates of being housebound (Gore et al., 2000) or increased rates of comorbid mental health problems which are known to be relatively common in individuals with COPD (Gore et al., 2000).

7.4.4 **Health Promotion, BMI and BP Recording Exception Rates:**

Higher median exception rates for the health promotion review (MH09), BMI recording (MH12) and Blood Pressure measurement (MH13) indicators in MMI compared to their respective comparator indicators in hypertension (CVD02), Diabetes (DM02) and Chronic Kidney Disease (CKD02) were reported in this study. These findings are of significant clinical concern. It is recognised that the increased morbidity and mortality experienced by individuals with MMI is largely due to a higher prevalence of modifiable risk factors, many of which are due to lifestyle choices (Parks et al., 2006). Therefore health promotion combined with the recording and monitoring of cardiovascular risk factors (such as BMI and BP) are important interventions in order to begin to address the gap in morbidity and mortality experienced by individuals with MMI.

In particular the finding of increased median rates of exception reporting for BMI recording is of particular clinical concern not only due to the high rates of obesity that are seen in patients with MMI (Ratliff et al., 2013: Allison et al., 1999) but also because of recent evidence to suggest that obesity in individuals with schizophrenia has a profound influence on cardiometabolic risk. Reasons for this increased risk associated with obesity are unclear but may in part be explained by poor diet and physical inactivity. Given the move towards primary prevention, higher median exception reporting for the recording of BMI and BP in MMI is of significant clinical concern as it suggests that opportunities for screening and for subsequent intervention to address cardiometabolic risk are being missed in this vulnerable patient group. The retirement of the BMI measurement indicator in MMI for the 2014/2015 QOF in England is also of concern (QOF England 2014/2015). These concerns have been further detailed in Chapter 6.

Although it is recognised that individuals with MMI have more physical health problems than the general population, inequalities are persistently reported for both the access to and the quality of a range of physical healthcare services (Lambert and Newcomer, 2009; de Hert 2011a). This study's findings of high rates of median exception reporting in Mental Health measurement indicators compared to measurement indicators in other chronic diseases supports the evidence of inequalities in access to some aspects of incentivised QOF care in Scotland.

7.5 Strengths and Limitations:

This is the first study to directly compare median exception rates for individual and composite mental health indicators with other individual and composite chronic disease indicators over time and so adds to previous work in this area. The national scope of this study represents a major strength but some potential limitations similar to those detailed in Chapter 6 are acknowledged. Firstly, some practices may not directly record all exceptions (if for example, the maximum payment threshold has been obtained) and so exception codes may be under-recorded. Secondly not all practices had exception rate data available. This is likely due to limitations in data extraction. However this meant that the number of practices whose data was available varied by indicator. While it may be the case that availability of exception rate data may be influenced by the indicator itself, due to the fact that most practices had exception rate data available (i.e. greater than 900 practices) it is likely that the effect of this was small. Thirdly, while it is recognised that individuals with a chronic disease are likely to have more than one (Barnett et al., 2012), it was not possible to assess the effect of multimorbidity on exception rates. Detailed auditing within practices, where reasons for exception could be examined across multiple indicator areas for the same person would allow this to be investigated further.

A further limitation of this work is that of the individual non-Mental Health indicators chosen for comparison with the comprehensive care plan indicator (MH06/MH10). Exception rates for the asthma review, COPD review, medication review in epilepsy and dementia care review indicators were chosen as proxy comparators: with the rationale being that these components (symptom review and medication review) should be included within a comprehensive care plan. While the skills, expertise and time required to complete the individual indicators may not be directly comparable, they represented the closest comparator indicators available within the QOF and were therefore felt to be a useful proxy measurement of equity in care across different chronic illnesses. Although the differences in the indicator definitions is a limitation to the design of this study.

The composite indicators generated in this study were also made up of different types of indicators (measurement and target indicators) and often contained different numbers of individual indicators (for example the Mental Health composite indicator contained nine individual indicators, while the CKD composite indicator contained four individual indicators). These factors may have influenced the median composite exception rate that was calculated for each chronic disease composite indicator. However the generation of a

median composite indicator exception rate for each chronic disease allowed a broad comparison over many chronic diseases and allowed general trends in median exception rates to be described. Although this technique has limitations, it has been detailed by others in this field (de Wet et al., 2012).

A further limitation to this study is that the different indicators investigated have been present in the QOF for different lengths of time. It is generally accepted that indicator exception rates decrease with time and then plateau (Reeves et al., 2010), and so differences in the exception rates observed in this study, may in part be explained by variations in the age of indicators. However by undertaking a longitudinal approach to exception rates, namely back to the inception of the QOF, this effect has been minimised.

7.6 Conclusions:

Although median rates of exception reporting varied across clinical indicators, there was evidence of higher rates of median exception reporting for composite and individual mental health indicators relative to a number of composite and individual comparator indicators for other chronic physical health problems. Although reductions in the gap between rates of median exception reporting in comprehensive care planning in mental health versus its comparator indicators have improved over time, the gap in median exception rates for health promotion indicators (including recording of BMI and BP) remain wide.

Despite the risk of increased exception rates in MMI being a concern highlighted by the Royal College of General Practioners (RCGP) at the inception of the QOF in 2004, higher exception rates and as such potential inequalities in healthcare provision appear to have continued over the following 9-10 years that the QOF has been in place. Further investigation, for example through detailed auditing of patient level data and monitoring of patterns of exception reporting over time, is required to ensure that the QOF indicators and exception reporting are appropriately used within primary care. Continued efforts must also be made to reduce barriers to care and improve integration of health services in order to provide higher quality healthcare for individuals with MMI. This will then act to help reduce inequalities in care.

Chapter 8: Increased mortality in Major Mental Illness (MMI): findings from The Glasgow Psychosis Clinical Information System (PsyCIS)

Chapter Overview:

This chapter describes and compares rate, age and primary cause of death of individuals with Major Mental Illness (MMI) within The Glasgow Psychosis Clinical Information System (PsyCIS) with the rate, age and primary cause of death of individuals living in the local (Glasgow) and wider (Scottish) areas. Rate of death was compared using Standardised Mortality Ratios (SMR). The impact of socioeconomic status on rate and primary cause of death between groups was also investigated. Finally a comparison of primary cause of death across the lifespan of individuals with schizophrenia and bipolar disorder was also undertaken.

8.1 Scottish Mortality within a European Setting:

As outlined in Chapter 1, individuals with MMI die 15-20 years younger than individuals without MMI; however work detailing mortality rates of individuals with MMI exclusively in Scotland has been limited. Scotland is often dubbed the "sick man of Europe" and the Glasgow Centre for Population Health (GCPH) has produced a 60 year overview of Scottish Mortality Rates in a European context (GCPH Still the Sick Man of Europe? 2012). They found that Scotland has had the highest mortality in Western Europe among working age (15-74 years old) men and women since the late 1970s. The GCPH also recognised that although mortality rates for Scottish men of working age have been falling at a similar rate to other Western European countries; they have remained consistently elevated compared to the Western European average. For women, although there has also been a reduction in mortality rates in Scotland, when compared to other Western European countries the reduction has been less than the European average; which has resulted in an increased gap in mortality rates with Scottish women experiencing higher mortality rates than their European counterparts. In 2010 it was estimated that Scottish male mortality rates were around 20% higher and female working age mortality rates were 30% higher than the Western European mean (GCPH Still the Sick Man of Europe? 2012).

The GCPH also highlighted another area potentially of greater concern: that of a plateauing mortality rate in younger working age adults (15-44 years). They reported that although

mortality rates have reduced from the 1950s until the mid-1980s, further reduction in mortality rate from the mid-1980s onwards has "stalled". This has been particularly evident in Scottish men since 1982 and in Scottish women since 1987. Additionally this plateauing of Scottish mortality rate, is unusual compared to other European Countries: where in all but one of the other nineteen European Countries (namely Northern Ireland) included in their overview, a reduction in mortality in men and women has continued to occur in recent years; albeit to varying extents. Subsequent to Scotland's plateau in mortality rate, its relative ranking for younger working age mortality has progressively worsened for both sexes over the last 55 years; in fact it was reported as the highest among the sixteen Western European countries in the study by the GCPH (GCPH Still the Sick Man of Europe? 2012).

More locally, when the Scottish younger working age mortality is compared to the younger working age mortality in England and Wales it was reported to be 46% higher for women and 54% higher for men in 2009 (GCPH Still the Sick Man of Europe? 2012). These findings highlight the unique challenges which face the healthcare system in Scotland.

8.2 Glasgow Mortality Rates:

Within Glasgow mortality rates are higher and age of death lower than that of Scottish averages (Scot PHO Public Health Information for Scotland, 2015). Although it is recognised that certain factors which impact on health; such as obesity, diabetes and diet, are not significantly different in Glasgow than elsewhere in Scotland, many health outcomes are worse. A substantial proportion of these differences can be explained by the socio-economic profile seen in Glasgow however it is recognised that this does not fully explain the differences seen.

The impact of deprivation on health outcomes has been recognised since health records began (Equally Well: Report of the Ministerial Task Force on Health Inequalities, 2008). As early as 1842 Edwin Chadwick reported this relationship in Aberdeen and it is recognised globally that mortality rates, life expectancy, rates of comorbidity and health related behaviour all vary between social group; with individuals from more deprived areas commonly experiencing more adverse outcomes and reduced life expectancy compared to individuals from more affluent areas (Hosseinpoor at al., 2012; MacIntyre and Ellaway, 2003).

Inequalities in socioeconomic status may arise in a number of different ways and interact with each other in a complex manner to affect both health related behaviour and health outcomes. Physical factors such as damp housing, air pollution and living in a threatening environment, along with individual psychological factors such as personal strengths and coping abilities will impact on health related behaviours such as smoking, diet and exercise. The relationship between these factors is complex and likely bidirectional; for example an individual with poor coping skills, may smoke and drink excessively while avoiding exercise in order to cope with living in a damp house where they feel threatened. Wider systems in place within the society that an individual lives; for example education systems, health care systems, working opportunities and taxation policies, will also impact on socioeconomic inequalities.

Although life expectancy and health behaviours have improved in Glasgow over the past 50 years, the rates of improvement have differed depending on an individuals' socioeconomic status. As Scotland's ranking in terms of European mortality rates have worsened over time, so too has the gap in life expectancy between the most affluent and most deprived areas (SPHSU, 2007). For example life expectancy at birth in Glasgow improved by 2.2 years (from 75.8 years in 1998-2000 to 78.0 years in 2008-2010) but in Edinburgh, life expectancy improved by 2.8 years (from 79.0 years in 1998-2000 to 81.8 years in 2008-2010) (GRO for Scotland Table 9, 2010). This highlights the particular challenges which face the healthcare system in Glasgow.

8.3 More than deprivation:

While it is known that the impact of deprivation on health and mortality is significant, the differences in life expectancy in Scotland compared to the rest of Europe and in Glasgow compared to the rest of Scotland cannot be fully explained by deprivation alone (Hanlon et al., 2001; McCartney et al., 2011). When all-cause mortality in Scotland was compared to all-cause mortality in England and Wales in 1981, it was 12% higher in Scotland, while in 2001, the Scottish all-cause mortality was 15% higher. When the Carstairs Deprivation Index was used to try and explain the rise in excess all-cause mortality over the 20 year period, the proportion that could be explained by differences in deprivation fell from 62% in 1981 to 47% in 2001 (McCartney et al., 2012). The gap in mortality (between Scotland and the rest of Europe) which cannot be explained by deprivation has been termed the "Scottish Effect".

This phenomenon has been replicated more locally on a city basis- namely in Glasgow. When premature mortality (deaths in those < 65 years) in Glasgow was compared to the similarly deprived English cities of Liverpool and Manchester, it was found that premature deaths were 30% higher in Glasgow than in Liverpool and Manchester and deaths at all ages were almost 15% higher. This excess has been shown for all adult age groups, for both sexes and across different neighbourhood types (both deprived and non-deprived). Of more concern is that the excess mortality appears to be greatest in the working-age groups (15-44 and 45-64), where it was 45% and 30% higher respectively. The gap in mortality seen in Glasgow that cannot be explained by deprivation alone has been termed the "Glasgow Effect." (GCPH Still the Sick Man of Europe? 2012).

As a consequence of these findings, much work has been undertaken by the GCPH comparing Glasgow, with Liverpool and Manchester in greater detail, to determine possible explanations for the "Glasgow Effect". Work is on-going within this field, but differences in Standardised Mortality Ratios (SMR) for certain causes of death between the three cities are consistently reported. For example when SMR are calculated for specific causes of death, such as lung cancer, suicide, alcohol and drug related deaths, deaths were 27% higher in relation to lung cancer, almost 70% higher for suicide, 2.3 times higher for alcohol-related causes, and almost 2.5 times higher for drug-related deaths in individuals living in Glasgow relative to individuals living in Liverpool and Manchester (GCPH Still the Sick Man of Europe? 2012). Clearly more detailed work is required to develop a better understanding of possible explanations for this.

Of note, and of potential hope, is that when analysis of long term trends in premature mortality for the three cities is dated back to the 1920s, the current trend of higher mortality rates in Glasgow compared to Liverpool and Manchester has not always been observed. This widening gap in mortality began to appear at the start of the 1980s and has continued over the past 25-30 years. This observation has led researchers to consider that the excess mortality and "Glasgow Effect" may be a relatively recent phenomenon. It is hypothesised that with the correct intervention this trend could be slowed and even reversed.

Given the unique mortality patterns and profile of the general population within Glasgow and Scotland, exploration of age and cause of death in individuals with MMI within a Glasgow and Scottish setting is of clinical interest and importance. This combined with the

paucity of research to date has led to the further investigation of the patterns of mortality included in this thesis.

8.4 Aims:

1. To describe the age and primary cause of death of individuals with major mental illness (MMI) within the Glasgow Psychosis Clinical Information System (PsyCIS) relative to the local (Glasgow) and wider (Scottish) populations.

2. To assess the impact of socioeconomic status on rate and primary cause of death in individuals with MMI (schizophrenia and bipolar disorder) relative to the local (Glasgow) and wider (Scottish) populations.

3. To compare calculated standardised mortality ratios (SMR), for individuals with MMI to the local (Glasgow) and wider (Scottish) populations.

4. To compare primary cause of death by ICD 10 diagnosis (schizophrenia and bipolar affective disorder), across the life-span.

8.5 Scientific Rationale:

While the increase in standardised mortality rates (SMR) for individuals with MMI compared to the general population is substantial (Crump et al., 2013; Hoang et al., 2011; Laursen et al., 2011; Wahlbeck et al., 2011), and reasonably well described, little work has assessed whether causes of mortality vary across the life-span. Although the relationship between age and suicide has been investigated (Gunnell and Middleton, 2003), with the recognition that suicide is a particularly important contributor to excess mortality in young males, little work has been done detailing other causes of death across the lifespan of individuals with MMI.

