

The Management of Hospital In-patients with Diabetes Mellitus

Dr Ketan Dhatariya

A thesis submitted for the degree of
PhD by Publication

Candidate Number 10088546

School of Medicine

University of East Anglia

Norwich, England

October 2017

©This copy of the thesis has been supplied on condition that anyone who consults it is understood to recognise that its copyright rests with the author and that use of any information derived there from must be in accordance with current UK Copyright Law. In addition, any quotation or extract must include full attribution

Abstract

Background:

In the UK, the prevalence of diabetes in adults in the general population is currently reported as just over 6% in 2014-15 [1]. This rose from a prevalence of 5.5% in 2010. However, the most recent data from the 2016 United Kingdom National Diabetes In-patient Audit reported that the prevalence of diabetes amongst hospitalised in-patients was 17% [2]. This represented a rise of over 15% since the first National Diabetes In-patient Audit was carried out in 2010, and was the same rise in prevalence seen in the general population during that time. Thus diabetes is disproportionately over represented in the in-patient population.

It has been recognised for many years that in-patients with diabetes experience 'glucose-related' harms. Any form of dysglycaemia is associated with increased harms – in terms of poor outcomes (however that is defined) and also increased mortality [3].

For many years it was well recognised that having long term high glucose concentrations was associated with an increased risk of developing the long term micro and macrovascular complications of diabetes. It was only with the publication of the two seminal trials, the Diabetes Control and Complications Trial in type 1 diabetes and the United Kingdom Prospective Diabetes Study in type 2 diabetes that showed conclusively that in an outpatient population tight glycaemic control was associated with a reduced risk of developing those complications [4,5]. However, to date whilst there are a great deal of data to show that high glucose concentrations are associated with harm in hospitalised in-patients with diabetes, there are almost

no data to show that improving glucose concentrations is associated with benefit. However, most authorities agree that glucose concentrations between 6.0 and 10.0mmol/l (with an acceptable range of 4.0 to 12.0mmol/l) are likely to be most beneficial (or rather, least likely to be associated with harm).

In the UK there is an organisation called the Joint British Diabetes Societies for In-patient Care group (JBDS), of which I am a senior member. JBDS is a group of professionals interested in the care of in-patients with diabetes. This group, which is funded by Diabetes UK and the Association of British Clinical Diabetologists and is a collaboration between these two national organisations and the National Diabetes In-patient Specialist Nurse Group, had as it's 'mission statement' the focus on producing evidence based or, where this was not possible, consensus based, clinical guidelines for the management of diabetes in hospitalised in-patients. These guidelines were designed to be used by non-specialists, and written in a user friendly way to make them clinically useful.

I have been involved in writing or contributing to most of the guidelines produced by the group, and have been the lead author on two of the most widely read / used documents – peri-operative care and diabetic ketoacidosis. Indeed, as a result of my involvement in these writing groups, I am now recognised as an international expert on these two subjects. I am regularly invited to speak on these subjects, but also invited to write about them as well.

This thesis is a journey through various aspects of my involvement in in-patient care for patients with diabetes from the time I was first appointed as a consultant in

Norwich in 2004 to the spring of 2017. In particular my hypothesis is that because of the work I and others have published, the management of in-patients with diabetes has improved the care of this vulnerable group.

Methods:

This thesis is a collection of some of the papers I have written over the last few years. I have divided it up into sections: admissions avoidance; general management of in-patients; outcomes of hyperglycaemia; diabetes in-patient treatment satisfaction; the management of diabetic ketoacidosis; and peri-operative diabetes care.

Each section is written chronologically as the papers relevant to that section were published. I have tried to tell a 'story' of the development of why that particular piece of work was done.

Part of my role as an educational supervisor is to help my junior colleagues do research and write this up. The papers that are written should have as part of their introduction a section on 'what is known', followed by a section on 'what is not known', with the end of the introduction being 'what we did to fill the gap in the unknown'. Similarly, in this thesis, each paper has an introduction dealing with the background to why the paper was written and the thinking behind it. There then follows a section on what the study added to the literature and what changed as a result of the paper. Finally, there is a section on what should have been done differently, a reflection on the paper, and its impact and how things could and (maybe) should, have been done differently. The more recently published works

have little in the last sections because they have not had time to be widely disseminated or discussed, but where I have managed to reflect on the works, I have done so.

Over the last few years, I have been part of the small team working with the Care Quality Commission (CQC) to ensure that diabetes care for hospital in-patients is now one of the very few 'disease-specific' areas that are included in the hospital inspections that they carry out. This is because of the realisation that diabetes patients are admitted under every speciality, that they have a complex set of unique needs that need to be delivered by a skilled, educated and committed workforce. Deficiencies in any area of care delivery will quickly show up, and the CQC has the power (the 'teeth') to ensure that hospitals deliver the standard of care that is necessary to prevent harm. In 2017, the CQC came up with a set of questions that individual Trusts must supply information on as part of their 'pre-inspection pack':

Results:

The work presented in this thesis shows that over the last decade or so, the care for in-patient diabetes has taken a greater prominence amongst diabetes professionals, but also at a higher level of NHS management. Inpatient diabetes has begun to take greater precedence within hospitals and the 2016 National Diabetes Inpatient Audit (NaDIA) results showed that several aspects of care had improved over the five years the audit had been running.

Hospital stay:

The 2011 NaDIA showed that only 58% of in-patients were seen by a member of the diabetes team. This had risen to 69% in 2016. Unfortunately, 28% of hospitals still did not have in-patient diabetes specialist nurses.

Hypoglycaemia:

The prevalence of all hypoglycaemic episodes decreased from 26% in 2011 to 20% in 2016. Looking more closely, the rates of mild (self-treated) hypoglycaemia fell from 23% in 2011 to 18% in 2016, and the rate of severe hypoglycaemia (i.e. requiring third party assistance) fell from 11% to 8% between those years. Within the latter category, the prevalence of severe hypoglycaemia requiring injectable rescue treatment fell from 2.2% in 2011 to 1.7% in 2016.

Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycaemia State (HHS):

Disappointingly, in 2016 4% of in-patients with type 1 diabetes developed DKA during their hospital stay, a rise from 3% in 2011. The incidence of HHS in in-patients with type 2 diabetes remained unchanged since 2015, at 0.2%.

Intravenous insulin:

The 2016 NaDIA data showed that there were fewer people on intravenous insulin infusions – 11% in 2011 and 8% in 2016. In addition, fewer people were on what was felt to be excessively long intravenous insulin infusions – 8% in 2011 to 6% in 2016. Finally, it was felt by the teams filling out the audit forms that the transfer from intravenous to subcutaneous insulin was better, with errors falling from 19% in 2011 to 14% in 2016.

Medication errors:

Despite the increasing use of electronic prescription charts, a proportion of drug charts still had at least one medication error. However, the rate decreased from 40% in 2011 to 38% in 2016. However this still meant that almost two out of five in-patient

drug charts had a drug error recorded. Drug chart errors were more likely to occur for patients on surgical wards – 41% – compared to patients on a medical ward – 37%. The 2016 NaDIA data also showed that prescription errors were less likely to occur if in-patients were treated in a hospital that used an electronic prescription chart – 19% – compared to hospitals that did not use have electronic charts – 25%. The data also showed that the number of hospitals using fully electronic prescribing has increased from 16.1% in 2013, to 27.8% in 2016, with the number using partial prescribing falling from 12.2% in 2013, to 9.8%.