While it is recognised that socioeconomic status has a significant impact on health and wellbeing and, with only a few exceptions, health outcomes are generally worse in deprived communities (Strickland et al., 1998), little work has specifically focused on the relationship between mortality and socioeconomic deprivation for individuals with MMI. This is therefore worthy of further exploration.

Historically it has been considered that bipolar disorder had a better prognosis than schizophrenia (Falret, 1854), however recent studies are increasingly recognising that the level of the increased mortality experienced by individuals with schizophrenia and bipolar disorder may be similar. Despite this, detailed comparisons of primary cause of death across the life span of individuals with schizophrenia and bipolar disorder are limited and again worthy of further exploration especially in a Scottish setting. These areas of investigation are the focus of this chapter.

8.6 Methods:

8.6.1 Sample:

All individuals with schizophrenia (F20-F29) or bipolar disorder (F30-F31) aged between 18 and 65 who had died between 2006 and 2010 and lived within the Greater Glasgow area covered by PsyCIS were identified. Date and cause of death were obtained by linkage to the Scottish Morbidity Records held by the Information Services Division (ISD) of NHS Scotland using patient Community Health Index (CHI) number. The International Statistical Classification of Diseases and Related Health Problems (ICD) was used to code cause of deaths, grouped into nine categories using information from the Scottish Government website: 1) cardiovascular disease, 2) cerebrovascular disease, 3) respiratory disease, 4) cancer, 5) alcohol related deaths, 6) mental and behavioural disorder due to drugs, 7) accidental, 8) suicide as defined by the Scottish suicide information database (which includes deaths of undetermined origin) and 9) other (GRO Website and GRO Suicide Definitions) (Table 8-1).

Main categories of cause of death	ICD 10 Codes
1) cardiovascular disease	I20-I25- including acute MI I219 & atherosclerotic heart disease I251 & I259
2) cerebrovascular disease	I60-I69- including subarachnoid haemorrhage I600, I609, brain stem intra cerebral haemorrhage I613, subdural haemorrhage I620, other unspecified stroke I64 & cerebral infarction I639, I693 & I679
3) respiratory disease	J00-J99- including, COPD J441 & J449, pneumonia J189, J22 & J690, emphysema J439, asthma J459 & bronchiectasis J459
4) cancer	C00-C97- including oral C069 & C329, GI tract C159, C169,19 & C20, lung C349, cervix C539, brain C719, skin C446, bladder C679 & lymphoma C819 & C851
5) alcohol related deaths	including mental and behavioural disorder due to use of alcohol F10, degeneration of nervous system due to alcohol G31.2, alcoholic polyneuropathy G62.1, alcoholic cardiomyopathy I42.6, alcoholic gastritis K29.2, alcoholic liver disease K70, chronic hepatitis, not elsewhere classified K73, fibrosis and cirrhosis of liver K74 (excluding K74.3-K74.5 – biliary cirrhosis), alcohol induced chronic pancreatitis K86.0, accidental poisoning by, and exposure to, alcohol X45
6) mental and behavioural disorder due to drugs	F11-F16 & F18-F19
7) accidental	Including transport accidents V01-V99, falls W00-W19, death due to fire X00, accidental poisoning X40-X49 (excluding X45), assault X04 & X59-Y09 and other accidents Y85 & Y86
8) suicide	As defined by the Scottish suicide information database (X60-X84 & Y87.0 and deaths of undetermined origin Y10-Y34) including- intentional self-poisoning X61 & X62, intentional hanging X70, intentional drowning X71, intentional jump from height X80, intentional jump before moving object X81, intentional death by fire X76, poisoning of undetermined intent Y11 & Y12, fall or jump from height of undetermined intent Y30 & undetermined cause of death Y34
9) other	Including all other codes not included in above 1-8. A00-B99, E00-E99, G00-G30, G32-G61, G62-G99, H00-H95, I00-I19, I26-I41, I43-I59, I70-I99, K00-K28, K30-KK69, K70-K85, K87-K93, L00-L99. M00-M99, N00-N99, O00-O99, Q00-Q99, R00-R99, in particular left ventricular failure I501, hypertensive disease I119, aortic aneurysm I711 & I713, peripheral vascular disease E145, ischaemic gut K550, cardiomegaly I517, cardiomyopathy I426 & I429, valvular disease I080, sarcoidosis D869, PE I269, obesity E668 & E669, unspecified cardiac arrest I469, unspecified diabetes E149, diabetic coma E140, diabetic ketoacidosis E141 and diabetes with renal complications E122, UTI N390, septicaemia A419, hypo-osmolality E871, phlebitis I803, GI haemorrhage K922, gastrointestinal ulcer K221, K254 & K264, appendicitis K37, intestinal obstruction K566 and renal failure N19.

Table 8-1   **ICD 10 Codes for Cause of death**

Scottish Index of Multiple Deprivation (SIMD) score was used as a measure of social deprivation (more detail is included in Appendix 1). Each individual was allocated to a SIMD category based on their postcode: where 1 is most deprived and 5 is most affluent.

8.6.2 **Analyses:**

Cause of death by 10 year age ranges, i.e. <25, 25-34, 35-44, 45-54 and 55-64, were calculated for the total deceased MMI population (schizophrenia and bipolar disorder combined) and compared to the local (Glasgow) population and the wider (Scottish)

population using annual mortality statistic data available from the General Register Office (GRO) for Scotland (GRO Scotland).

Cause of death by SIMD quintile for the total deceased MMI population (schizophrenia and bipolar disorder combined) was also calculated and compared with cause of death in the local (Glasgow) and wider (Scottish) population, using annual mortality statistic data. Rates and patterns in cause of death by deprivation quintile were compared in individuals with MMI to the local Glasgow and wider Scottish populations. Both all-cause mortality rate and mortality rate excluding suicide in the MMI population were calculated. The rationale being that as suicide is a major contributor to premature death in MMI it may in itself be influenced by socioeconomic status.

Standardised mortality ratios (SMR) were calculated in the 10 year age ranges for the whole deceased MMI population and further analysed by schizophrenia and bipolar disorder diagnosis and gender. SMR for all causes of death, all causes excluding suicides, and causes due to cardiovascular disease, cerebrovascular disease and cancer, were calculated.

For local (Glasgow) SMR calculations, the expected rate of death was derived by applying the Glasgow death rate stratified by age, sex and cause to the PsyCIS cohort. For the wider (Scotland) SMR calculations, the expected rate of death was derived by applying the Scotland death rate stratified by age, sex and cause to the PsyCIS cohort (Figure 8-1).

Glasgow expected number of deaths	= Glasgow death rate x number in PsyCIS cohort
	1000
Glasgow Standardised Mortality Ratio (SMR)	= actual number of deaths in the PsyCIS cohort
	Glasgow expected number of deaths
Scotland expected number of deaths	= Scotland death rate x number in PsyCIS cohort
	1000
Scotland Standardised Mortality Ratio (SMR)	= actual number of deaths in PsyCIS cohort
	Scotland expected number of deaths

Figure 8-1   Standardised Mortality Ratio (SMR) Calculations

8.7 Results:

8.7.1 Age and primary cause of death in individuals with MMI:

The primary cause of death in individuals with MMI differed from that in the local Glasgow and wider Scottish populations (Table 8-2). When age at death was considered, a higher proportion of individuals with MMI who had died were aged 25-34 and 35-44 compared to individuals who had died in Scotland (7.8% vs. 5.8%, p<0.001 and 16.5% vs. 12.5%, p<0.001) (Table 8-2). The proportion of deaths by age group in individuals with MMI was more similar to the pattern observed locally in Glasgow (Table 8-2).

The proportion of men that died in each group was similar: 67.8% of deaths in those with MMI were in men, 64.5% of deaths in Glasgow were in men (p=0.298) and 61.9% of deaths in Scotland were in men (p=0.063) (Table 8-2).

Cause of death differed between the three groups: for example, death due to cancer occurred less frequently in individuals with MMI compared to the local Glasgow and wider Scottish populations (14.3% vs. 27.3%, p<0.001 and 33.2%, p<0.001) (Table 8-2). Alcohol related deaths were also lower (6.5% (MMI) vs. 12.8% (Glasgow), p=0.005 and 9.7% (Scotland), p=0.099) (Table 8-2). The proportion of deaths due to suicide was higher in individuals with MMI compared to that of the local Glasgow and wider Scottish populations (14.8% vs. 7.0%, p<0.001 and 6.5%, p<0.001), as were drug related deaths (7.8% vs. 5.1%, p=0.065 and 3.2%, p<0.001) (Table 8-2). The proportion of deaths due to cardiovascular disease were similar across the three groups (14.8% in those with MMI, 13.2% in those living in Glasgow (p=0.546) and 13.7% in those living in Scotland (p=0.626) (Table 8-2).

	Combined MMI Group (n=230)	Glasgow City (n=8,094)	P[1]	Scotland (n=54,590)	P[2]
Cause of death (n, %)					
Cerebrovascular Disease	8 (3.5)	304 (3.8)	0.833	2186 (4.0)	0.685
Cardiovascular Disease	34 (14.8)	1069 (13.2)	0.546	7465 (13.7)	0.626
Cancer	**33 (14.3)**	**2211 (27.3)**	**<0.001**	**18129 (33.2)**	**<0.001**
Respiratory disease	**24 (10.4)**	606 (7.5)	0.096	**3451 (6.3)**	**0.001**
Alcohol Related	**15 (6.5)**	**1032 (12.8)**	**0.005**	5319 (9.7)	0.099
Accidental Deaths	11 (4.8)	400 (4.9)	0.912	2882 (5.3)	0.734
Suicide	**34 (14.8)**	**568 (7.0)**	**<0.001**	**3533 (6.5)**	**<0.001**
Other	53 (23.0)	1492 (18.4)	0.076	9869 (18.1)	0.05
Mental & behavioural disorder due to drugs	**18 (7.8)**	412 (5.1)	0.065	**1756 (3.2)**	**<0.001**
Male (n, %)	156 (67.8%)	5218 (64.5%)	0.298	33772 (61.9%)	0.063
Rate of death/age group (n,%)					
<25	3 (1.3)	238 (2.9)	0.144	1902 (3.5)	0.07
25-34	**18 (7.8)**	559 (6.9)	0.588	**3186 (5.8)**	**<0.001**
35-44	**38 (16.5)**	1250 (15.4)	0.656	**6841 (12.5)**	**<0.001**
45-54	72 (31.3)	2171 (26.8)	0.131	13841 (25.4)	0.039
55-64	99 (43.0)	3876 (47.9)	0.147	28820 (52.8)	0.003
Death Rate/Quintile (n, %)					
5 Most affluent	11 (4.8)	257 (3.2)	0.173	5974 (10.9)	0.003
4	15 (6.5)	450 (5.6)	0.531	8244 (15.1)	0.0003
3	34 (14.8)	732 (9.0)	0.003	10338 (18.9)	0.108
2	64 (27.8)	**1286 (15.9)**	**<0.001**	12643 (23.2)	0.09
1- Most deprived	**106(46.1)**	**5369 (66.3)**	**<0.001**	**17391 (31.9)**	**<0.001**

Table 8-2   Cause of Death of the Deceased PsyCIS Cohort compared to Glasgow and Scottish Populations
Bold if significant (p<0.001) p[1] Chi squared combined MMI group vs. Glasgow City, p[2] Chi squared combined MMI group vs. Scotland

Compared to the local Glasgow and wider Scottish population, individuals with MMI had a different pattern of cause of death across the life span (Table 8-3 & Figure 8-2). Suicide was the single leading cause of death in individuals with MMI aged <25 (100%), 25-34 (27.8%) and 35-44 (26.3%). For individuals with MMI aged 45-54, suicide and cardiovascular disease were the leading causes of death (both 12.5%), while in the 55-64 age group cardiovascular disease was the single most common cause of death (21.2%), followed by cancer (20.2%).

In the Scottish population, accidental deaths were the leading cause of death in the <25 (35.5%) and 25-34 age groups (21.5%), whereas in the 35-44, 45-54 and 55-64 age groups, cancer was the single leading cause of death (18.7%, 31.4% and 41.1% respectively).

In the Glasgow population suicide and accidental deaths were the most common causes of death in the <25s (29.4% and 24.8% respectively) while in the 25-34 age group drug related deaths and suicide were the most common causes of death (both 27.8%). In the 35-44 age group alcohol related deaths were the leading cause of death (20.3%) while in the 45-54 and 55-64 age groups cancer was the leading cause of death (26.5% and 36.4% respectively) (Table 8-3 & Figure 8-2).

	<25	25-34	35-44	45-54	55-64
Cardiovascular disease					
MMI vs. Glasgow n, (%)	0 (0) vs. 1 (0.4) p=0.91	1 (5.6) vs. 14 (2.5) p=0.423	3 (7.9) vs. 99 (7.9) p=0.909	9 (12.5) vs. 310 (14.3) p=0.671	21 (21.2) vs. 645 (16.6) p=0.229
MMI vs. Scotland n, (%)	0 (0) vs. 8 (0.4) p=0.910	1 (5.6) vs. 77 (2.4) p=0.389	3 (7.9) vs. 609 (8.9) p=0.811	9 (12.5) vs. 2042 (14.8) p=0.591	21 (21.2) vs. 4729 (16.4) p=0.198
Cerebrovascular disease					
MMI vs. Glasgow n, (%)	0 (0) vs. 5 (2.1) p=0.80	0 (0) vs. 7 (1.3) p=0.633	1(2.6) vs. 31 (2.5) p=0.999	4(5.6) vs. 100 (4.6) p=0.706	3 (3.0) vs. 161 (4.2) p=0.579
MMI vs. Scotland n, (%)	0 (0) vs. 20 (1.1) p=0.856	0 (0) vs. 49 (1.5) p=0.596	1(2.6) vs. 230 (3.4) p=0.803	4(5.6) vs. 613 (4.4) p=0.643	3 (3.0) vs. 1274 (4.4) p=0.501
Respiratory disease					
MMI vs. Glasgow n, (%)	0 (0) vs. 9 (3.8) p=0.73	0 (0) vs. 8 (1.4) p=0.609	3 (7.9) vs. 52 (4.2) p=0.2953	7(9.7) vs. 138 (6.4) p=0.253	14 (14.1) vs. 399 (10.3) p=0.215
MMI vs. Scotland n, (%)	0 (0) vs. 45 (2.4) p=0.787	0 (0) vs. 75 (2.4) p=0.510	3 (7.9)vs.233 (3.4) p=0.130	7(9.7) vs. 676 (4.9) p=0.058	**14 (14.1) vs.2422 (8.4) p=0.04**
Cancer					
MMI vs. Glasgow n, (%)	0 (0) vs. 19 (8.0) p=0.61	2 (11.1) vs. 48 (8.6) p=0.708	3(7.9) vs. 157 (12.6) p=0.287	**8 (11.1) vs.576 (26.5) p=0.003**	**20 (20.2) vs.1411(36.4) p<0.001**
MMI vs. Scotland n, (%)	0(0) vs. 139 (7.3) p=0.627	2(11.1) vs. 301 (9.4) p=0.810	3(7.9)vs1286 (18.8) p=0.086	**8 (11.1)vs. 4455(32.2) p<0.001**	**20 (20.2) vs.11948 (41.5) p<0.001**
Alcohol Related Deaths					
MMI vs. Glasgow n, (%)	0 (0) vs. 4 (1.7) p=0.82	1 (5.6) vs. 46 (8.2) p=0.683	**1 (2.6) vs. 254 (20.3) p=0.008**	8(11.1) vs.358 (16.5) p=0.224	5 (5.1) vs. 370 (9.5) p=0.131
MMI vs. Scotland n, (%)	0 (0) vs. 19 (1.0) p=0.862	1 (5.6) vs. 210 (6.6) p=0.860	**1 (2.6) vs. 980 (14.3) p=0.039**	8(11.1) vs. 1947 (14.1) p=0.472	5 (5.1) vs. 2163 (7.5) p=0.355
Mental & behavioural disorder due to drugs					
MMI vs. Glasgow n, (%)	0 (0) vs. 29 (12.2) p=0.519	5 (27.8) vs.143 (25.6) p=0.834	5(13.2) vs.179 (14.3) p=0.704	**7 (9.7) vs. 49 (2.3) p<0.001**	1(1.0) vs. 12 (0.3) p=0.228
MMI vs. Scotland n, (%)	0 (0) vs. 263 (13.8) p=0.488	(27.8) vs. 666 (20.9) p=0.475	(13.2) vs.608 (8.9) p=0.357	**7 (9.7) vs. 188 (1.4) p<0.001**	**1 (1.0) vs. 31 (0.1) p=0.007**
Accidental Deaths					
MMI vs. Glasgow n, (%)	0 (0) vs. 59 (24.8) p=0.321	1 (5.6) vs. 63 (11.3) p=0.447	1(2.6) vs. 94 (7.5) p=0.205	**7(9.7) vs. 90 (4.1) p=0.022**	2 (2.0) vs. 94 (2.4) p=0.495
MMI vs. Scotland n, (%)	0 (0) vs. 584 (30.78) p=0.249	1 (5.6) vs. 502 (15.8) p=0.236	1(2.6) vs. 586 (8.6) p=0.192	**7(9.7) vs. 604 (4.4) p=0.027**	2 (2.0) vs. 606 (2.1) p=0.954
Suicide					
MMI vs. Glasgow n, (%)	**3 (100) vs. 70 (29.4) p=0.008**	5(27.8) vs. 139(24.9) p=0.779	**10(26.3)vs.161 (12.9) p=0.014**	**9 (12.5)vs.123 (5.7) p=0.015**	**7 (7.1) vs. 75 (1.93) p<0.001**
MMI vs. Scotland n, (%)	3 (100)vs. 474 (24.9) p=0.31	5(27.8) vs. 751(23.6) p=0.675	**10(26.3)vs986 (14.4) p=0.038**	**9 (12.5)vs.815 (5.9) p=0.018**	**7 (7.1) vs. 507 (1.8) p<0.001**
Other					
MMI vs. Glasgow n, (%)	0 (0) vs. 42 (17.6) p=0.423	3 (16.7) vs. 91 (16.3) p=0.965	11(28.9) vs. 223 (17.8) p=0.071	13 (18.1) vs. 427 (19.7) p=0.735	**26 (26.3) vs.709 (18.3) p=0.044**
MMI vs. Scotland n, (%)	0 (0) vs. 350 (18.4) p=0.411	3 (16.7) vs. 555(17.4) p=0.93	11 (28.9) vs. 1323(19.3) p=0.135	13(18.1) vs. 2501 (18.1) p=0.998	**26 (26.3) vs.5140 (17.8) p=0.029**
All Cause of death					
MMI vs. Glasgow	3 vs. 238	18 vs. 559	38 vs. 1250	72 vs. 2171	99 vs. 3876
MMI vs. Scotland	3 vs. 1902	18 vs. 3186	38 vs. 6841	72 vs. 13841	99 vs. 28820

Table 8-3 Cause of death in PsyCIS Population compared to the Glasgow and Scottish Population by age group Bold if significant (p<0.05)
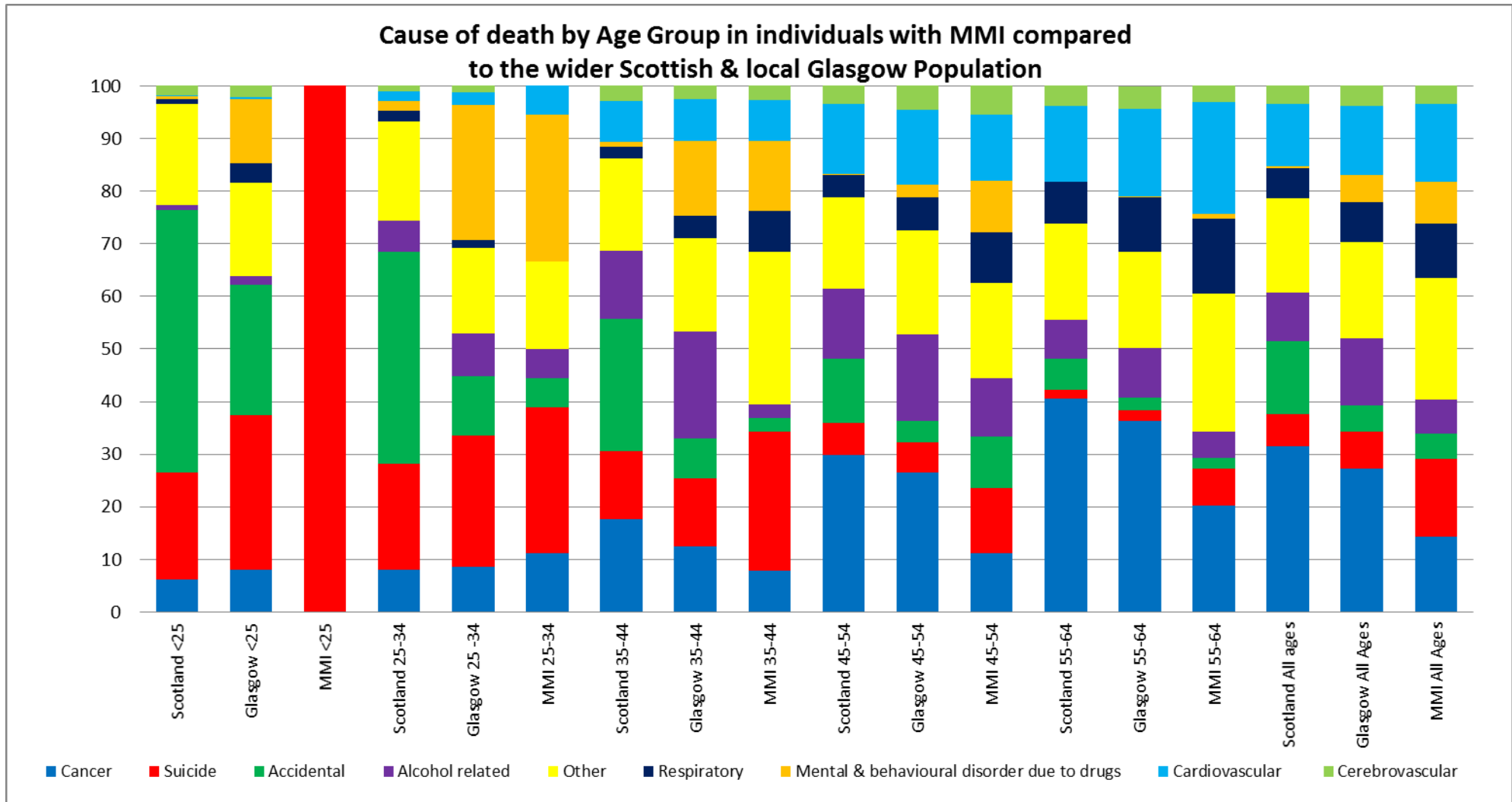
Figure 8-2   Cause of death by Age Group in individuals with MMI compared to the wider Scottish and local Glasgow population by age group

8.7.2 **Impact of socioeconomic status on rate and primary cause of death:**

The rate of death per 10,000 population over the 5 years for MMI compared to the local Glasgow and wider Scottish populations was higher across all socioeconomic quintiles and persisted even when suicide was excluded as a cause of death (Figure 8-3). For example, in the most deprived cohort, the rate of death (excluding suicide) in individuals with MMI was 697.2 per 10,000 population compared to a rate of 252.4 per 10,000 population for Scotland and 274.7 per 10,000 population for Glasgow.
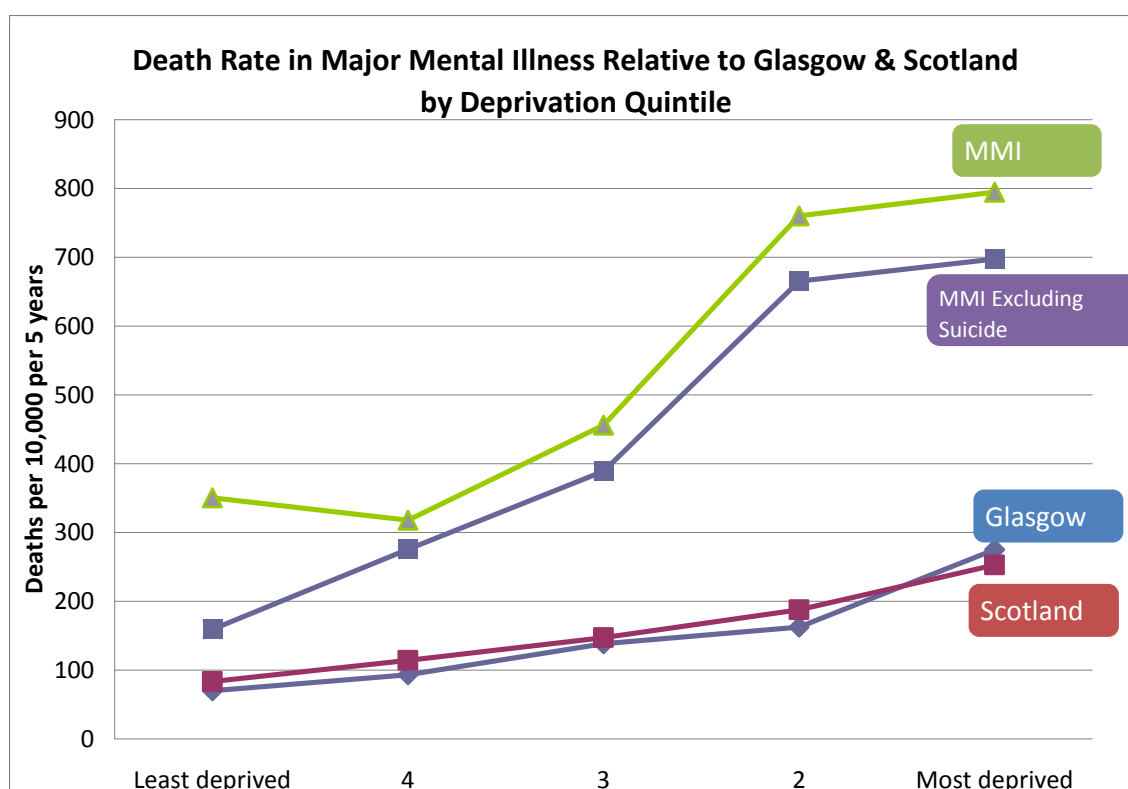
Figure 8-3   **Death Rate/10,000 population per 5 years for those with MMI and for the general population living in Glasgow and Scotland by deprivation quintile**

There appeared to be a graded relationship between increasing level of deprivation and death rate in MMI, mirroring that seen in the local Glasgow and wider Scottish general population. When suicide was excluded as a cause of death for individuals with MMI, this graded relationship appeared most prominent.

When the primary cause of death for individuals with MMI was reported in more detail by deprivation quintile, and compared to the local Glasgow and wider Scottish populations, a number of differences were identified. For individuals living in the most deprived cohort, higher drug-related deaths occurred in MMI compared to the local Glasgow and wider Scottish population rates (12.3% vs. 5.9%, p<0.001 and 5.1% p=0.002 respectively). A

lower proportion of deaths due to cancer in individuals with MMI living in the most deprived quintile were also observed, relative to the local Glasgow and wider Scottish populations (12.3% vs. 25.1% p=0.013 and 26.3% p<0.001) (Table 8-4).

The proportion of suicide was significantly higher in individuals with MMI living in the most affluent quintile relative to the local Glasgow and wider Scottish populations (54.6% vs. 5.8%, p<0.001 and 5.5%, p<0.001). Similarly, an increase in proportion of suicide was observed for individuals with MMI living in the most deprived quintile compared to the local Glasgow and wider Scottish population (12.3% vs. 6.9%, p=0.05 and 6.9%, p=0.05) (Table 8-4)