In 2017, the questions that the CQC will ask individual Trusts when inspecting hospitals as part of their 'pre-inspection pack' are as follows:

1. That the Trust participates in the annual national diabetes in-patient audit (NaDIA) programme
2. That the Trust has a credible and overarching written strategy for in-patient diabetes care across the entire Trust as part of an approved Trust governance framework
3. That the Trust has a written policy for the safe prescribing and administration of insulin, linked to direct or online mandatory training of all staff, with evidence of adoption of national guidance on in-patient diabetes care and insulin use, and programmes to review improvement in outcomes
4. That the Trust has a dedicated in-patient diabetes specialist service as one of their core services, with routine and planned access to this service for all in-patients with diabetes, not just emergency admissions
5. That the Trust has a foot multidisciplinary team (MDT) for in patients with acute diabetic foot problems and /or high risk feet while in-patients

6. That the Trust has a robust system in place to identify all current in-patients with a known diabetes diagnosis, with evidence of a rapid referral system to the specialist in-patient diabetes team for those experiencing diabetes management problems

Conclusions:

The prevalence of diabetes continues to rise unabated, and the consequence will be that more people with diabetes will be admitted to hospital – for the most part not because of diabetes, but they will have diabetes in addition to the condition that necessitated admission. As I have tried to describe throughout this thesis, patients with diabetes in hospital unfortunately come to greater harm than those without diabetes. However I hope that the work that I have done, or contributed to, has in some way mitigated these harms. Furthermore, that unifying practice across the UK and elsewhere, has improved the care for people in hospital with diabetes.

Guidelines in particular, can go a long way to helping standardise and improve the care of this vulnerable patient group, but they are not the whole answer. As these and other data show, there has only been partial success in their implementation and utilisation. Whilst a lot has been done over the last few years, there is a very long way to go before it can be said that the care of hospital in-patients is good and safe at all times. There are many areas of outstanding practice and an equally large number of areas where standards need to be improved.

As with general diabetes care in the 1950's onwards, we need to collect the data in a meaningful way that shows what outcomes are not as good as for those without

diabetes, then intervene and see if we can reduce those differences. We need to collect the data to show that harm is being done, before we can do something about it. My small contributions to the field continue because there remains a huge amount of work to be done.

Table of Contents

Abstract.....	3
Table of Contents	11
Figure	14
Tables.....	15
Acknowledgements	16
Abbreviations Used in this Dissertation	22
List of Papers Used in this Dissertation.....	24
Objective of this Thesis and my Hypothesis	27
Background and Introduction	28
A Brief History of Treating In-patients with Diabetes.....	31
Diabetes Related Emergencies	31
Diabetes in In-patients	37
Variations in Care.....	41
List of Publications – to August 2017	47
Original Peer Reviewed Papers.....	47
Miscellaneous	54
Editorials (* peer reviewed).....	55
Reviews (* peer reviewed).....	57
Book Chapters (* peer reviewed).....	57
Admissions Avoidance	59
Gooday C, Hallam C, Sieber C, Mtariswa L, Turner J, Schelenz S, Murchison R Messenger G, Morrow D, Hutchinson R, Williams H, Dhatariya K (2013); An antibiotic formulary for a tertiary care foot clinic: admission avoidance using intramuscular antibiotics for borderline foot infections in people with diabetes. Diabetic Med 30: 581-589.....	60
Gooday C, Murchison R, Dhatariya K (2013); An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic Foot & Ankle 4: 21757	70
General Management of Patients in Hospital with Diabetes	75
Daultrey H, Gooday C, Dhatariya K (2011); Increased length of in-patient stay and poor clinical coding: audit of patients with diabetes. J R Soc Med Sh Rep 2: 83 ..	76
Narwani V, Swafe L, Stavrika C, Dhatariya K (2014); How frequently are bedside glucose levels measured in hospital in-patients on glucocorticoids? Clinical Medicine 14: 327-328	81
Outcomes of In-patient Hyperglycaemia	86

Evans NR, Dhatariya KK (2012); Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. Clin Med JRCPL 12: 137-139.....	87
Haddadin F, Clark A, Evans N, Dhatariya K (2014); Admission blood glucose helps predict 1 year, but not 2 years, mortality in an unselected cohort of acute general medical admissions. Int J Clin Pract 69: 643-648.....	92
Dhatariya K (2013); Should in-patient hyperglycaemia be treated? Br Med J 346: f134.....	97
The Benefits of a Diabetes In-patient Specialist Nurse.....	101
Sampson MJ, Dozio N, Ferguson B, Dhatariya K (2007); Total and excess bed occupancy by age, speciality and insulin use for nearly one million diabetes patients discharged from all English Acute Hospitals. Diabetes Res Clin Pract 77: 92-98	102
Sampson MJ, Brennan C, Dhatariya K , Jones C, Walden E (2007); A national survey of in-patient diabetes services in the United Kingdom. Diabetic Med 24: 643-649.....	106
Sampson MJ, Crowle T, Dhatariya K , Dozio N, Greenwood, R, Heyburn PJ, Jones C, Temple RC, Walden E (2006); Trends in bed occupancy for in-patients with diabetes before and after the introduction of a diabetes in-patient specialist nurse service. Diabetic Med 23: 1008-1015	113
The Diabetes In-patient Treatment Satisfaction Study (DIPSat)	118
Sampson MJ, Singh H, Dhatariya KK , Jones C, Walden E, Bradley C (2009); Psychometric validation and use of a novel diabetes in-patient treatment satisfaction questionnaire. Diabetic Med 26: 729-735	119
Rutter CL, Jones C, Dhatariya KK , James J, Irvine L, Wilson EC, Singh H, Walden E, Holland R, Harvey I, Bradley C, Sampson MJ (2013); Determining in-patient diabetes treatment satisfaction in the UK—the DIPSat study. Diabetic Med 30: 731-738	124
The Management of Diabetic Ketoacidosis	129
Dhatariya KK (2007); Diabetic ketoacidosis. Br Med J 334: 1284-1285.....	130
Savage MW, Dhatariya KK , Kilvert A, Rayman G, Rees JA, Courtney CH, Hilton L, Dyer PH, Hammersley MS (2011); Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. Diabetic Med 28: 508-515	134
Rudd B, Patel K, Levy N, Dhatariya K (2013); A survey of the implementation of the NHS diabetes guidelines for management of diabetic ketoacidosis in the intensive care units of the East of England. Journal of the Intensive Care Society 14: 60-64.....	143
Dhatariya KK , Nunney I, Higgins K, Sampson MJ, Icton G (2016); A national survey of the management of diabetic ketoacidosis in the UK in 2014. Diabetic Med 33: 252-260	148
Dhatariya K , Nunney I, Icton G (2016); Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. Diabetic Med 33: 269-270	154

Edge JA, Nunney I, Dhatariya KK (2016); Diabetic ketoacidosis in an adolescent and young adult population in the UK in 2014: a national survey comparison of management in paediatric and adult settings. <i>Diabetic Med</i> 33:1352-1359.....	158
Peri-operative Diabetes Care	164
Dhatariya K , Levy N, Kilvert A, Watson B, Cousins D, Flanagan D, Hilton L, Jairam C, Leyden K, Lipp A, Lobo D, Sinclair-Hammersley M, Rayman G (2012); NHS Diabetes guideline for the perioperative management of the adult patient with diabetes. <i>Diabetic Med</i> 29: 420-433	165
Rollins KE, Varadhan KK, Dhatariya K , Lobo DN (2016); Systematic review of the impact of HbA _{1c} on outcomes following surgery in patients with diabetes mellitus. <i>Clin Nutr</i> 35: 308-316.....	174
Summary and Conclusions	178
References	186

Figure

Figure 1 – Data from Mike Sampson. Feedback from 104 hospitals – first shown at
Diabetes UK March 2013 140

Tables

Table 1 – Classification for the severity of diabetes related foot disease, taken from the Infectious Diseases Society of America (IDSA) and the International Working Group for the Diabetic Foot [102,106].	65
Table 2 – Our modified severity classification, including the admissions avoidance category ‘Moderate infection – borderline admission’ [107].	66
Table 3 – Award winning diabetic foot antibiotic prescribing guideline generated from our modification of the IDSA guideline [107].	67

Acknowledgements

The bulk of the published work on which this thesis is based is my own. My contribution to each of the publications is detailed at the start of each paper discussed, with a comment from a co-author on my contribution if I am on a multi-author paper.

There are however notable contributions to the body of work from a number of friends and colleagues.

Firstly I would like to thank my consultant colleagues, in particular Professor Mike Sampson who has invited me to participate in many of the research projects that he was involved in and encouraged me to develop my own work. His leadership of the Joint British Diabetes Societies for In-patient Care group remains inspirational. It was his involvement in in-patient diabetes that was my introduction to the subject. I also thank Professor Jeremy Turner as clinical director for allowing me to divert my attention for a few months to concentrate on this thesis. I am also grateful to Professor Gerry Rayman who has been an enthusiastic supporter of my various endeavours over the last few years. That we have the same interests in in-patient diabetes and the diabetic foot is probably no coincidence, and I fully acknowledge that I have probably been unconsciously coerced into this. I am very pleased to report that I am happy to have been pushed in this direction.

For each chapter in this thesis I have many people to thank.

Admissions Avoidance

It is a blessing to be allowed to call myself the lead of a fantastic foot team at the Norfolk and Norwich Hospital. In particular, my 'partner in crime' Catherine Gooday who, together with Rachel Murchison has helped to build what is, in my humble opinion, one of the premier foot clinics in the UK. In addition, I thank the legions of medical students who have wanted to come and work with us, and have then done some sterling work.

In addition, I also work with an outstanding cadre of diabetes nurses who do amazing work under sometimes difficult circumstances. To them, I say a big 'Thank You!'

General Management of In-patients with Diabetes

One of the first things I did when I started working at the Norfolk and Norwich was to start encouraging medical students to work in our department. As a result, some of the work that I present in this section of the thesis has been done by them. In particular Alec Beaney, Coral Stark, Harriet Daultrey, Thomas Murray, Zahra Essackajee, Elizabeth Swan, Edwin Li Ping Wah-Pun Sin, Francesca Li, Joyce Cheng, Anson Yue, Will Fry, Sean McCafferty, David Maxey, Nishchay Kakkar, Meera Patel, and Maithili Varadarajan. They have helped look through our reams of data and put it together in such a way that we have managed to publish. Much of their work is not included in this thesis, but could very well have been so, and should I ever want to do another PhD on the 'diabetic foot', then their work will be included.

Outcomes of Hyperglycaemia in Hospitalised In-patients with Diabetes

Apart from medical students, there have been a number of junior doctors who have been interested in the work that I have done have also taken part. There remains so much to do, and it has been an uphill struggle to convince journals and reviewers that improving the management of in-patients with diabetes is an important subject – and that the first step on the pathway of that improvement is measuring what is wrong, and not necessarily looking at intervention. I am grateful to the medical students and junior doctors on three counts – for them seeing the same vision that I have; for them doing the actual work on collecting the data; and then having the continued patience whilst I try and persuade journals to accept the papers. For the papers in this section, I would like to acknowledge the work done by Nicholas Evans and Firas Haddadin. If the journals ever accept the other work that I have been trying to publish, then this section would have a few more papers in it.

The Benefits of a Diabetes In-patient Specialist Nurse

At the start of my time at the Norfolk and Norwich Hospital I was invited by Mike Sampson to be involved with the work that he had already been doing on the impact of in-patients with diabetes, and then to take the next step – a natural evolution of the work he had already done – looking at the impact of the diabetes in-patient specialist nurses. I am indebted to Esther Walden, the senior DISN, who allowed me to join in and contribute my tuppence worth without being too scathing at my suggestions.

Diabetes In-patient Treatment Satisfaction

My involvement in this project was also thanks to Mike Sampson who invited me to be part of this novel piece of work. Working with national luminaries such as June James, Claire Bradley and our outstanding JBDS administrator Chris Jones was such a privilege for me. For most of the time I felt like a little boy in short trousers being allowed to play at the top table – a feeling I continue to have to this day. I am very grateful to them for making me feel so much part of the group and not treating me like the small child I think I am in front of them.

Diabetic Ketoacidosis

I thank my anaesthetic colleague with whom I had a discussion in 2006 about why physicians used normal saline in diabetic ketoacidosis. His doubt on the utility of normal saline started the process which led to the publication of an editorial in the British Medical Journal. As a result of that publication I was invited to join the Joint British Diabetes Societies for In-patient Care writing group for the management of diabetic ketoacidosis.

I thank all of my co-authors, in particular Professor Mark Savage and Dr Ann Kilvert who had led the work to that point and then allowed me to make my own contributions. For the national surveys, I am very deeply indebted to Gilly Icton for helping me create the data collection forms, and then, for putting the data into the spreadsheet when it came in. That she continued to do this even after she had retired was a testament to her belief in the project and her work ethic.

Ian Nunney deserves a special mention, not just for the DKA work, but for a lot of the work on feet, most of which goes unmentioned in this thesis. Without him none of the work on the national DKA survey presented in this thesis would have been possible.

My most recent collaboration with Professor Guillermo Umpierrez from Atlanta, Georgia is the fulfilment of a dream of mine. Guillermo is an international superstar in the world of in-patient diabetes. For him to agree to be a co-author on an editorial for the Lancet Diabetes and Endocrinology, criticising the American Diabetes Association DKA guideline that he was on the writing group for makes me believe that maybe I can help to change things for the better.

Perioperative Diabetes Care

Nicholas Levy has been a major driver in this field. I am fully aware that his enthusiasm for this subject and his vision has helped to carry me along this road. For us to be able to work together so well is a testament to how we respect and acknowledge each other's strengths and ensure that we use them to the benefit of patients. It is our fervent hope that as time passes, the importance of this subject becomes apparent to all, and that glycaemic control is high on the anaesthetic and surgical agendas for safe surgical practice around the world. It is largely thanks to the work that we have done together that in 2017, the National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) started a 2 year project on peri-operative diabetes care. He is of course, also instrumental in much of the DKA work I have done.

Of course, it would be remiss of me to not acknowledge the many co-authors on the JBDS peri-op guideline, and the reviewing group of the first and second editions.

Finally, my family. Special mention must be made of my parents. I am totally in their debt. Until recently I was not able to fully appreciate the sacrifices that they made when my brother and I were children, to build us the foundations of the lives we live now. Even now, I am sure that I have no idea of the magnitude of their love. To paraphrase Isaac Newton, I have only been able to achieve the things that I have by standing on the shoulders of giants. For me, my parents are giants in my world.

However, the final word goes to Vasu, Ishika and Krishna, without whom life would be meaningless. In particular I am forever indebted to Vasu, who over the last 2 decades and more has always accommodated my selfish desire for self-improvement. She knows the drive I have is insatiable, and she reminds me all too frequently that I have only attained my goals at work and in life in general because of her. As with almost everything else, she is right of course.