Cause of Death	n, (%)	SIMD Category				
		Most Affluent				Most deprived
Accidental	MMI vs. Glasgow	0 (0) vs. 9 (3.5) p=0.535	0 (0) vs. 21 (4.7) p=0.40	1 (2.9 vs. 23 (3.1) p=0.94	5 (7.8) vs. 59 (4.6) p=0.265	5 (4.7) vs. 88 (5.4) p= 0.02
	MMI vs. Scotland	0 (0) vs. 273 (4.7) p=0.45	0 (0) vs. 6491(6.0) p=0.345	1 (2.9) vs. 601 (5.8) p=0.49	5 (7.8) vs. 618 (4.9) p=0.31	5 (4.7) vs.899(5.2) p=0.84
Alcohol	MMI vs. Glasgow	1 (9.1) vs. 18 (7.0) p=0.693	0(0) vs. 38 (8.4) p=0.26	1(2.9) vs.78 (10.7) p= 0.178	10 (15.6) vs.152 (11.8) p= 0.425	**8 (2.8) vs. 746 (13.9) p= 0.003**
	MMI vs. Scotland	1 (9.1) vs.336 (5.8) p=0.64	0(0) vs. 530 (6.4) p=0.326	1 (2.9) vs. 864 (8.4) p=0.282	10 (15.6) vs.1275 (10.1) p= 0.196	**8 (2.8) vs.2314 (13.3) p=0.004**
Cancer	MMI vs. Glasgow	**0 (0) vs. 109 (42.4) p=0.03**	1(6.7) vs.163 (36.2) p=0.067	1 (32.4) vs.236 (32.2) p= 0.992	**8 (12.5) vs.357 (27.8) p= 0.0312**	**13(12.3) vs. 1346.(25.1) p= 0.013**
	MMI vs. Scotland	**0 (0) vs. 2726 (47.0) p=0.025**	**1(6.7) vs.3287 (39.9) p=0.050**	11 (32.4) vs. 3606 (34.9) p=0.829	**8 (12.5) vs.3942 (31.2) p=0.011**	**1 (12.3) vs.4568 (26.3) p=0.008**
Cardiovascular	MMI vs. Glasgow	2 (18.2) vs. 33 (12.8) p=0.44	1 (6.7) vs. 47 (10.4) p=0.66	2 (5.9) vs. 109 (14.9) p=0.191	8 (12.5) vs.171 (13.1) p= 0.872	21 (19.8) vs. 709 (13.2) p= 0.09
	MMI vs. Scotland	2 (18.2) vs. 734 (12.7) p=0.608	1(6.7)vs.1048(12.7) p=0.525	2 (5.9) vs. 1463 (14.2) p=0.213	8 (12.5) vs.1802 (19.3) p=0.727	21(19.8) vs.2418 (13.9) p=0.138
Cerebrovascular	MMI vs. Glasgow	1(9.1) vs. 13 (5.1) p=0.58	2(13.3) vs.20 (4.4) p=0.14	1 (2.9) vs. 27 (3.7) p=0.826	0 (0) vs.3.4 (44) p= 0.139	4 (3.8) vs. 200 (3.7) p= 0.979
	MMI vs. Scotland	1(9.1) vs. 253 (4.4) p=0.455	2(13.3) vs.378 (4.6) p=0.138	1 (2.9) vs. 390 (3.8) p=0.806	0 (0) vs. 478 (3.8) p=0.120	4 (3.8) vs. 687 (4.0) p=0.929
Mental & behavioural disorder due to drugs	MMI vs. Glasgow	0(0) vs. 4 (1.6) p=0.68	**2(13.3) vs. 12 (2.7) p=0.028**	2 (5.9)vs.23 (3.1) p= 0.40	1 (1.6) vs.58 (4.5) p= 0.275	**13 (12.3) vs. 315 (5.9) p <0.001**
	MMI vs. Scotland	0(0) vs. 72(1.2) p=0.716	**2 (13.3) vs.1.7(138) p=0.001**	2 (5.9) vs. 238 (2.3) p=0.183	1 (1.6) vs. 422 (3.3) p=0.44	**13 (12.3) vs. 886 (5.1) p=0.002**
Other	MMI vs. Glasgow	1 (9.1) vs. 4.5 (17.5) p= 0.52	5(33.3) vs.91 (20.2) p=0.34	8 (23.5)vs. 133 (18.2) p=0.521	16(25.0) vs.258 (20.1) p= 0.44	23 (21.2)) vs. 965 (18.0) p= 0.418
	MMI vs. Scotland	1 (9.1) vs.1043 (18.0) p=0.525	5 (33.3) vs. 1447 (17.6) p=0.207	8(23.5) vs.1899 (18.4) p=0.528	16(25.0 vs.2381(1838) p=0.310	23 (21.2) vs. 3099 (17.8) p=0.393
Respiratory	MMI vs. Glasgow	0 (0) vs. 11 (4.3) p= 0.49	2(13.3) vs. 25 (5.6) p=0.257	3(8.8) vs. 45 (6.1) p=0.287	8 (12.5) vs.98 (7.6) p=0.199	11 (10.4) vs. 427 (8.0) p=0.405
	MMI vs. Scotland	0 (0) vs.217 (3.7) p=0.527	2(13.3) vs.406 (4.9) p=0.169	3(8.8) vs. 621 (6.0) p=0.522	8 (12.5) vs. 888 (7.0) p=0.121	11 (10.4) vs. 1319 (7.6) p=0.322
Suicide	MMI vs. Glasgow	**6 (54.6) vs. 15 (5.8) p<0.001**	2 (13.3) vs. 33 (7.3) p= 0.433	5 (14.7) vs. 58 (7.9) p=0.208	8 (12.5) vs. 82 (6.9) p= 0.08	**13 (12.3) vs. 373 (6.9) p= 0.054**
	MMI vs. Scotland	**6 (54.6) vs. 320 (5.5) p<0.001**	2(13.3) vs.519 (16.3) p=0.308	5 (14.7) vs.656 (6.3) p=0.07	8 (12.5) vs. 837 (6.6) p=0.086	**13(12.3) vs. 1201 (6.9) p=0.05**
All Cause of death	MMI vs. Glasgow	11 vs. 257	15 vs.450	34 vs. 732	64 vs. 1286	106 vs.5369
	MMI vs. Scotland	11 vs. 5947	15vs.8244	34 vs. 10388	64 vs. 12643	106 vs.17391

Table 8-4   Cause of death in individuals with MMI compared to Glasgow and Scotland by SIMD Quintile
Bold if significant (p<0.05)

8.7.3 **Standardised Mortality Ratios (SMR):**

Scotland Standardised mortality ratios (Scotland SMR) and Glasgow Standardised mortality ratios (Glasgow SMR) were elevated in all age ranges for the combined schizophrenia/bipolar (MMI) group (Table 8-5), with an overall Scotland SMR across all age ranges of 2.7 (95% CI 2.4-3.1) and Glasgow SMR of 1.8 (95% CI 1.6-2.0). When suicide was excluded as a cause of death, the overall Scotland SMR remained elevated at 2.3 (95% CI 2.0-2.7) and the Glasgow SMR was 1.5 (95% CI 1.3-1.8). In the younger age groups (<25, 25-34 and 35-44), Scotland SMR and Glasgow SMR were markedly elevated for individuals with MMI (Table 8-5).

Deaths due to cardiovascular disease were higher in individuals with MMI over the age of 25 and were particularly elevated in the 25-34 age group (Scotland SMR 9.6 (95% CI 0.2-53.2), Glasgow SMR 16.7 (95% CI 0.4-93.1)) although confidence intervals were wide. Similarly, cancer deaths for MMI were significantly elevated in the 25-34 age group (Scotland SMR 4.8 (95% CI 0.6-17.4), Glasgow SMR 9.7 (95% CI 1.2-35.2)) but were lower in the 45-54 and 55-64 age groups (Scotland SMR 0.5 (95% CI 0.2-0.9), Glasgow SMR 0.8 (95% CI 0.3-1.5) and Scotland SMR 0.5 (95% CI 0.3-0.8), Glasgow SMR 0.8 (95% CI 0.5-1.2) respectively) (Table 8-5).

SMR (95% CI)	<25	25-34	35-44	45-54	55-64	All ages
All cause Male & Female						
Scotland SMR	38.3 (7.9-111.8)	8.3 (4.9-13.0)	4.1 (2.9-5.6)	2.7 (2.1-3.4)	2.1 (1.7-2.6)	2.7 (2.4-3.1)
Glasgow SMR	40.8 (8.4-119.4)	7.5 (4.4-11.9)	2.6 (1.8-3.5)	1.8 (1.4-2.3)	1.4 (1.1-1.7)	1.8 (1.6-2.0)
	(n=3)	(n=18)	(n=38)	(n=72)	(n=99)	(n=230)
All cause Male						
Scotland SMR	30.5 (0.4-11.0)	6.9 (3.8-11.3)	3.5 (2.3-5.0)	2.4 (1.8-3.2)	2.1 (1.6-2.7)	2.6 (2.2-3.0)
Glasgow SMR	47.7 (5.8-172.2)	9.1 (5.1-15.0)	2.9 (2.0-4.2)	2.0 (1.5-2.6)	1.7 (1.3-2.1)	3.3 (2.8-3.9)
	(n=2)	(n=15)	(n=29)	(n=47)	(n=63)	(n=156)
All cause Female						
Scotland SMR	52.1 (1.3-290.2)	8.1 (1.7-23.7)	4.3 (1.9-8.1)	3.1 (2.0-4.6)	2.1 (1.5-2.9)	2.7 (2.1-3.4)
Glasgow SMR	31.7 (0.8-177.0)	4.0 (0.8-11.6)	1.8 (0.8-3.4)	1.6 (1.0-2.3)	1.1 (0.7-1.5)	2.4 (1.9-3.1)
	(n=1)	(n=3)	(n=9)	(n=25)	(n=36)	(n=74)
All cause excluding suicide						
Scotland SMR	0 (1-47.1)	6.0 (3.2-10.2)	3.0 (2.0-4.3)	2.4 (1.8-3.1)	2.0 (1.6-2.4)	2.3 (2.0-2.7)
Glasgow SMR	0 (0-50.2)	5.4 (2.9-9.3)	1.9 (1.2-2.7)	1.6 (1.2-2.0)	1.3 (1.0-1.6)	1.5 (1.3-1.8)
	(n=0)	(n=13)	(n=28)	(n=63)	(n=92)	(n=196)
Cardiovascular disease						
Scotland SMR	0 (0-6587.3)	9.6 (0.2-53.2)	1.8 (0.4-5.2)	1.1 (0.5-2.2)	1.4 (0.8-2.1)	1.4 (0.9-1.9)
Glasgow SMR	0 (0-11938.1)	16.7 (0.4-93.1)	2.5 (0.5-7.4)	1.6 (0.7-3.0)	1.8 (1.1-2.7)	1.8 (1.3-2.5)
	(n=0)	(n=1)	(n=3)	(n=9)	(n=21)	(n=34)
Cerebrovascular disease						
Scotland SMR	0 (0-6587)	0 (0-49.8)	1.6 (0.04-8.97)	1.7 (0.5-4.3)	0.7 (0.1-2.1)	1.1 (0.5-2.2)
Glasgow SMR	0 (0-2386.1)	0 (0-123.2)	2.7 (0.7-15.1)	2.2 (0.6-5.6)	1.0 (0.2-2.9)	1.5 (0.7-3.0)
	(n=0)	(n=0)	(n=1)	(n=4)	(n=3)	(n=8)
Cancer						
Scotland SMR	0 (0-399.2)	4.8 (0.6-17.4)	0.9 (0.2-2.5)	0.5 (0.2-0.9)	0.5 (0.3-0.8)	0.6 (0.4-0.8)
Glasgow SMR	0 (0-628.0)	9.7 (1.2-35.2)	1.6 (0.3-4.7)	0.8 (0.3-1.5)	0.8 (0.5-1.2)	0.9 (0.6-1.2)
	(n=0)	(n=2)	(n=3)	(n=8)	(n=20)	(n=33)

Table 8-5   SMRs for all individuals with MMI (Schizophrenia and Bipolar Disorder) by cause of death and age group

8.7.4 Comparison of Age and Primary Cause of death in Schizophrenia versus Bipolar Disorder:

6.3% of individuals with schizophrenia (163 from a sample of 2583) and 4.9% of individuals with bipolar disorder (67 from a sample of 1355) (p=0.086) died during the 5 year study period. Suicide occurred more frequently in individuals with bipolar disorder than in individuals with schizophrenia (22% vs. 11.7% p=0.04). All other causes of death occurred at similar rates (Table 8-6). There was no difference in death rate by socioeconomic quintile between individuals with schizophrenia and bipolar disorder.

	Schizophrenia (n=163)	Bipolar Disorder (n=67)	p value
Death Rate (n, %)			
All (males + females)	163/2583 (6.3%)	67/1655 (5%)	0.086[1]
Males	120/1854 (6.5%)	36/534 (7%)	
Female	43/729 (5.9%)	31/821 (4%)	
	p= 0.653[2]	p=0.015[2]	
Mean age of death, (standard deviation)			
Males	49.3 (0.79)	50.2 (1.57)	
Females	52.2 (1.45)	51.7 (1.79)	
	p=0.1077[2]	p= 0.1962[2]	
Cause of death (n, %)			
Cerebrovascular Disease	6 (3.7%)	2 (3%)	0.794[1]
Cardiovascular Disease	25 (15.3%)	9 (13%)	0.712[1]
Cancer	25 (15.3%)	8 (12%)	0.504[1]
Respiratory disease	19 (11.7%)	5 (8%)	0.345[1]
Alcohol Related	11 (6.7%)	4 (6%)	0.828[1]
Accidental	8 (4.9%)	3 (5%)	0.889[1]
Suicide	**19 (11.7%)**	**15 (22%)**	**0.037[1]**
Mental & behavioural disorder due to drugs	14 (8.6%)	4 (6%)	0.502[1]
Other	36 (22.1%)	17 (25%)	0.591[1]
Ethnicity White (n, %)	158 (96.9%)	66 (99%)	0.675[1]
Death Rate/Quintile (n, %)			
5 Most affluent	3/147 (2.0%)	8/178 (5%)	0.223[1]
4	10/271 (3.7%)	5/216 (2%)	0.383[1]
3	24/490 (4.9%)	10/290 (3%)	0.338[1]
2	45/619 (7.3%)	19/287 (7%)	0.723[1]
2- Most deprived	81/1056 (7.7%)	25/384 (7%)	0.456[1]

Table 8-6 **Demographics of deceased PsyCIS Cohort (Schizophrenia vs. Bipolar Disorder)**
Bold if significant (p<0.05) [1] (Chi squared Schizophrenia vs. Bipolar Disorder) [2] (Chi squared males vs. female)

In individuals with schizophrenia aged <25, 25-34 and 35-44, suicide was the leading cause of death (100%, 28.6% and 22.2% of deaths respectively) (Figure 8-4). In individuals with bipolar disorder aged <25 and 35-44, suicide was also the leading cause of death (100% and 36% of deaths respectively), although drug-misuse related deaths (75%) were the leading cause of death in the 25-34 age group (Figure 8-4).

Deaths due to cardiovascular disease accounted for 7.1% of deaths in individuals with schizophrenia aged 25-34 and remained an important cause of death as age increased: 7.4% of deaths in the 35-44 age group, 10.7% of deaths in the 45-54 age group and 25.0% of deaths in the 55-64 age group (Figure 8-4). Deaths due to respiratory disease occurred at a younger age in the schizophrenia cohort compared to the bipolar disorder cohort (11.1%, 12.5% and 14.1% in the 35-44, 45-54 and 55-64 age groups in the schizophrenia cohort respectively vs. none in the 35-44 and 54-54 age groups and 14% in the 55-64 age group in the bipolar disorder cohort) (Figure 8-4).