Norwich October 2017

Abbreviations Used in this Dissertation

AABGI – Association of Anaesthetists of Great Britain and Ireland

ABCD – Association of British Clinical Diabetologists

BSPED – British Society for Paediatric Endocrinology and Diabetes

CQC – Care Quality Commission

DCCT – Diabetes Control and Complications Trial

DISN – Diabetes In-patient Specialist Nurse

DKA – Diabetic Ketoacidosis

DUK – Diabetes UK

FRIII – Fixed Rate Intravenous Insulin Infusion

HbA_{1c} – Glycated Haemoglobin

HDU – High Dependency Unit

HES – Hospital Episode Statistics

HHS – Hyperosmolar Hyperglycaemic Syndrome

HRG – Healthcare Resource Group

IDSA – Infectious Diseases Society of America

IQR – Interquartile Range

ISPAD – International Society for Pediatric and Adolescent Diabetes

ITU – Intensive Care Unit / Intensive Therapy Unit

IWGDF – International Working Group for the Diabetic Foot

JBDS – Joint British Diabetes Societies for In-patient Care group

SD – Standard Deviation

SIRS – Systemic Inflammatory Response Syndrome

NaDIA – National Diabetes In-patient Audit

NCEPOD – National Confidential Enquiry in Patient Outcomes and Death

NICE – National Institute for Health and Care Excellence

UKPDS – United Kingdom Prospective Diabetes Study

VRIII – Variable Rate Intravenous Insulin Infusion

List of Papers Used in this Dissertation

Admissions Avoidance

Gooday C, Hallam C, Sieber C, Mtariswa L, Turner J, Schelenz S, Murchison R, Messenger G, Morrow D, Hutchinson R, Williams H, **Dhatariya K** (2013); An antibiotic formulary for a tertiary care foot clinic: admission avoidance using intramuscular antibiotics for borderline foot infections in people with diabetes. *Diabetic Med* 30(5): 581-589

Gooday C, Murchison R, **Dhatariya K** (2013); An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. *Diabetic Foot & Ankle* 4: 21757

General Management of In-patients

Daultrey H, Gooday C, **Dhatariya K** (2011); Increased length of in-patient stay and poor clinical coding: audit of patients with diabetes. *J R Soc Med Sh Rep* 2: 83

Narwani V, Swafe L, Stavraka C, **Dhatariya K** (2014) How frequently are bedside glucose levels measured in hospital in-patients on glucocorticoids? *Clinical Medicine* 14(3):327-328

Outcomes of Hyperglycaemia in In-patients

Evans NR, **Dhatariya KK** (2012); Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. *Clin Med JRCPL* 12(2): 137-139

Haddadin F, Clark A, Evans N, **Dhatariya K** (2014); Admission blood glucose helps predict 1 year, but not 2 years, mortality in an unselected cohort of acute general medical admissions. *Int J Clin Pract* 69(6): 643-648

Dhatariya K (2013); Should in-patient hyperglycaemia be treated? *Br Med J* 346: f134

The Benefits of a Diabetes In-patient Specialist Nurse

Sampson MJ, Dozio N, Ferguson B, **Dhatariya K** (2007); Total and excess bed occupancy by age, speciality and insulin use for nearly one million diabetes patients discharged from all English Acute Hospitals. *Diabetes Res Clin Pract* 77: 92-98

Sampson MJ, Brennan C, **Dhatariya K**, Jones C, Walden E (2007); A national survey of in-patient diabetes services in the United Kingdom. *Diabetic Med* 24: 643-649

Sampson MJ, Crowle T, **Dhatariya K**, Dozio N, Greenwood, R, Heyburn PJ, Jones C, Temple RC, Walden E. (2006); Trends in bed occupancy for in-patients with diabetes before and after the introduction of a diabetes in-patient specialist nurse service. *Diabetic Med* 23: 1008-1015

Diabetes In-patient Treatment Satisfaction

Sampson MJ, Singh H, **Dhatariya KK**, Jones C, Walden E, Bradley C (2009); Psychometric validation and use of a novel diabetes in-patient treatment satisfaction questionnaire. *Diabetic Med* 26: 729-735

Rutter CL, Jones C, **Dhatariya KK**, James J, Irvine L, Wilson EC, Singh H, Walden E, Holland R, Harvey I, Bradley C, Sampson MJ (2013); Determining in-patient diabetes treatment satisfaction in the UK—the DIPSat study. *Diabetic Med* 30: 731-738

The Management of Diabetic Ketoacidosis

Dhatariya KK (2007); Diabetic ketoacidosis. *Br Med J* 334: 1284-1285

Savage MW, **Dhatariya KK**, Kilvert A, Rayman G, Rees JA, Courtney CH, Hilton L, Dyer PH, Hammersley MS (2011); Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. *Diabetic Med* 28: 508-515

And the main document from which this paper was derived:

Dhatariya K, Savage M, Kelly T, Sampson M, Walton C, Claydon A, Dyer P, Evans P, Khan A, Kilvert A, Leech N, Levy N, Rayman G, Rees A, Sinclair-Hammersley M (2013) Joint British Diabetes Societies In-patient Care Group. The management of diabetic ketoacidosis in adults. Second edition. Update: September 2013
<http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm>

Rudd B, Patel K, Levy N, **Dhatariya K** (2013); A survey of the implementation of the NHS diabetes guidelines for management of diabetic ketoacidosis in the intensive care units of the East of England. *Journal of the Intensive Care Society* 14: 60-64

Dhatariya KK, Nunney I, Higgins K, Sampson MJ, Icceton G (2016); A national survey of the management of diabetic ketoacidosis in the UK in 2014. *Diabetic Med* 33: 252-260

Dhatariya K, Nunney I, Icceton G (2016); Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. *Diabetic Med* 33: 269-270

Edge JA, Nunney I, **Dhatariya KK** (2016); Diabetic ketoacidosis in an adolescent and young adult population in the UK in 2014: a national survey comparison of management in paediatric and adult settings. *Diabetic Med* 33: 1352-1359

Perioperative Diabetes Care

Dhatariya K, Levy N, Kilvert A, Watson B, Cousins D, Flanagan D, Hilton L, Jairam C, Leyden K, Lipp A, Lobo D, Sinclair-Hammersley M, Rayman G (2012); NHS Diabetes guideline for the perioperative management of the adult patient with diabetes. *Diabetic Med* 29: 420-433

And the main document from which this paper was derived:

Dhatariya K, Flanagan D, Hilton L, Kilvert A, Levy N, Rayman G, Watson B, Cousins D, Jairam C, Leyden KM, Lobo DN, Sinclair-Hammersley M (2015) Management of adults with diabetes undergoing surgery and elective procedures: Improving standards. Revised September 2015 http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_Surgical_Guideline_2015_Full.pdf

Rollins KE, Varadhan KK, **Dhatariya K**, Lobo DN (2016); Systematic review of the impact of HbA_{1c} on outcomes following surgery in patients with diabetes mellitus. *Clin Nutr* 35: 308-316

Objective of this Thesis and my Hypothesis

The objective of this thesis is to highlight some of the key peer reviewed publications that I have written or contributed to in the management of hospital in-patients with diabetes. My hypothesis is that because of the work I and others have published, the management of in-patients with diabetes has improved.

As the prevalence of diabetes in the general population has continued to increase, the number of people in hospital with the condition has also risen. However, until the mid-2000's the care of hospital in-patients with diabetes was not an area that had received much attention, nor had it been the focus of much research. In particular, because of the lack of awareness of the poor outcomes associated with in-patient hypo- or hyperglycaemia, specific care pathways or guidelines had not been developed, or where they had been, were often limited to use in the hospital in which they had been written.

I have been actively involved in the care of in-patients with diabetes since I was a junior trainee in the mid-1990's, but since the mid-2000's I have published widely on the subject, including many national guidelines used to standardise the treatment of in-patients across the UK and in many parts of the world. It is possible, (although virtually impossible to prove), that the improved quality of care documented over the last few years by the National Diabetes In-patient Audit has, in part, been due to the work I have contributed to.

Background and Introduction

Diabetes mellitus is a complex metabolic disorder characterised by chronic hyperglycaemia resulting from defects in insulin secretion or insulin action, or both. In 2015, the prevalence of diabetes in the UK was estimated to be in the region of between 4.6% and 6.0%, representing about 3.2 million people [6,7]. This is likely to rise over time, to an estimated 5 million by 2025 [7]. The number of people in hospital with diabetes is far greater than the prevalence in the general population, with a mean of 17%, and a range of between 4 to over 35% of hospital in-patients having the condition [2]. Most of the estimated 1.087million people this represents are admitted to hospital *with* their diabetes rather than *because* of it [8]. There is a systemic national issue with poor in-patient diabetes care in the UK. Work presented in this thesis shows that people with diabetes in hospital experience substantial shortfalls in the quality of care, and in-patient safety. This has been demonstrated as avoidable excess mortality and morbidity, and in diabetes treatment satisfaction. People with diabetes are more likely to be admitted; less likely to have day case surgery; have longer hospital stays; and experience more harms than those without diabetes admitted for the same conditions [9-11]. In 2013, the National Diabetes Information Service looked at over 10 million general hospital admissions between 2010 and 2012. After carefully adjusting for case mix, they reported in 2013 that there had been an excess diabetes specific mortality of 2300 deaths during those 2 years [12]. There are wide variations between hospitals in the UK in these outcomes, but the increased mortality was not due to differences in standardised mortality rates, suggesting this was a true excess diabetes specific rise in mortality.

In addition to excess mortality, the morbidity incurred by poor in-patient diabetes care issues incurs substantial excess treatment costs. The National Diabetes In-patient Audit (NaDIA) is a snapshot of diabetes in hospitalised in-patients carried out over 1 day in individuals hospitals, during 1 particular week per year. This audit has taken place annually since 2011 (except 2014) and has produced a wealth of data. In particular, the data have shown very high rates of medication errors, errors associated with insulin infusion use, frequent severe in-patient hypoglycaemia, limited access to diabetes specialist input, poor assessment of high risk foot problems, and wide geographical variability [2].

These shortfalls are deep rooted, systemic, and are often so large in scale that they have become essentially invisible to many acute hospitals. There are service models and interventions of proven benefit in reducing the excess morbidity and mortality experienced by in-patients with diabetes that are relatively simple and cost effective, but which many hospitals do not use. With increasing awareness of these harms that having diabetes presents, there has been a move in the last 10 years or so to address the issues that these often vulnerable patients' experience.

In the UK there has been the formation of the Joint British Diabetes Societies for In-patient Care group (JBDS). This is a collaboration formed in 2009 of senior diabetes health professions made up from representatives of Diabetes UK, the main charity for people with diabetes in the UK; the Association of British Clinical Diabetologists (ABCD), the main organisation in the UK representing diabetes consultants and trainees; and the Diabetes In-patient Specialist Nurse group. Together this group has made major advances in the management of in-patients with diabetes. They have

produced several guidelines that are aimed at the non-specialists who treat the majority of patients admitted to hospital. These guidelines have been widely adopted or adapted across the UK and further afield. Some of these guidelines are discussed in this thesis. More recently, in the United States, where the health economy is more fragmented than in the UK, a group of endocrinologists has come together to address the issues as well, calling the consortium they have formed Planning Research in In-patient Diabetes (PRIDE) [13].

This thesis is a personal journey through my own involvement with in-patient diabetes over the last few years. In particular, it will focus on the areas that I have been involved with. In each chapter I will outline the background and history of what had gone before, and move on to why the work presented was undertaken. After describing what each paper added to the literature, each presented manuscript will then be analysed to suggest how the care for people with diabetes in hospital has changed as a direct or indirect result of the work. Of course, with the benefit of hindsight, one would always like to have done things differently, and where this is the case, these will be discussed. Finally, at the end of each discussion there is a short section of what further work could be undertaken as a result of the paper presented. As stated, my hypothesis is that some of the work that I have done and contributed to has helped to improve that care of hospital in-patients with diabetes.

As with many areas of health care, change is a gradual process and in many instances the goals change as more evidence emerges. However, how the work presented fits into these changes will be discussed.

A Brief History of Treating In-patients with Diabetes

Diabetes Related Emergencies

Type 1 Diabetes – the Pre-Insulin Era

Diabetes, with its symptoms of polydipsia, polyuria and loss of weight, was first described by Aretaeus of Cappadocia, as a ‘melting of the flesh into urine’ [14]. For most of human history, type 1 diabetes was universally fatal within a few months of initial diagnosis. One of the earliest descriptions of ‘the diabetic coma’ in the ‘modern’ era was from 1886 [15]. In it the author – a German pathologist – described how, for those individuals who developed type 1 diabetes, life was miserable, and usually very short. It had previously been recognised that fasting (or rather, enforced rationing) had relieved the glycosuria of diabetes during the German siege of Paris in 1870 and this led to the development of severe, carbohydrate free diets. By the end of the 19th Century several eminent diabetes specialists such as Fredrick Allen in the USA, or Bernard Naunyn in Germany, managed to keep people alive for a few months, or even a year or two on these strict, unpalatable regimens of a combination of alcohol, laxatives, castor oil, citrate of potassium, caffeine and other ‘circulatory stimulants’ [16]. All of this changed almost overnight with the discovery of insulin in 1922 by Fred Banting and Charles Best [17].

The discovery of insulin in 1922-23 was possibly the greatest medical breakthrough of the 20th Century. What dogged those pioneering physicians who were ‘early adopters’ of the new ‘wonder drug’ was how to use it – how often, how much, and so on, and how to balance the glucose lowering effects with the risks of going too low or not administering enough to prevent ketosis. It was on this background that the management of diabetic ketoacidosis (DKA) evolved.

High Dose Insulin

An early report on the management of DKA during the first 20 years after the availability of insulin documented that between January 1923 and August 1940 12% of patients died if they presented with DKA. The report stated that they were given, on average, 237 units of insulin in the first 24 hours – with a mean of 83 units being given in the first 3 hours [18]. The author went on to report that between August 1940 and May 1944, only 1.6% of patients died, and the average insulin dose given in the first 24 hours was 287 units (range 50 to 1770 units), with a mean of 216 units being given in the first 3 hours [18]. Thus, high dose insulin treatment for the management of DKA became the ‘norm’. In 1949, Black and Malins from Birmingham reported a case series of 170 consecutive cases of DKA treated with an average of 265 units (range 140 and 500 units) of intravenous insulin for those who were drowsy but rousable, an average of 726 units (range 250 to 1400 units) for those who were rousable with difficulty, and an average of 870 units (range 500 to 1400 units) for those who were unconscious on admission [19]. What was lacking, of course in those very early reports was aggressive fluid management. Black and Malins reported that they would usually give ‘a pint [568 mls] of saline over 15 – 30 minutes, followed by a second pint given at the same rate, and then perhaps a third, followed by 5% glucose given at a pint per hour’ [19]. They were, however, also amongst the first to describe a classification of severity for DKA, something that the American Diabetes Association continues to advocate [20].

Low Dose Insulin and Aggressive Fluid Replacement

In the very early days after insulin had been discovered, it was initially in short supply meaning that small doses were used to treat DKA [21]. However, as insulin became

more widely available, the high dose regimen described previously took over as the accepted standard of care. Early work had showed that low dose insulin infusions worked as well as high dose infusions [22,23]. However, it was not until Sönksen et al in 1972 [24], Alberti et al in the same year [25], and subsequently Kidson et al [26] and Page et al [27] in back to back publications in the British Medical Journal who showed that low dose insulin infusions given intravenously, adequately lowered ketone and glucose concentrations. It was only after these publications that low dose regimens were put into every day practice. The doses used were 1.2 to 9.6 units per hour from Kidson et al, and a fixed rate of 6 units per hour from Page et al. In addition, the 6 units per hour that Kidson et al administered resulted in a plasma insulin concentration of ~100 $\mu\text{U/ml}$. This was compared with a pancreatic output in a healthy individual of ~40 – 50 $\mu\text{U/ml}$ [26]. Further work by Alberti et al [28] prompted Kitabchi et al and Sacks et al in the USA to undertake some of the first randomised trials comparing low dose vs high dose based on these data [29,30]. Further seminal work by Kitabchi et al established that there was no role for the routine use of phosphate or bicarbonate replacement in DKA [31,32].

The weight based fixed rate intravenous insulin infusion (FR_{III}) has also now been used successfully for several decades [20,33]. The concept of an FR_{III} is well established in paediatric diabetes [34], and the question often arises ‘when does a child become an adult’?