Suicide was an important cause of death throughout the life-span of individuals with bipolar disorder, accounting for 19% of deaths in the 45-54 age group and 17% of deaths in the 55-64 age group. Notably, rates of suicide were significantly higher in individuals with bipolar disorder aged 55-64 compared to individuals of the same age with schizophrenia (17% vs. 1.2% p=0.009) (Figure 8-4).
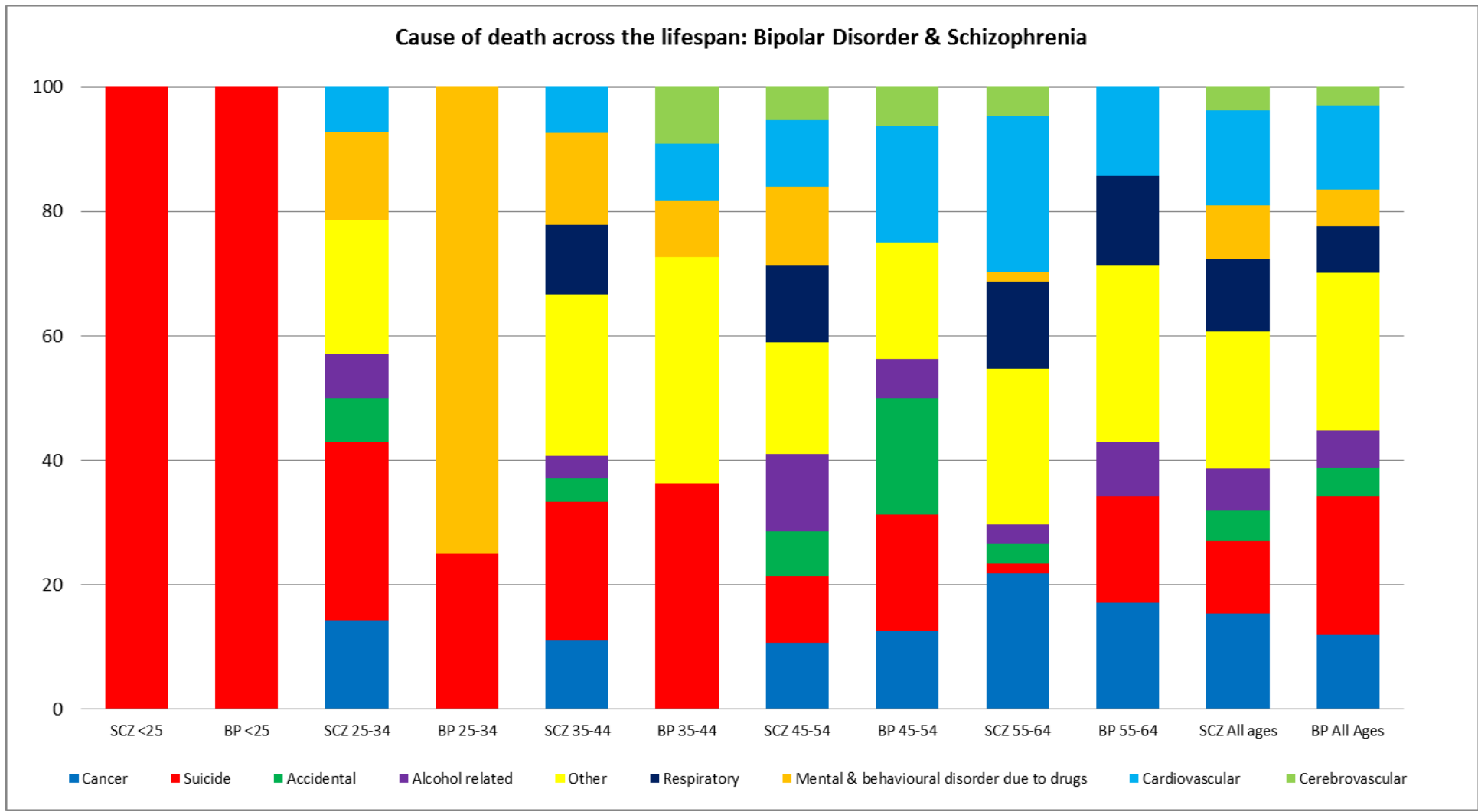
Figure 8-4   Cause of death in individuals with Schizophrenia and Bipolar Disorder by age group
(Where SCZ= schizophrenia and BP= bipolar disorder)

For all causes of death for men and women, the calculated Scotland and Glasgow SMR were elevated across all age groups for individuals with schizophrenia and bipolar disorder (Table 8-7). For individuals with schizophrenia the Scotland and Glasgow SMR were consistently higher than those calculated for the bipolar disorder group, although the absolute difference appeared to be small. For example for all cause of death for all ages Scotland SMR for individuals with schizophrenia was 3.0 (95% CI 2.5-3.4) versus 2.2 (95% CI 1.7-2.8) for all cause of death for all ages in individuals with bipolar disorder (Table 8-7 & Figure 8-5). When suicide was excluded as a cause of death, the Scotland and Glasgow SMR for both the schizophrenia and bipolar group were consistently elevated in individuals aged over 25.

	<25	25-34	35-44	45-54	55-64	All ages
Schizophrenia Group						
All cause (M+F)						
Scotland SMR (95% CI)	51.0 (6.2-184.3)	9.9 (5.4-16.7)	4.2 (2.7-6.1)	3.2 (2.4-4.2)	2.2 (1.8-2.9)	3.0 (2.5-3.4)
Glasgow SMR (95% CI)	54.5 (6.6-196.8)	9.0 (4.9-15.1)	2.6 (1.7-3.8)	2.1 (1.6-2.8)	1.5 (1.1-1.9)	2.0 (1.7-2.3)
	(n=2)	(n=14)	(n=27)	(n=56)	(n=64)	(n=163)
All Cause Excluding suicide (M+F)						
Scotland SMR (95% CI)	0 (0-39.6)	7.1 (3.4-13.0)	3.2 (2.0-5.0)	2.9 (2.1-3.8)	2.2 (1.7-2.8)	2.7 (2.3-3.1)
Glasgow SMR (95% CI)	0 (0-100.5)	6.4 (3.1-11.9)	2.0 (1.3-3.1)	1.9 (1.3-3.1)	1.4 (1.1.-1.8)	2.8 (1.5-2.1)
	(n=0)	(n=10)	(n=21)	(n=50)	(n=63)	(n=144)
All cause Male Scotland SMR (95% CI)	40.6 (4.9-146.8)	6.4 (3.2-11.5)	3.3 (2.1-5.0)	2.6 (1.8-3.5)	2.1 (1.5-2.7)	2.6 (2.2-3.1)
All cause Male Glasgow SMR (95% CI)	63.5 (7.7-229.5)	8.5 (4.2-15.2)	2.8 (1.7-4.2)	2.1 (1.5-2.9)	1.6 (1.2-2.2)	3.3 (2.7-3.9)
	(n=2)	(n=11)	(n=22)	(n=39)	(n=46)	(n-120)
All cause Female Scotland SMR (95% CI)	0 (0-1152.8)	23.6 (4.9-69.1)	4.9 (1.6-11.5)	4.2 (2.4-6.7)	2.2 (1.3-3.5)	3.2 (2.3-4.4)
All cause Female Glasgow SMR (95% CI)	0 (0-703.2)	11.6 (2.4-33.9)	2.1 (0.7-4.9)	2.1 (1.2-3.4)	1.1 (0.7-1.8)	3.0 (2.2-4.0)
	(n=0)	(n=3)	(n=5)	(n=17)	(n=18)	(n=43)
Bipolar Disorder Group						
All Cause (M+F)						
Scotland SMR (95% CI)	25.5 (0.6-142.1)	5.2 (1.4-13.3)	3.9 (1.9-6.9)	1.8 (1.0-2.9)	1.9 (1.4-2.7)	2.2 (1.7-2.8)
Glasgow SMR (95% CI)	27.2 (6.9-1517.3)	4.7 (1.3-12.1)	2.4 (1.3-4.3)	1.2 (0.7-2.0)	1.3 (0.9-1.8)	1.4 (1.1-1.8)
	(n=1)	(n=4)	(n=11)	(n=16)	(n=35)	(n=67)
All Cause Excluding suicide(M+F)						
Scotland SMR (95% CI)	0 (0-94.4)	3.9 (0.8-11.4)	2.5 (1.0-5.1)	1.5 (0.8-2.5)	1.6(1.1-2.3)	1.7 (1.3-2.2)
Glasgow SMR (95% CI)	0 (0-100.5)	3.5 (0.7-10.3)	1.5 (0.6-3.2)	1.0 (0.5-1.7)	1.0 (0.7-1.5)	1.1 (0.8-1.5)
	(n=0)	(n=3)	(n=7)	(n=13)	(n=29)	(n=52)
All cause Male Scotland SMR (95% CI)	0 (0-224.9)	8.6 (2.3-21.9)	4.3 (1.7-8.8)	1.8 (0.8-3.5)	2.2 (1.3-3.5)	2.5 (1.8-3.5)
All cause Male Glasgow SMR (95% CI)	0 (0-351.6)	8.5 (1.8-24.9)	2.1 (0.6-5.3)	1.3 (0.5-2.7)	1.5 (0.9-2.5)	2.8 (1.9-4.0)
	(n=0)	(n=4)	(n=7)	(n=8)	(n=17)	(n=36)
All cause Female Scotland SMR (95% CI)	62.5 (1.6-348.2)	0 (0-15.2)	3.6 (1.6-9.3)	2.0 (0.9-3.9)	2.0 (1.2-3.1)	2.2 (1.5-3.0)
All cause Female Glasgow SMR (95% CI)	38.1 (0-140.6)	0 (0-7.5)	1.2 (0.2-3.4)	0.8 (0.3-1.7)	0.8 (0.4-1.3)	1.4 (0.9-2.1)
	(n=1)	(n=0)	(n=4)	(n=8)	(n=18)	(n=31)

Table 8-7   Standardised Mortality Ratios (SMR) for individuals with Schizophrenia and Bipolar Disorder
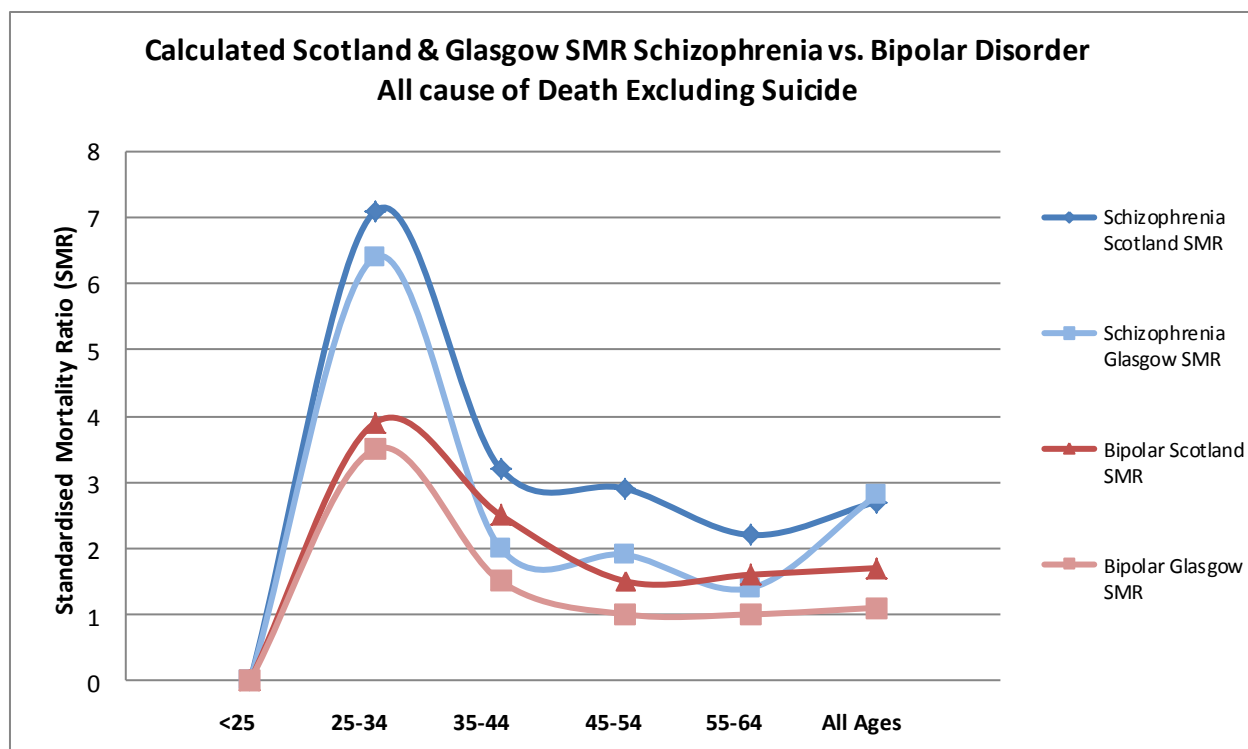
Figure 8-5 **Calculated All cause of death excluding suicide Scotland & Glasgow SMR for Schizophrenia vs. bipolar disorder**

8.8 Discussion:

This cohort of individuals with MMI had higher mortality rates compared to both the local Glasgow and wider Scottish populations, consistent with several other studies which have used similar secondary care mental health registers (Baxter, 1996). SMR in individuals with MMI were elevated in all age categories across both sexes and were profoundly elevated in younger age groups. The proportion of deaths by age group was similar to that seen in the local Glasgow population, but differed from that of the wider Scottish population, with a larger proportion of deaths occurring in individuals aged 25-44 years with MMI. As occurs in the general population, increasing socioeconomic deprivation appeared to be associated with an increased overall rate of death in MMI.

8.8.1 Differences in the rate, age and cause of death:

Although individuals with MMI died at a younger age than individuals in the Scottish population, the age at death was similar to the local Glasgow population. This is potentially in keeping with the "Glasgow Effect" whereby average age at death in Glasgow is lower than the Scottish average. However despite this, differences in cause and rate of death between the MMI and Glasgow groups were apparent.

In particular, deaths due to cancer were lower in the MMI group compared to the Glasgow group. To date, the literature surrounding cancer deaths in individuals with MMI has been mixed, with some studies reporting elevated rates (Kisely et al., 2015; Tran et al., 2009), while others report lower rates of cancer deaths (Oksbjerg et al., 2003). A recent meta-analysis of incidence of cancer (Catt et al., 2008), reported that pooled overall rates of cancer incidence were not significantly increased in individuals with schizophrenia compared to controls (Standardised Incidence Rate (SIR) 1.05, 95% CI 0.95-1.15) and although incidence of lung cancer was increased, when adjusted for smoking there was no difference in incidence rates. This study also reported that the incidence of several cancers unrelated to smoking was reduced in individuals with schizophrenia (Catt et al., 2008). Given the current inconsistent evidence in this area, there is a need for further longitudinal research.

The finding of a lower proportion of alcohol related deaths in MMI, compared to the local Glasgow and wider Scottish populations was also surprising, especially given the high rates of comorbid alcohol and illicit substance misuse reported in individuals with MMI (Rosenberg et al., 1998). This may in part be explained by the elevated population levels of alcohol related deaths in Scotland compared to other countries: for example in 2011 the Scottish male alcohol mortality rate was 28.4/100,000 compared to the UK average of 17.2/100,000 while in women the Scottish alcohol mortality rate was 13.9/100,000 compared to the UK average of 8.3/100,000. (Alcohol Related Mortality, Institute of Alcohol Studies, 2013). The finding of a trend towards significantly higher proportions of drug related and "other" causes of death (which included a wide range of causes) within the MMI cohort may also partly explain this finding. Given that only the primary cause of death was obtained from the GRO, rates of alcohol as a secondary cause of death within this cohort are unknown. This may also explain our finding of lower rates of primary cause of death being due to alcohol in this cohort.

Increased suicide rates in the under 25s explained the large increase in SMR in this age group but did not account for the excess mortality in the other age groups to the same extent (when suicide was excluded as a cause of death, SMR remained significantly elevated in the 25-34, 35-44, 45-54 and 55-64 age groups). The proportion of cardiovascular disease deaths in MMI was only marginally higher compared to Glasgow and Scotland, with a trend towards an increase in deaths from cardiovascular disease in younger age groups (25-34 and 35-44). This is in keeping with other studies which have found similar rates of cardiovascular deaths in individuals with MMI compared to their

local population (Colton and Manderscheid, 2006). However given the small sample size in this study the ability to draw definitive conclusions is limited.

8.8.2 Overall mortality rates across the life-span:

In this cohort, the magnitude of the raised SMR (both the Scotland and Glasgow SMR) appeared to reduce as age increased in both the schizophrenia and bipolar disorder cohorts. This apparent diminution of mortality with age has been described in other cohorts (Chang et al., 2010). Chang and colleagues, (2010) reported a SMR of 4.47 95 % CI 3.49-5.64 in individuals aged 15-44 compared to a SMR of 3.1 95% CI 2.61-3.66 in individuals aged 45-64, although this was for any MMI and for all-cause mortality. The finding of a trend towards a greater elevation in mortality rates from cardiovascular disease and cancer in the 25-34 and 35-44 age groups in this cohort is also of particular interest given that many physical health screening programmes are focused on older patient groups.

The apparent reduction in magnitude of premature mortality associated with MMI across the lifespan is likely to be multifactorial. It may be due in part to differences in the nature of the underlying mental illness in people presenting at different ages or may be due to differences in levels of engagement and treatment compliance with both mental and physical health services.

8.8.3 The role of deprivation:

In this cohort, as with the local Glasgow and wider Scottish populations, rate of death in individuals with MMI increased as deprivation increased. The magnitude of the elevation in mortality associated with deprivation was similar; however, when suicide was excluded as a cause of death, the magnitude of increase in mortality associated with deprivation was greatest for the MMI cohort. This association between deprivation and mortality in individuals with MMI appear similar to that reported in the general population.

Of important clinical note, was the finding of a significantly higher proportion of suicide in MMI in both the least and most deprived quintiles. While a negative correlation between suicide and socioeconomic status has been found in Australia (Taylor et al., 1998) and the US (Kposowa, 1999), a more complex relationship has been identified by others in the UK (Hawton et al., 2001; Osborn et al., 2008). In particular, Osborn and colleagues, (2008) reported that although suicide rates were increased across all age groups of individuals

with MMI, individuals who were least socially deprived were particularly at risk (Osborn et al., 2008).

Despite the negative impact of deprivation on health outcomes: for example, individuals living in the most deprived areas are more likely to have unplanned admissions to hospital than individuals living in the most affluent areas (Payne et al., 2013) as well as the premature onset of multimorbidity (Barnett et al., 2012), studies investigating the relationship between socioeconomic status and mortality in individuals with MMI are limited. While there are studies looking at the impact of socioeconomic status on parasuicide (Gunnell et al., 1995), suicide (Osborn et al., 2008; Congdon 2013) and cause of death in major depressive disorder (Surtees et al., 2008; Scafato 2012), generalised anxiety disorder (Phillips et al., 2009) and alcohol misuse (Singh and Hoyert, 2000), only one study specifically focused on the impact of socioeconomic status on mortality in bipolar disorder (Schneider et al., 2001) and no studies have specifically focused on the impact of socioeconomic status on mortality in schizophrenia. The study which explored the impact of socioeconomic factors on cause and rate of death in bipolar disorder was limited due its small sample size of only 30 deaths (Schneider et al., 2001).

8.8.4 The "Scottish" and the "Glasgow" Effects:

Life expectancy and health behaviours have improved in Glasgow over the past 50 years; but the rates of improvement have differed depending on the individuals' socioeconomic status. As Scotland's ranking in terms of European mortality rates have worsened over time, so too has the gap in life expectancy between the most affluent and most deprived areas within Scotland (SPHSU, 2007). This inequality associated with socioeconomic status has been mirrored by an inequality in life expectancy associated with MMI: whereby the gap in life expectancy between individuals with MMI and individuals without MMI appears to be increasing (Saha et al., 2007; Hoye et al., 2011; Walker et al., 2015).

As detailed above, although the impact of deprivation on health and mortality is marked, the differences in life expectancy in Scotland compared to the rest of Europe, and in Glasgow compared to the rest of Scotland, cannot be fully explained by deprivation alone. The "Scottish" and "Glasgow Effects" were reflected in this study, where the gap in mortality rate for individuals living in the most deprived cohort with MMI was highest. This "Glasgow Effect" appeared in our study, where mortality rates for those with MMI were even higher than both the Scottish and Glasgow averages. The differences in

mortality between individuals with MMI and individuals without MMI also appeared largest for those living in the most deprived quintiles.

This study of all-cause mortality in individuals with MMI in Glasgow has identified a trend towards increasing mortality associated with worsening deprivation; however more work is required to investigate this relationship further. It remains unclear the extent to which each factor (deprivation and MMI) contribute to the increased mortality observed and whether these effects are cumulative as deprivation worsens.

8.8.5 Inverse Care Law:

Inequalities in health outcomes based on social status have long been recognised. As early as 1842 Edwin Chadwick reported this relationship in Aberdeen. With the advent of a free at the point of access healthcare system in 1948, it was thought that these inequalities would improve. However in 1968 Titmuss reported that "from 15 years' experience of the Health Service (we have learned) that the higher income groups know how to make better use of the service; they tend to receive more specialist attention; occupy more of the beds in better equipped and staffed hospitals; receive more elective surgery; have better maternal care, and are more likely to get psychiatric help and psychotherapy than low-income groups- particularly the unskilled" (Titmuss, 1968). This inequality in access to healthcare was further described by Julian Tudor Hart in 1971 who described the Inverse Care Law whereby "the availability of good medical care tends to vary inversely with the need for the population served" (Tudor Hart, 1971).

It is widely recognised that individuals living in deprived areas have higher rates of long term illness and disability compared to individuals in more affluent areas (The Kerr Report 2005). Multimorbidity is more common and occurs 10-15 years earlier in the most deprived areas compared to the most affluent areas (Barnett et al., 2012: Salisbury et al., 2011). The level of deprivation influences not only the amount of multimorbidty but also the type of multimorbidity which influences the complexity of care (Mercer et al., 2012). Despite the steep gradients in health needs by socioeconomic status that occur in Scotland (Barnett et al., 2012), number of General Practioners (GPs) remains stable across socioeconomic status (MacKay et al., 2005). This can lead to longer time in accessing primary care with subsequent lower satisfaction with access to care in the most deprived areas compared to the more affluent ones (Mercer and Watt, 2007). While it is also recognised that patients in the most deprived areas often have more problems to discuss

(especially psychosocial problems) clinical encounter length is often shorter (Mercer and Watt, 2007).

This high burden of morbidity in deprived areas leads to high demands on primary care. This can paradoxically result in poorer access to care, shorter consultation time, lower patient enablement (specifically for encounters for psychosocial problems) and higher GP stress (Mercer and Watt, 2007). This can then lead to negative impacts on patient outcomes. For example in a recent study of individuals with depression, for those living in deprived areas, depression was more common and early outcomes were poorer compared with affluent areas (Jani et al., 2012). While patient-centered consulting appears to improve early outcomes, it is recognised that this is difficult to achieve in deprived areas because of the inverse care law and the burden of multimorbidity (Jani et al., 2012). This therefore suggests that even in today's National Health Service (NHS) the Inverse Care Law still exists and impacts on patients.

The Inverse Care Law is reported throughout Europe (Pederson and Vedsted 2014) and New Zealand (Sandiford et al., 2015) and is therefore not only a phenomenon associated with the NHS. For individuals with MMI who tend to experience downward social drift (Aro et al., 1995) the Inverse Care Law may be especially pertinent. With current plans in NHS England to distribute healthcare resources based on age, there is the potential for a worsening in the manifestations of the Inverse Care Law: where such a change would in essence take money away from practices in deprived areas, where fewer people survive into old age (Hawkes, 2012).

8.8.6 Differences between the schizophrenia and bipolar cohorts:

No significant difference in rate of death for individuals with schizophrenia and bipolar disorder was found in this cohort. This highlights the similarities in the level of increased mortality experienced by individuals with schizophrenia and bipolar disorder and challenges the idea that bipolar disorder has a better prognosis than schizophrenia. Although the pattern of rate of death and age at death was more similar in the bipolar disorder and schizophrenia cohorts compared to that of the broader Scottish population, a number of notable differences were identified. Suicide was more common in the bipolar disorder cohort compared to the schizophrenia cohort, there were more drug related deaths in the schizophrenia cohort (except the 25-34 age group) and there were more deaths due to respiratory disease at a younger age in the schizophrenia cohort. The higher mortality

due to respiratory disease in individuals schizophrenia is in keeping with the higher smoking rates reported in individuals with schizophrenia compared to individuals with bipolar disorder (Dikerson et al., 2013) and the higher suicide rate in individuals with bipolar disorder has also been reported elsewhere (Ilgen et al., 2010; Nordentoft et al., 2013). The higher drug related deaths observed in the schizophrenia cohort is of note given the general consensus that substance misuse is more prevalent amongst individuals with bipolar disorder than schizophrenia (Regier et al., 1990) and this warrants further investigation.

8.9 Strengths and Limitations:

In this study the primary cause of death throughout the life-span of individuals with MMI was described and compared to both the local Glasgow and wider Scottish population in detail, allowing patterns of cause of mortality to be reported by age. Standardised mortality rates with suicide excluded as a cause of death were calculated and described by ICD 10 diagnosis, gender and age group. This approach is novel and helps improve the understanding of premature mortality patterns throughout the adult life-span and may help aid the development of age specific strategies to improve the life expectancy of individuals with MMI. The local nature of this study is also valuable for clinicians working within NHS Greater Glasgow and Clyde, as much of the mortality research to date has been carried out in Sweden, Denmark, Western Australia and Canada, although some research undertaken in London has been published.

The finding of a gradient in level of deprivation and magnitude of increase in mortality in MMI is also novel. To my knowledge, this is the first study to investigate the impact of deprivation on rate and cause of death in schizophrenia and bipolar disorder and as such may help inform the development of population-based strategies to improve the life expectancy of individuals with MMI. Additional strengths of this study include the large, comprehensive and prospective nature of the PsyCIS database, which is representative of a large clinical population accessing mental health services in a defined urban area. Regular checks of data accuracy are carried out by the senior medical practitioners involved in case management, thereby maintaining the reliability of diagnoses along with clinical and sociodemographic data.

Limitations of this work include the relatively small number of deaths which occurred during our limited study timeframe. Further limitations include the exclusion of a small

number of individuals with psychosis who are managed exclusively in primary care. As PsyCIS is a database set within secondary care, inclusion of all individuals with psychosis in the geographical area would require linkage of the database to primary care records, which is not currently possible. Although some individuals with psychosis live independently in the community without input from secondary services, further study is required to ascertain the numbers of such individuals living in Glasgow. PsyCIS also excludes individuals who are under 16, over 65 years old and who are not managed by general adult community services, such as individuals whose psychotic illness is managed exclusively in addictions psychiatry, old age psychiatry or learning disability services. These numbers are likely to be relatively small because the majority of individuals of working age with a psychotic disorder are managed by general adult psychiatric services. SIMD is a relative measure of deprivation and given the impact of socioeconomic drift in the PsyCIS cohort, wider Glasgow and Scottish population during our five year timeframe, its use has a number of limitations. A further limitation was that of the impact of age on death rates - although adjustment for age profile of the populations were made, full standardisation was not possible due to small sample sizes.

Although the PsyCIS cohort contains information for individuals aged 18-25, the GRO mortality data used to calculate Scotland SMR for under 25s included individuals aged 15, 16 and 17. This may have resulted in an artificial reduction in the Scotland SMR calculated for the under 25s and represents a limitation in the study. However, given the small numbers of deaths in the wider Scottish population under the age of 25, and in particular between the ages of 15, 16 and 17, inclusion of this data was felt to be important.

Standardised Mortality Ratios (SMR) are used to indirectly standardise for confounding effects of age and gender, and are often compared across different age groups and by gender. However changes in SMR may reflect changes in the mortality rate within the general population rather than the population being studied. In this study calculating SMR using data from both a local and national level, occurred with the aim of limiting this effect.

Although SIMD is recognised as a reliable method for describing deprivation, it is worth noting that the health domain contains information regarding mortality, morbidity and rates of psychotropic medication prescribing. As mortality was an outcome of this study, and individuals with a diagnosis of bipolar disorder or schizophrenia will likely be prescribed psychotropic medication, perhaps a single domain within SIMD (such as income) could

have been used to measure deprivation. A sensitivity analysis could have been carried out to determine if this had an effect on results. While this does represent a limitation of the study, it is also worth noting that within the SIMD model, the health domain is one of 6 other domains and carries a weight of only 14%.

8.10 Conclusion:

In this cohort of individuals with MMI the rate and cause of death differed from that of the local Glasgow and wider Scottish populations. Within individuals with MMI, cause of death varied across the life span and by ICD 10 diagnosis. Standardised mortality rates were increased for men and women with MMI in all age groups. In the under 25s, suicide accounted for the majority of the increase in SMR but in the 25-34 and 35-45 age groups, deaths from cardiovascular disease, cerebrovascular disease and cancer were all increased. There also appeared to be a gradient effect of deprivation on mortality, which was largest for individuals with MMI when suicide was excluded as a cause of death. This pattern of rising mortality across deprivation categories may represent evidence of inequalities in health outcomes for the most deprived individuals with MMI and more work is required to investigate this relationship further. These findings may help inform age and deprivation specific interventions for health care organisation, health promotion and screening for individuals with MMI in Glasgow and in Scotland.

Chapter 9 Conclusion:

Chapter Overview:

This concluding chapter will discuss the main findings of each of the studies carried out in Chapters 4 through 8. It will discuss how the findings are related to the main themes of this thesis and it will discuss the extent to which the original aims have been met. The limitations of the work carried out will also be discussed and the implications of the findings at both a research and clinical level will be highlighted. Potential directions for future research will also be outlined.

9.1 Summary of Main Findings and Clinical Implications:

The findings in Chapter 4, which detail the patterns of increased physical health comorbidities in individuals with schizophrenia and bipolar disorder, complements existing literature in this area. Using the SPICE data of the thirty two most common physical health conditions investigated, sixteen occurred significantly more frequently in individuals with schizophrenia and fourteen occurred more frequently in individuals with bipolar disorder. In particular viral hepatitis, constipation, Parkinson's disease, diabetes, bronchitis and chronic pain occurred most frequently. Due to the large nature of the dataset used in this study, adjustment for age, sex and socioeconomic status was possible and so these findings help to enrich the limited data which is available in this field and adds to the understanding of the type and pattern of physical health comorbidity reported in individuals with schizophrenia and bipolar disorder. This also has important clinical implications in that clinicians need to more readily consider potential co-existing physical illness in this group of patients. Clinicians should also be vigilant for physical symptoms which may be due to undiagnosed physical illness and always be aware of the potential for diagnostic over-shadowing.