What was still missing from the report by Kidson et al was the fluid replacement regimen. Page et al comment that they gave 3.66L (range 1.5 to 6L) in the first six hours, and a mean of 5.5L (range 2.75 to 9L) in the first 12 hours. Thus an

aggressive fluid regimen given together with a low dose intravenous insulin infusion regimen became the standard of care for the management of DKA for the next 4 decades.

Ketone and Venous Blood Gas Measurement

In 1972 it was Hockaday and Alberti who suggested that a plasma ketone body concentration of greater than 3mmol/L would equate to 'severe' acidosis [35]. However, the technology needed to measure ketones meant that it was not routinely available. The development of urine ketone monitoring was a major advance, and the recommended standard of care when monitoring the treatment of DKA [36]. As the physiology of ketosis became better understood, it became apparent that whilst urine ketone sticks detected aceto-acetic acid, it was poor at detecting β -hydroxybutyrate, the predominant ketone in the blood. With the advent of hand held bedside ketone monitoring equipment [37], and the better understanding that the pathological problem in DKA is the ketosis/acidosis rather than the hyperglycaemia [38], the management of DKA continued to be refined. An example of this is the evidence that the difference between arterial and venous pH and bicarbonate is not large enough to alter management and is far less invasive for the patient [39-41]. This has led the UK guidelines to recommend that venous blood gasses be used for monitoring of treatment once a diagnosis of DKA has been made [42].

Type 2 Diabetes and Hyperosmolar Hyperglycaemic Syndrome – the Pre-Medication Era

What we now know as type 2 diabetes was initially described in the late 1600's as a condition associated with the 'upper classes', and in particular to those who were

described as 'corpulent'. But it was in 1886, during the Bradshawe lecture delivered by Dreschfeld in 1886, that he described 3 types of diabetic coma [15]. The first one he described as a gradual coma that is in older adults (age > 40 years) in overweight adults without the characteristic acetone breath or acetone in the urine. The second form was that of alcoholic ketosis, where nothing was noted to be abnormal about the breathing, but large quantities of sugar in the urine. The final form (described later) was that of "coma from acetonemia" [15].

Subsequently increasing reports of this form of diabetic coma appeared in the literature [43,44]. After these cases, several authors described diabetic coma in which polydipsia, polyuria was accompanied by hyperglycemia but without the characteristic Kussmaul breathing seen in DKA [45-48]. Unlike patients with DKA, there were no ketones or beta-hydroxybutyrate. In addition, these patients were 'stout' [15], and very physically unlike those with the characteristics of DKA, rapid weight loss and Kussmaul breathing with the smell of acetone on their breath [45]. The full extent of the metabolic derangements seen with HHS were not fully described till the 1950's [49,50]. In these papers, the authors reported the severe hyperglycemia accompanied by osmotic diuresis but without ketonuria. They also suggested measurement of electrolytes such as sodium and chloride and that the treatment of this condition should be large quantities of fluid, with only a little insulin [50].

It was only around that time, in about 1955, that the first oral medications became available to treat type 2 diabetes, the sulfonylureas. These were developed as a result of the profound hypoglycaemia that was noted to occur in some soldiers given

sulpha containing antibiotics during World War 2. The other widely used agent, metformin was discovered in 1922, but was only used to treat humans in 1957 [51].

But despite the availability of oral agents that could treat type 2 diabetes, these relatively expensive drugs meant that many people remained at risk of hyperglycaemic emergencies. In 1971 Gerich et al [52] then Arieff and Carroll [53] described the diagnostic criteria for HHS and coined the term hyperglycemic hyperosmolar nonketotic coma (HHNK or HONK). These criteria have been subsequently revised and updated by the American Diabetes Association [20].

In the UK DKA and HHS are considered different conditions and thus have different management guidelines [42,54]. In the USA, the management of DKA and HHS has been amalgamated into a single pathway [20]. A comparison between the approaches to treatment between the UK and the USA has recently been published [55].

The Diabetes Specialist Team

Over the last thirty years diabetes has developed into a medical speciality in its own right. Many of the people who were appointed in the 1970's and 1980's as 'General physicians with an interest in diabetes' have now been overtaken by 'Consultants in diabetes and general medicine'. This shift, whilst apparently minor, has had implications for the management of patients with diabetes in general, but in particular for those presenting with diabetes related emergencies. It was demonstrated in the late 1990's that when a patient with DKA was looked after by a doctor specialising in diabetes, their outcomes were better than when compared to the care given by

'general physicians' [56]. With the advent of the Diabetes In-patient Specialist Nurse [57], there has been a wholesale move towards diabetes care being delivered by the specialist diabetes team. As such diabetes specialist nurses in particular provide a valuable service to people with diabetes and act as a vital link between hospital services, primary care and the patients themselves [58]. Indeed, with the recent implementation of the Best Practice Tariff for DKA, there is now a financial incentive for hospitals to provide such a service [59].

Diabetes in In-patients

Those Known to Have Diabetes

The prevalence of diabetes in the general population of Western Europe is in the region of 6-7%. This is expected to rise significantly over the next 20-30 years [6]. The prevalence in other parts of the world is much higher, in the United States the prevalence of diabetes is reported to be between 9.3% and 10.9% [6,60]. It has been recognised that having diabetes more than doubles the risk of being hospitalised for any given condition [9]. This is reflected in the high prevalence of diabetes in hospitalised patients. Data from the 2016 UK National Diabetes In-patient Audit (NaDIA) showed that the prevalence of hospital in-patients with diabetes ranged from 4% to over 35% [2]. Previous work has shown that people with diabetes have a longer length of hospital stay and higher mortality rates than those without the condition [12]. This translates to greater costs. In the UK it has been estimated that diabetes accounts for over 10% of the entire budget of the National Health Service, with the excess costs of in-patients with diabetes equating to between £573 million and £686 million per annum [8]. In the USA, data suggests that in 2012, 20% of the

health budget was spent on diabetes, equating to \$245 billion, with over 40% of this being attributed to direct in-patient costs [61].

Those Not Known to Have Diabetes

In addition to those admissions of people who are known to have diabetes prior to admission, there are a number of people with hyperglycaemia who are admitted without a prior diagnosis of diabetes. These include those people not previously known to have diabetes but who continued to have it after they were discharged. However, some patients may develop transient hyperglycaemia (a fasting glucose concentration of >7.0 mmol/l, 126 mg/dl) or a random blood glucose concentration of >11.1 mmol/l, 200 mg/dl) during their in-patient stay which normalises after discharge – so called stress hyperglycaemia [62,63]. Taken together the numbers of people in hospital with either diabetes or transient hyperglycaemia is very large, with observational data reporting a prevalence of between 32% to 38% on general wards [64,65], and between 28 and 80% of patients with critical illness or cardiac surgery [65-67].

Evidence of Harm from In-Hospital Hyperglycaemia and Effect of Glucose Lowering

Prior to the publication of large randomised control trials in the 1990s, it had been well recognised that poor diabetes control in ambulatory people with either Type 1 or Type 2 diabetes was associated with poor outcomes. It was only with the publication of the DCCT [4] and UKPDS [68] that it was shown that interventions to improve glycaemic control maintained over many years were associated with improved outcomes. In the world of in-patient diabetes, there is compelling evidence that high blood glucose concentrations are associated with a higher in-hospital morbidity and

mortality, prolonged length of stay, unfavourable post-discharge outcomes and significant excess health care costs in medical and surgical specialities [11,64,69-71]. Umpierrez et al. showed that patients with new hyperglycaemia had a striking 18-fold increase in in-hospital mortality, while patients with known diabetes had a 2.7-fold increase in in-hospital mortality, when compared with normoglycaemic patients [64]. In 2004, a joint position statement from the American College of Endocrinology and the American Association of Clinical Endocrinologists on in-patient diabetes and metabolic control concluded that hyperglycaemia in hospitalised patients is a common, serious and costly health care problem. There was a strong recommendation for early detection of hyperglycaemia and an aggressive management approach to improve outcomes [9]. In the UK, JBDS have produced a series of guidelines in managing various aspects of in-patient diabetes care, which also recommend aggressive glucose control [72].