The finding of significantly increased rates of multimorbidity in individuals with schizophrenia and bipolar disorder that is also detailed in this chapter is novel, and is of scientific and clinical importance given the paucity of literature in this field.

Evidence for inequalities in access to healthcare, which may partly contribute to the gap in life expectancy experienced by individuals with MMI, were found within the studies included in this thesis. Chapter 4 provided evidence of under-reporting of cardiovascular-related conditions in individuals with schizophrenia and bipolar disorder in primary care in

Scotland and also provided evidence for less intensive prescribing patterns for individuals with schizophrenia and bipolar disorder who had comorbid hypertension and coronary heart disease (CHD) compared to individuals with hypertension and CHD who did not have schizophrenia or bipolar disorder. This too has important clinical implications in that an opportunity to deliver the best evidence-based practice is being lost.

Further evidence for inequalities in access to care, was explored in Chapter 5, where there was evidence that despite higher smoking rates, the rate of recording of smoking cessation advice in MMI was significantly lower compared to that in diabetes, hypertension and CHD. Evidence for inequalities in prescribing, similar to those reported in Chapter 5, was then further reinforced by the finding of a significantly lower odds ratio of NRT prescription in individuals with MMI without diabetes compared to individuals with diabetes without MMI. Similarly when rates of NRT prescription in individuals with MMI without CHD and MMI without hypertension were compared to individuals with CHD without MMI and individuals with hypertension without MMI, rates of NRT prescription were significantly lower in the MMI cohort. The presence of a physical comorbidity improved rates of recording of smoking cessation advice and NRT prescription in individuals with MMI. This appears to reinforce evidence of inequalities in prescribing between patient groups.

Additional evidence of inequalities in access to healthcare was explored at a National Level, through analysis of incentivised QOF data and is detailed in Chapters 6 and 7. In particular across the UK, payment and population achievement rates for the recording of BMI and BP in MMI were significantly reduced compared to payment and population achievement rates for the recording of BMI and BP in diabetes and chronic kidney disease. In Scotland there was also evidence of higher exception rates for most of the individual and composite mental health indicators compared to their proxy individual comparator and composite physical health indicators. The inequalities reported in Scotland appear to have persisted over the past nine years since the inception of the QOF and despite evidence of some improvement in certain indicators (for example comprehensive care plan recording), there remain significant and clinically important gaps in indicators associated with preventative interventions in particular the recording of BMI and BP. While inequalities in screening have been reported for individuals with MMI, the findings of inequality in access to incentivised healthcare, on a UK wide basis using QOF data is novel. These findings therefore enhance the current available literature and understanding of potential reasons and sources of health inequalities.

Finally, in keeping with the literature described in Chapter 1, an increase in Standardised Mortality Ratios (SMR) for individuals with MMI was found in Chapter 8 using data from the PsyCIS cohort. Similarly these data also showed that SMR in individuals with MMI were elevated in all age categories across both sexes and were more profoundly elevated in younger age groups. The finding that increasing socioeconomic deprivation appeared to be associated with an increased overall rate of death in MMI is novel and to date has not been explicitly explored in other linkage studies. The differences in primary cause of death by deprivation quintile for individuals with MMI compared to the local Glasgow and wider Scottish populations detailed in Chapter 8, is again novel. While some patterns in cause of mortality were perhaps predicted; for example higher drug-related deaths in individuals with MMI living in the most deprived quintile compared to the local Glasgow and wider Scottish population rates, some were more surprising: for example a lower proportion of deaths due to cancer in individuals with MMI living in the most deprived quintile and a higher proportion of suicides in individuals with MMI living in the most affluent quintile relative to the local Glasgow and wider Scottish populations. These findings add to the limited studies investigating mortality in MMI in a Scottish setting and are of local clinical and wider scientific importance.

This study also reported no significant difference in rate of death for individuals with schizophrenia and bipolar disorder and challenges the preconception that bipolar disorder has a better prognosis than schizophrenia. Although suicide occurred more frequently in individuals with bipolar disorder than in individuals with schizophrenia, all other causes of death occurred at similar rates. These findings add to the limited research currently available comparing causes of death in individuals with schizophrenia and bipolar disorder.

9.2 Revisit of Aims & Research Questions:

Throughout the body of this thesis, I have attempted to address its aims as fully as possible. The narrative review of the literature set the thesis in context and allowed gaps in current knowledge and research, to became apparent. This allowed the generation of the research questions around which the remaining thesis aims were addressed.

The second aim of this thesis was to gain a more detailed understanding of the patterns of multiple physical health comorbidities in individuals with schizophrenia and bipolar disorder. Optimisation of the SPICE database have, been helpful in contributing to a greater understanding of patterns of physical health comorbidities in individuals with

schizophrenia and bipolar disorder. An introductory exploration into rates of multimorbidity in individuals with MMI has also been undertaken-although this is an area which warrants much further in-depth study.

The third aim of this thesis was to better understand possible explanations for the health inequalities that are reported in individuals with schizophrenia and bipolar disorder. By examining prescribing data from primary care and national incentivised QOF data an attempt to explore possible reasons for the inequalities reported has been undertaken. Inequalities in prescribing for individuals with MMI across a range of clinical settings, within Scottish primary care were found. Evidence of inequalities in payment, population achievement and exception rates for a wide range of incentivised aspects of health care in Scotland and indeed across the whole of the UK across a number of years were also found. Therefore through analysis of these data the third aim of this thesis has been addressed.

The final aim of this thesis was to gain a more detailed understanding of the causes of premature mortality in individuals with schizophrenia and bipolar disorder. Using the PsyCIS database this has been explored in detail and a novel finding of the impact of socioeconomic status on rate and primary cause of death has also been detailed.

9.3 Limitations:

As this thesis compromised largely of retrospective, cross-sectional, epidemiological secondary data, there are a number of limitations which require to be acknowledged. In addition to the limitations detailed at the end of each Chapter, there are a number of general limitations to this work; firstly in the datasets used and secondly in the design of the studies included in this thesis.

The SPICE dataset used in Chapters 4 and 5, is a primary care dataset, which contains information from approximately one third of the Scottish Population. While all general practices in Scotland were invited to participate 314 practices opted in. Differences between participating and not participating general practices (non response bias) need to be considered and potentially could affect generalisability. The data is anonymised and arises from the primary care clinical record and so the quality of the data retrieved is reliant on the quality of the data entry and completeness of the contributing General Practices- this is likely to vary across the whole of Scotland and may therefore affect results. The data used

in the studies were extracted in March 2007 and so are now almost eight years old and represents a further limitation of this work.

The QOF data analysed in Chapters 6 and 7, are collected nationally as a payment rather than quality monitoring system and thus quality and accuracy of data is reliant on type of clinical computing system used and also on local practice factors. These may vary across geographical location. Data was also available only at a practice level and so consideration at patient level was not possible.

The PsyCIS dataset used in Chapter 8, was originally designed as a clinical governance and audit tool, and although has undergone significant diagnostic validation, there is nevertheless the possibility for inaccuracies in data recording; either by the clinicians locally or when local returns are centrally uploaded. Clinical diagnosis, albeit by an experienced Consultant Psychiatrist, rather than by a structured interview was used for diagnostic stratification and so represents a limitation of the data. Limitations within the construct of the PsyCIS database (i.e. exclusion of under 16s and over 65s) are also acknowledged. The factors outlined above are all limitations of the datasets utilised in this thesis.

In terms of study design, all studies included were cross-sectional in nature, and so no directionality or temporality can be attributed to the association between factors investigated, nor can any association confirm a causal relationship. Although this is a limitation for all the studies detailed in Chapters 4 through 8 given the datasets that were available and the gaps in current knowledge, each study design was felt to be the most pragmatic one possible. The findings highlighted in this thesis however I feel can be used to form the basis for further prospective and longitudinal studies.

9.4 Implications of Findings:

The findings of the studies included in this thesis have shown that while mortality rates, causes of death and patterns of physical health comorbidity are different in individuals with MMI compared to the general population, there is evidence of inequalities in: access to healthcare advice, prescribing patterns and recording of basic health indices in individuals with MMI. This has important implications at both a clinical and research level.

Adequate healthcare resources at both a primary and secondary care level need to be targeted in response to the increased burden of physical health comorbidity identified by the studies included in this thesis. In particular primary care, has an important role in translating policy into evidence based practice (Planner et al., 2014). In a healthcare system which has become increasingly specialised and at times fragmented, greater attention is needed to ensure that the healthcare that is being delivered by all clinicians is as holistic and efficient as possible. System design which often leads to separation between physical and mental healthcare also needs to be addressed. Druss and Newcomer (2007) described four types of separation: geographic (whereby there is a lack of co-located physical and mental health services), financial (whereby there are separate finding streams for physical and mental health service), organisational (whereby there is difficulty sharing information and expertise across these systems) and lastly cultural (whereby providers focus on symptoms or single disorders, rather than the whole patient) (Druss and Newcomer, 2007). Strategies therefore to ensure that healthcare systems have enough flexibility to respond to the challenges of multimorbidity, stigma and variability in help seeking behaviour also require to be developed.

For psychiatric inpatients pathways to improve access to non-urgent secondary care need to be developed (Moore et al., 2015). Integrated healthcare teams and records would potentially make this easier, as there is evidence that within secondary care, merging medical and psychiatric electronic records, can lead to lower readmission rates and shorter lengths of stay (Kozubal et al., 2013). For outpatients, integrating care may in some ways be more challenging. The debate over who should be responsible for the monitoring of physical health in individuals with MMI should be resolved. Mental health providers although may be the primary point of healthcare contact for individuals with MMI, may not be familiar with the current monitoring of physical health issues. This can inadvertently lead to sub-standard care. GPs, may have difficulty engaging individuals with MMI and the short appointment times make it challenging to address the physical healthcare needs of patients with MMI who may lack motivation and concentration and be thought disordered (Moore et al., 2015). Therefore strategies to address this need to be developed.

For clinicians in both primary and secondary care, an increased awareness of the impact of age and socioeconomic status on cause of death for individuals with MMI is important to help target resources and ensure that both the physical and mental health needs of all individuals are being met. At a wider level, public health strategies, in combination with healthcare policies need to take into account these unique healthcare needs in order to

ensure that there is no further worsening of the health inequalities and widening of the gap in life expectancy experienced by individuals with MMI compared to individuals without MMI.

The findings of inequality in access to care, at a healthcare advice, prescribing and health indices recording level are also important for clinicians to be aware of. Raising awareness of the potential bias that may occur in the delivery of patient care may be helpful in changing practice to reduce bias and improve equality in health care.

For researchers, the relationship between deprivation, mortality rate and cause of death requires further exploration using other cross sectional data. More in-depth study to investigate the mechanisms underpinning the findings of increased morbidity and mortality in individuals with MMI is required to allow the development of interventions aimed at reducing the gap in mortality. A better understanding of the possible reasons for inequalities in healthcare delivery is also required in order to inform potential strategies aimed at reducing this inequality.

9.5 Future Work:

Given the identification of elevated rates of physical health comorbidity and elevated rates of multimorbidity, further prospective longitudinal studies to investigate the temporal relationship between physical and mental health comorbidity would be helpful to determine if the comorbid medical conditions assessed predated or precipitated the diagnosis of schizophrenia or bipolar disorder (and conversely whether schizophrenia or bipolar disorder was an antecedent for some of the medical conditions).

Mechanistic studies to determine possible genetic and/or epigenetic factors associated with comorbid mental and physical illnesses could also be undertaken to help better understand possible common pathways in the development of these conditions. Further studies investigating the role of inflammation in the development of comorbidity and multimorbidty may also be helpful.

Finally, consideration to the modification of healthcare services from the current single, disease orientated, hierarchical nature of care, to a more integrated collaborative approach should occur. As the current single, disease orientated system can lead to fragmented care, greater integration of psychiatric services with primary care and with specialist medical

services may be helpful in achieving better, more holistic and more effective healthcare. Strategies such as Community Engagement (CE) which have been shown to be effective in engaging hard to reach individuals (Lamb et al., 2014) should be evaluated in the context of MMI. Collaborative care, which aims to develop closer working relationships between primary and secondary care (Reilly et al., 2013) is an important strategy which may improve the quality of care for individuals with MMI. While collaborative care models have been used in the management of depression (Coventry et al., 2015), only one study looking at collaborative care in MMI has been undertaken (Bauer et al., 2006). Therefore more work is required to develop, design and evaluate an integrated model of care for individuals with MMI and physical health comorbidity.

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Appendices

Appendix 1 Narrative review search methodology:

For the literature search for evidence of increased physical health comorbidity in Major Mental Illness (MMI) the same terms to search for MMI were: Major Mental Illness (MMI), Severe Mental Illness (SMI), schizophrenia, bipolar disorder and bipolar affective disorder. Physical health comorbidity was searched using the terms: physical health, comorbidity, multimorbidity and morbidity. Titles and abstracts of identified papers were reviewed and suitability was based on definition of MMI, definition of comorbidity and cohort size. Given the overlap in the literature pertaining to schizophrenia and bipolar disorder, searches using both terms were performed, although papers relevant to either condition were considered and reported separately.

For Evidence for inequalities in health outcomes experienced by individuals with Major Mental Illness (MMI) the same terms to search for MMI were used. To search for inequalities in healthcare, the terms: inequality, inequities, disparity, healthcare, health promotion, screening, prescribing, outcomes were used. Titles and abstracts of identified papers were reviewed and their suitability was assessed.

For the search regarding evidence of premature mortality in Major Mental Illness (MMI) search terms included were: premature mortality, mortality, deaths, Major Mental Illness (MMI), Severe Mental Illness (SMI), Serious Mental Illness, schizophrenia, bipolar disorder and bipolar affective disorder. Titles and abstracts of identified papers were reviewed. Given the overlap in the literature pertaining to schizophrenia and bipolar disorder, searches using both terms were performed, although papers relevant to either condition were considered and reported separately. Study suitability was based on definition of MMI, measure of premature mortality, length of follow up and cohort size This allowed a systematic narrative review of the literature surrounding premature mortality in MMI to be undertaken.

The initial search was performed in June 2014 and was updated in July 2015.