For surgical patients, there are data to show that hyperglycaemia in the peri-operative period is associated with poor outcomes in several surgical specialities [11,71,73]. These can be measured as a variety of outcomes, such as length of hospital stay, development of urinary tract infections, surgical site infections, time in the intensive care unit, and mortality. The reasons for these adverse outcomes are multi-factorial, but includes failure to identify patients with diabetes and/or hyperglycaemia [74]; multiple co-morbidities including microvascular and macrovascular complications [75-78], complex polypharmacy and insulin prescribing errors [79]; increased perioperative and postoperative infections [11,80,81]; associated hypoglycaemia and hyperglycaemia [11]; lack or inadequate institutional guidelines for management of in-patient diabetes and/or hyperglycaemia [11,82]; and

inadequate knowledge of diabetes and hyperglycaemia management amongst staff delivering care [83].

There are also data to show that having a diagnosis of diabetes prior to having surgery is associated with a lowering of risk [71]. This lowering of risk is despite having a high glucose concentration. Thus the knowledge that a patient has diabetes is somehow protective. It may well be that patients with diabetes have more attention paid to them, and thus have more contact with nursing and medical staff. This may mean that post-operative problems are picked up sooner. What remains to be determined is whether it is the high glucose concentrations per se that causes the increased harm, or whether the high glucose is a marker for underlying disease severity.

Whilst there are reasonably robust data showing that high peri-operative glucose concentrations are associated with harm, the data showing an association with high pre-operative HbA_{1c} is currently lacking [84]. There are very few good quality prospective observational studies in the area of preoperative glycaemic control – as measured by HbA_{1c} – as a predictive factor of postoperative morbidity and mortality. Recent work has suggested that risks increase when pre-operative HbA_{1c} is greater than 64 mmol/mol (8%), and the UK JBDS guideline also recommends a pre-operative concentration of less than 69 mmol/mol (8.5%) [73].

Disappointingly, to date, despite the findings that high glucose concentrations are associated with harm for medical and surgical patients, except for a very few clinical specialities such as cardiac surgery and, more recently liver transplant surgery, there

is yet to be any convincing evidence to show that achieving good glycaemic control whilst an in-patient is associated with improved outcomes [85].

Variations in Care

Over time, whilst there has been significant progress in the 'broad brush' of how diabetes should be treated in an attempt to prevent harm in the short and long term, what has remained is the variation in the small details on how these broad themes should be achieved. For example, it is accepted that lower glucose concentrations are associated with better long term outcomes, but how should one achieve them? The pharmaceutical companies develop newer agents, but the US Food and Drug Administration only mandates that a new product should lower HbA_{1c} when compared to placebo or metformin (a surrogate marker for outcomes [86]), and that they do not mandate that any newer agent should be compared to other drug classes. Because large scale trials of new agents are expensive, (and of course there is the risk that doing a comparative trial may show that the competitors' drug is better!), and because there is no regulatory need to conduct such trials pharmaceutical companies do not commonly do them. This means that when national and international guidelines are developed, because there are little data comparing drug classes directly, all of the different classes become 'second line' agents after metformin [87,88].

Similarly with in-patient diabetes, currently there are a lot of data to show that hyperglycaemia in in-patients is associated with harm, but there are almost no data (other than in those undergoing cardiac surgery or liver transplant surgery) that

achieving glucose concentrations similar to those without dysglycaemia is associated with any benefit [85].

On this background, there have developed differences in care pathways in how an outcome should be achieved. This variation is thought to be part of the reason why outcomes are different in different geographical locations when dealing with the same condition – not just in diabetes [89-91], but for a wide variety of conditions [92]. Variation in care was one of the factors that were found to be responsible at the public inquiry into the increased mortality rate found at the Mid Staffordshire NHS Foundation Trust (the Francis Report). They reported that “Commissioners.....must insist on quality and challenge the inefficiencies of providers, particularly unevidenced variations in clinical practice” [93].

For in-patient diabetes very little ‘formal’ data exist on variations of care. However, anecdotally, from my own experience as a medical registrar it was common for me when I moved from one hospital to the next to be asked by my consultant to ‘re-write the DKA guideline’. My question was always ‘Why? What is wrong with the current one?’ There was never a satisfactory answer and moving between several hospitals as part of my registrar training it became clear that whilst most of the guidelines were very similar (fluids, insulin, and potassium replacement), there were subtle variations between hospitals, often based on the consultants’ (largely non-evidence based) preferences. There was no data to show that the outcomes from one hospital were any different from the neighbouring hospitals, because a) no-one did that form of comparison, and b) the small differences made them difficult to compare because very large numbers would be needed to tease out what was better out one guideline

compared to any other. Thus, it was clear that harmonisation of treatment was needed. I believe that this is one of the reasons why the guidelines produced by the JBDS have been so welcomed, and so quickly adopted (or adapted) across the UK, and other parts of the world.

There remain some differences however, across the world. In particular the management of DKA and HHS is subtly different in the USA compared to the UK [20,42,55]. However, I strongly believe that the US DKA guideline is outdated and is in need of revision. I believe that it should move towards the UK guideline in many respects – something that a senior author on the US guideline has recently acknowledged with me [94].

Where Are We Now?

By the late 1990's and early 2000's there was a consensus to show that the best way to treat DKA was with aggressive fluid management and a low dose intravenous insulin infusion. HHS was treated differently due to the greater age, and lower physiological reserve of the patients, as well as the presence of co-morbidities. With DKA, it was agreed that regular monitoring of blood gases aided management decisions. For both conditions, it was also recognised that electrolyte deficiencies were common and that for some – potassium in particular – replacement was necessary. What there was no consensus about, however, was how much fluid, which fluid, how much insulin, in DKA, whether to use venous or arterial gases, how much potassium, bicarbonate yes or no, phosphate yes or no, and so on. Thus it was often left to individual hospitals to come up with their own DKA and HHS guidelines (and for the incoming registrar to rewrite them!). It was in 2006 that the

Association of British Clinical Diabetologists (ABCD) asked two leading clinicians to construct a set of guidelines that would form the basis of standardised treatment regimen for DKA [95]. It quickly became clear that there was an appetite for such a document, for use by those at the 'front door'. However, it needed to be more detailed and more evidence based for emergency teams to accept its use. It was at this time that the Joint British Diabetes Societies In-patient Care Group was also formed. A collaboration between ABCD, Diabetes UK, and the National Diabetes In-patient Nurse Group it was made of individuals interested in in-patient care. The authors of the initial ABCD DKA guideline were joined by others and a more comprehensive document was written [42], and then revised in 2013 [96]. The JBDS also then wrote a guideline for HHS [54].

The use of the updated DKA guideline was surveyed in 2014 and it showed that most hospitals in the UK use them [97,98].

For DKA and HHS, there remain areas of controversy, and the guidelines are dynamic documents that will be updated in due course as and when new data become available.

Much of the work in this chapter has come from two of my publications [99,100]. Permission to reproduce sections are shown.

Dhatariya Ketan (RM1) Norfolk and Norwich University Hospital

From: Gregory Rob - Diabetes Consultant <Rob.Gregory@uhl-tr.nhs.uk>
Sent: 08 September 2016 17:51
To: Dhatariya Ketan (RM1) Norfolk and Norwich University Hospital;
editor.bjdv@diabetologists.org.uk; p.narendran@bham.ac.uk
Cc: Kong Marie-France - Consultant Physician Diabetes & Endocrinology, Walton, Chris
Subject: RE: request to publish a paper in a PhD thesis please

Dear Ketan,

I am sure Chris and I gave permission as directors of BJDM did a few months ago. I am copying to relevant editorial staff. Do you need a letter on headed note paper or what?