Appendix 2: List of the thirty two most common physical health conditions and there definitions assessed in Chapters 4 and 5

Condition	Definition
Atrial Fibrillation (AF)	Read code ever recorded
Hypertension	Read Code ever Recorded
Coronary Heart Disease (CHD)	Read code ever recorded
Cancer	Read code first recorded in last 5 years
Peripheral Vascular Disease (PVD)	Read code ever recorded
Rheumatoid Arthritis (RA)	Read code ever recorded
Prostate Disease	Read code ever recorded
Glaucoma	Read code ever recorded
Multiple Sclerosis (MS)	Read code ever recorded
Chronic Kidney Disease (CKD)	Read code ever recorded
Diverticular Disease	Read code ever recorded
Bronchiectasis	Read code ever recorded
Crohn's Disease	Read code ever recorded
Stroke	Read code ever recorded
Sinusitis	Read code ever recorded
Heart Failure	Read code ever recorded
Hearing Loss	Read code ever recorded
Asthma	Read code ever recorded AND any prescription in last 12 months
Migraine	≥ 4 prescription only medicine anti-migraine prescriptions in last year
Chronic Obstructive Pulmonary Disease (COPD)/Bronchitis	Read code ever recorded
Psoriasis or Eczema	Read code ever recorded AND ≥ 4 related prescriptions in last 12 months (excluding simple emollients)
Pain	≥ 4 prescription only medicine analgesic prescriptions in last 12 months OR ≥ 4 specified anti-epileptics in the absence of an epilepsy Read code in last 12 months
Thyroid Disease	Read code ever recorded
Blindness	Read code ever recorded
Diabetes	Read code ever recorded
Irritable Bowel Syndrome (IBS)	Read code ever recorded OR ≥ 4 prescription only medicine antispasmodic prescription in last 12 months
Liver Disease	Read code ever recorded
Dyspepsia	≥ 4 prescriptions in last 12 months BNF 0103% excluding antacids AND NOT (≥ 4 NSAIDS OR ≥ 4 aspirin/clopidogrel)
Epilepsy	Read code ever recorded AND antiepileptic prescription in last 12 months
Parkinson's Disease	Read code ever recorded
Constipation	≥ 4 laxative prescriptions in last year
Viral Hepatitis	Read code ever recorded

Appendix 3: Detailed breakdown of Scottish Index of Multiple Deprivation (SIMD) Domains:

Income Domain:

Count or proportion of people defined as income deprived. This is a combined count of claimants on the following benefits:
- Adults and Children in Income Support (IS) or Income-based Employment and Support Allowance Households;
- Adults and Children in Job Seekers Allowance (JSA) households;
- Adults in Guarantee Pension Credit Households;
- Adults and Children in Tax Credit Households on low incomes

Each person will only be counted once.

Employment Domain:

Count or proportion of people defined as employment deprived. This is a combined count of claimants on the following benefits:
- Working Age Unemployment Claimant Count averaged over 12 months;
- Working Age Incapacity Benefit claimants, or Employment and Support Allowance recipients;
- Working Age Severe Disablement Allowance claimants;

Each person will only be counted once.

Crime Domain:

Rate of recorded crime taken from the following:
- Recorded Crimes of Violence
- Recorded Sexual Offences
- Recorded Domestic housebreaking
- Recorded Vandalism
- Recorded Drugs Offences
- Recorded Common Assault

Sum of the recorded crimes/offences in each of the above indicators.

Education Domain:

The Education Domain gives an education deprivation rank using the following indicators:
- School pupil absences
- Pupil performance on SQA at stage 4
- Working age people with no qualifications
- 17-21 year olds enrolling into higher education
- People aged 16-19 not in education, employment or training

Health Domain:

The Health Domain gives a Health deprivation rank using the following indicators:
- ➢ Standardised Mortality Ratio
- ➢ Hospital stays related to alcohol use
- ➢ Hospital stays related to drug use
- ➢ Comparative Illness Factor
- ➢ Emergency stays in hospital
- ➢ Estimated proportion of population being prescribed drugs for anxiety, depression or psychosis
- ➢ Proportion of live singleton births of low birth weight, <2500g

Housing Domain:

The Housing Domain uses rates for the following:
- ➢ Persons in households without central heating
- ➢ Persons in households that are overcrowded

To calculate housing deprivation.

Geographical Access to services Domain:

This indicator is intended to capture the issues of financial cost, time and inconvenience of having to travel to access basic services and uses the population weighted average drive time in minutes as a measure of geographical access to services. This is based on
- ➢ drive time to: GPs, shopping facilities, a petrol station, schools and a post office and
- ➢ public transport time to GPs, a post office and to shopping facilities.

Appendix 4: Possible Smoking Status Read Codes

Read Code		coding
137D.	Admitted tobacco cons untrue ?	0
137J.	Cigar smoker	1
137P.	Cigarette smoker	1
137L.	Current non-smoker	3
137R.	Current smoker	1
137O.	Ex-cigar smoker	2
137N.	Ex-pipe smoker	2
137S.	Ex-smoker	2
137A.	Ex-heavy smoker (20-39/day)	2
1378.	Ex-light smoker (1-9/day	2
1379.	Ex-moderate smoker (10-19/day)	2
137F.	Ex-smoker - amount unknown	2
1377.	Ex-trivial smoker (<1/day)	2
137B.	Ex-very heavy smoker (40+/day)	2
1375.	Heavy smoker - 20-39 cigs/day	1
137C.	Keeps trying to stop smoking	1
1373.	Light smoker - 1-9 cigs/day	1
1374.	Moderate smoker - 10-19 cigs/d	1
1371.	Never smoked tobacco	3
137I.	Passive smoker	0
137H.	Pipe smoker	1
137M.	Rolls own cigarettes	1
137Q.	Smoking started	1
137K.	Stopped smoking	2
137..	Tobacco consumption	1
137Z.	Tobacco consumption NOS	1
137E.	Tobacco consumption unknown	0
1372.	Trivial smoker - < 1 cig/day	1
137G.	Trying to give up smoking	1
1376.	Very heavy smoker - 40+cigs/day	1

Missing/excluded data =0, current smoker =1, ex-smoker=2, never smoked=3

Appendix 5: Possible Smoking Cessation Advice Read Codes

Read Code	Descriptor	Coding
13P1.	Smoking status at 4 weeks	1
13p..	Smoking cessation milestones	1
13p0.	Negotiated date for cessation of smoking	1
13p1.	Smoking status at 4 weeks	1
13p2.	Smoking status between 4 and 52 weeks	1
13p3.	Smoking status at 52 weeks	1
13p4.	Smoking-free weeks	1
13p5.	Smoking cessation programme start date	1
6791	Health education - smoking	1
67A3.	Pregnancy smoking advice	1
67H1.	Lifestyle advice re: smoking	1
8B2B.	Nicotine replacement therapy	1
8B3F.	Nicotine replacement therapy provided free	1
8B3Y.	Over-the-counter nicotine replacement therapy provided free	1
8B3y.	Over-the-counter nicotine replacement therapy provided free	1
8CAL.	Smoking cessation advice	1
8CAl.	Smoking cessation advice	1
8H7I.	Referral to smoking cessation adviser	1
8H7i.	Referral to smoking cessation adviser	1
8HTK.	Referral to stop-smoking clinic	1
8HTk.	Referral to stop-smoking clinic	1
9N2k.	Seen by smoking cessation adviser	1
9N4M.	Did not attend smoking cessation advice	0
9OO..	Anti-smoking monitoring administration	1
9OO1.	Attends stop-smoking monitor	1
9OO2.	Refuses stop-smoking monitor	1
9OO3.	Stop-smoking monitor default	1
9OO7.	Stop-smoking monitor verbal interview	1
9OO9.	Stop-smoking monitoring deletion	1
9OOA.	Stop-smoking monitor check done	1
9OOZ.	Stop-smoking monitor administration NOS	1
9Oo..	Anti-smoking monitoring administration	1

Where 0= no smoking cessation advice and 1= smoking cessation advice given

Appendix 6: Possible Prescription Format of NRT

LastNicotineRep	Code
NICORETTE	1
NICORETTE CHEWING GU 2-P42	1
NICORETTE CHEWING GUM	1
NICORETTE GUM	1
NICORETTE INHALATOR	1
NICORETTE NASAL SPRA LIQ 500-P42	1
NICORETTE NASAL SPRAY 10MG/ML-P42	1
NICORETTE PATCH	1
NICORETTE PATCH 10-P42	1
NICORETTE PATCH 15-P42	1
NICORETTE PATCHES	1
NICORETTE chewing gum 2mg-P42	1
NICORETTE inhalator cartridge 10mg-P42	1
NICORETTE patch 10mg-P42	1
NICORETTE patch 15mg-P42	1
NICORETTE patch PAT 15mg-P42	1
NICORETTE plus chewing gum 4mg-P42	1
NICORETTE-P42	1
NICOTINE REPLACEMENT THERAPY	1
NICOTINE TRANSDERMAL PATCH 30CM-P42	1
NICOTINE cartridge - (for inhalation) 1	1
NICOTINE chewing gum 2mg fruit-P42	1
NICOTINE inh cartridge 10mg-P42	1
NICOTINE patch 10mg-P42	1
NICOTINE patch 14mg-P42	1
NICOTINE patch 15mg-P42	1
NICOTINE patch 21mg-P42	1
NICOTINE patch 7mg-P42	1
NICOTINELL	1
NICOTINELL 10 TTS-P42	1
NICOTINELL 20 TTS-P42	1
NICOTINELL 30 TTS-P42	1
NICOTINELL GUM	1
NICOTINELL LOZENGES	1
NICOTINELL PATCHES	1
NICOTINELL TTS	1
NICOTINELL TTS 30 patch NON NHS 11/97-P	1
NICOTINELL TTS PATCH	1
NICOTINELL TTS PATCH 20 SQ CM-P42	1
NICOTINELL TTS PATCHES	1
NICOTINELL TTS patch 10 square cm-P42	1
NICOTINELL TTS patch 30 square cm-P42	1
NICOTINELL TTS patch PAT 10 sq cm-P42	1
NICOTINELL TTS patch PAT 20 sq cm-P42	1
NICOTINELL TTS patch PAT 30 sq cm-P42	1

NIQUITIN	1
NIQUITIN CQ	1
NIQUITIN CQ 21MG PATCHES	1
NIQUITIN CQ PATCH	1
NIQUITIN CQ PATCH 24 HRS	1
NIQUITIN CQ PATCHES	1
NIQUITIN CQ patch 14mg-P42	1
NIQUITIN CQ patch 21mg-P42	1
NIQUITIN CQ patch 7mg clear-P42	1
NIQUITIN CQ patch 7mg-P42	1
NIQUITIN CQ patch PAT 14mg-P42	1
NIQUITIN CQ patch PAT 21mg-P42	1
NIQUITIN CQ patch PAT 7mg-P42	1
NIQUITIN LOZENGES	1
Nicotine Patches 14mg	1
NiQuitin CG	1
NiQuitin CQ	1
NiQuitin CQ 14mg	1
NiQuitin CQ 21mg	1
NiQuitin CQ 7mg	1
NiQuitin CQ PATCHES	1
NiQuitin CQ Patches	1
NiQuitin CQ clear	1
NiQuitin CQ pastilles	1
NiQuitin Lozenges	1
NiQuitin QC	1
Nicorette	1
Nicorette 10mg patches	1
Nicorette 15mg Patches	1
Nicorette 15mg patches	1
Nicorette 16hr patch	1
Nicorette 5mg patches	1
Nicorette Chewing Gum	1
Nicorette Gum	1
Nicorette Inhalator	1
Nicorette Microtab	1
Nicorette Nasal Spray	1
Nicorette Patch	1
Nicorette Patch 5mg-P42	1
Nicorette Patches	1
Nicorette Step 1	1
Nicorette inhalator cartridge refill pa	1
Nicorette microtabs	1
Nicorette patch	1
Nicotine	1
Nicotine CQ Patches	1
Nicotine Chewing Gum (as resin)	1
Nicotine Chewing Gum 2mg-P42	1
Nicotine Inhalation	1

Nicotine Inhalation Cartridge	1
Nicotine Lozenge 1mg-P42	1
Nicotine Lozenge 2mg	1
Nicotine Lozenge 4mg	1
Nicotine Medicated Chewing Gum 2mg	1
Nicotine Medicated Chewing Gum 4mg	1
Nicotine Patch	1
Nicotine Patches	1
Nicotine Patches 15mg	1
Nicotine Patches 16 Hours	1
Nicotine Patches 16 hours	1
Nicotine Patches 24 Hours	1
Nicotine Patches 24 hours	1
Nicotine Replacement Lozenges	1
Nicotine Replacement Therapy	1
Nicotine TTS Patches	1
Nicotine Transdermal Patch 10mg in 16hr	1
Nicotine Transdermal Patch 14mg in 24hr	1
Nicotine Transdermal Patch 15mg in 16hr	1
Nicotine Transdermal Patch 21mg in 24hr	1
Nicotine Transdermal Patch 5mg in 16hrs	1
Nicotine Transdermal Patch 7mg in 24hrs	1
Nicotine chewing gum	1
Nicotine lozenges	1
Nicotine microtab	1
Nicotine patches	1
Nicotine replacement therapy	1
Nicotinell	1
Nicotinell patches	1
Nicotinell 14mg Patch	1
Nicotinell 14mgs	1
Nicotinell 21mgs	1
Nicotinell Chewing Gum	1
Nicotinell Gum	1
Nicotinell Lozenge	1
Nicotinell Mint Lozenge	1
Nicotinell Patches	1
Nicotinell TTS	1
Nicotinell TTS 20	1
Nicotinell TTS Patch	1
Nicotinell TTS Patches	1
Nicotinell Tts 10	1
Nicotinell Tts 20	1
Nicotinell Tts 30	1
Nicotinell programme	1
Nicotinelle	1
Niquitin	1
Niquitin 21mg	1
Niquitin CQ	1

Niquitin CQ Lozenge	1
Niquitin CQ Patches (10 week course)	1
Niquitin CQ Patch	1
Niquitin CQ Patch 14mg-P42	1
Niquitin CQ Patch 21mg-P42	1
Niquitin CQ Patch 7mg-P42	1
Niquitin CQ Patches	1
Niquitin CQ Tab	1
Niquitin CQ patches	1
Niquitin Cq	1
Niquitin Cq Lozenge	1
Niquitin patches	1
nicorette	1
nicorette 16hr	1
nicorette 5mg patches	1
nicorette gum	1
nicorette gum 2mg	1
nicorette inhalator	1
nicorette inhalator refills	1
nicorette microtab	1
nicorette microtabs	1
nicorette nasal spray	1
nicorette patch 10mgms 16hr	1
nicorette patches	1
nicorette patches 10mg	1
nicorette patches 15mg	1
nicotine	1
nicotine patch	1
nicotine gum	1
nicotine patch	1
nicotine patches	1
nicotine patches	1
nicotine replacement	1
nicotine replacement therapy	1
nicotine replacement therapy patches	1
nicotine sublingual tabs	1
nicotine transdermal	1
nicotinell	1
nicotinell 14 mg	1
nicotinell 20	1
nicotinell 30	1
nicotinell TTS	1
nicotinell TTS 24hr patch	1
nicotinell TTS 30	1
nicotinell gum	1
nicotinell gum 1mg	1
nicotinell patch	1
nicotinell patches	1
nicotinell tts 10	1

nicotinelle	1
nicotinelle patches	1
niquitin CQ	1
niquitin CQ lozenge	1
niquitin CQ lozenges	1
niquitin cq	1
niquitin cq lozenges 2 mgms	1
niquitin cq lozenges 4mgms	1
niquitin cq patches	1
niquitin cq patches mg	1