Regs,
Rob

From: Dhatariya Ketan (RM1) Norfolk and Norwich University Hospital | <mailto:ketan.dhatariya@nnt.nhs.uk>
Sent: 08 September 2016 16:27
To: editor.bjdv@diabetologists.org.uk; p.narendran@bham.ac.uk
Cc: Gregory Rob - Diabetes Consultant
Subject: RE: request to publish a paper in a PhD thesis please

Hello

I sent you this email a few months ago and you said that you'd send it to me, but I have not heard from you. It is now getting a bit more urgent. Could I ask you to let me know whether I can reproduce this paper ASAP please.

Rob, I am copying you in as you will know more as to what is happening at the journal at the tool, and who can give permissions – please see my email below

Kind regards

Ketan

Dr Ketan Dhatariya
Consultant in diabetes, endocrinology and general medicine
Helen Ewart Diabetes Centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Conyng Lane
Norwich
NR4 7UY
Tel: 44 1603 288170
Fax: 44 1603 288434

From: Dhatariya Ketan (RM1) Norfolk and Norwich University Hospital
Sent: 05 June 2016 09:09
To: 'editor.bjdv@diabetologists.org.uk'; 'p.narendran@bham.ac.uk'
Subject: request to publish a paper in a PhD thesis please

Hello,

Re: Dhatariya K (2015); The evolution of DKA management. Br J Diabetes Vasc Dis 15: 31-33

I'm not sure who to ask about this. I am writing a PhD by publication on the management of diabetes in hospital inpatients and would like to include this paper in my thesis. I am writing for permission to reprint the entire paper in my thesis. The distribution will be limited to a copy to the University of East Anglia Library, a copy to my supervisor and one for me.

**JOHN WILEY AND SONS LICENSE
TERMS AND CONDITIONS**

Apr 04, 2017

This Agreement between Ketan Dhatariya ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

The publisher has provided special terms related to this request that can be found at the end of the Publisher's Terms and Conditions.

License Number	4047690860629
License date	
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Wiley Books
Licensed Content Title	Textbook of Diabetes, 5th Edition
Licensed Content Author	Richard I. G. Holt (Editor), Clive Cockram (Editor), Allan Flyvbjerg (Editor), Barry J. Goldstein (Editor)
Licensed Content Date	Feb 1, 2017
Licensed Content Pages	1104
Type of use	Dissertation/Thesis
Requestor type	University/Academic
Format	Print and electronic
Portion	Text extract
Number of Pages	3
Will you be translating?	No
Title of your thesis / dissertation	The management of hospital inpatients with diabetes
Expected completion date	Jan 2017
Expected size (number of pages)	300
Requestor Location	Ketan Dhatariya Elsie Bertram Diabetes Centre Norfolk and Norwich University Hospital Colney Lane Norwich, other NR4 7UY United Kingdom Attn: Ketan Dhatariya
Publisher Tax ID	EU826007151
Billing Type	Invoice
Billing Address	Ketan Dhatariya Elsie Bertram Diabetes Centre Norfolk and Norwich University Hospital Colney Lane Norwich, United Kingdom NR4 7UY Attn: Ketan Dhatariya
Total	0.00 GBP

List of Publications – to August 2017

Many of the papers that are listed in this bibliography are not discussed in this thesis.

Those publications that are in *italics* are related to in-patient diabetes care, and those publications which are underlined are included in this thesis. A line has been added to explain why the papers that are in italics have been included in this thesis.

Almost none of my work on the ‘diabetic foot’ has been included in this thesis, because much of it is not relevant to the in-patient setting. In addition, the majority of the work that I did as a research fellow at the Mayo Clinic between 2001 and 2003 is not applicable to in-patients.

Original Peer Reviewed Papers

1. **Dhatariya K**, Bigelow, ML, Nair KS. The effect of dehydroepiandrosterone replacement on insulin sensitivity and lipids in hypoadrenal women. *Diabetes* 2005;54(3):765-769
2. Nair KS, Rizza RA, O’Brien P, **Dhatariya K**, Short K, Nehra A, Vittone J, Klee G, Basu A, Basu R, Cobelli C, Toffolo G, Dalla Man C, Tindall D, Melton III LJ, Smith G, Khosla S, Jensen M. DHEA in elderly women and DHEA or testosterone in elderly men. *New England Journal of Medicine* 2006;355(16):1647-1659
3. Sampson MJ, Crowle T, **Dhatariya K**, Dozio N, Greenwood RH, Heyburn PJ, Jones C, Temple RC, Walden E. Trends in bed occupancy for in-patients with diabetes before and after the introduction of a diabetes in-patient specialist nurse service. *Diabetic Medicine* 2006;23(9):1008-1015

These data showed the beneficial impact of a dedicated diabetes in-patient specialist nurse in terms of reducing bed occupancy.

4. Sampson MJ, Dozio N, Ferguson BA, **Dhatariya K**. Total and excess bed occupancy by age, specialty and insulin use for nearly one million diabetes patients discharged from all English Hospitals. *Diabetes Research Clinical Practice* 2007;77(1):92-98

These data showed the absolute excess hospital bed occupancy in England for people with diabetes compared to those without diabetes.

5. Sampson MJ, Brennan C, **Dhatariya K**, Jones C, Walden E. A national survey of in-patient diabetes services in the UK. *Diabetic Medicine* 2007;24(6):643-649

These data showed the paucity of speciality in-patient diabetes services across the UK.

6. Karakelides H, Asmann YW, Bigelow ML, Short KR, **Dhatariya K**, Coenen-Schimke J, Kahl J, Mukhopadhyay D, Nair KS. Effect of insulin deprivation on muscle mitochondrial ATP production and gene transcript levels in type 1 diabetic subjects. *Diabetes* 2007;56(11):2683-2689
7. **Dhatariya KK**, Greenlund JL, Bigelow ML, Thapa P, Oberg A, Ford GC, Schimke JM, Nair KS. DHEA replacement therapy in hypoadrenal women: Protein anabolism and skeletal muscle function. *Mayo Clinic Proceedings* 2008;28(11):1218-1225
8. **Dhatariya K**. *People with type 1 diabetes using short acting analogue insulins are less dehydrated than those using human soluble insulin prior to onset of diabetic ketoacidosis. Medical Hypotheses* 2008;71(5):706-708
9. Henderson GC, **Dhatariya K**, Ford GC, Klaus KA, Basu R, Rizza RA, Jensen MD, Khosla S, O'Brien P, Nair KS. Higher muscle protein synthesis in women than men across the lifespan, and failure of androgen administration to amend age-related decrements. *FASEB Journal* 2009;23(2):631-641
10. Srinivasan M, Irving BA, **Dhatariya K**, Klaus KA, Hartman SJ, McConnell JP, Nair KS. Effect of dehydroepiandrosterone replacement on lipoprotein profile in hypoadrenal women. *Journal of Clinical Endocrinology and Metabolism* 2009;94(3):761-764
11. Sampson MJ, Singh H, **Dhatariya K**, Jones C, Walden E, Bradley C. A novel psychometrically validated diabetes treatment satisfaction questionnaire for in-patients (DTSQ-IP) to assess in-patient diabetes care. *Diabetic Medicine* 2009;26(7):729-735

These data described the development of the first validated diabetes treatment satisfaction questionnaire for hospital in-patients.

12. *Bhupal E, Darkins A, **Dhatariya K**. Differential effects of intravenous and subcutaneous insulin sliding scales in a tertiary care setting. *Journal of Diabetes Nursing* 2009;13(5):170-175*
13. *Stansby G, Wealleans V, Wilson L, Morrow D, Gooday C, **Dhatariya K**. Clinical experience of a new NPWT system in diabetic foot ulcers and post-amputation wounds. *Journal of Wound Care* 2010;19(11):496-502*
14. *Savage MW, **Dhatariya KK**, Kilvert A, Rayman G, Rees JAE, Courtney CH, Hilton L, Dyer PH, Sinclair Hamersley M for Joint British Diabetes Societies (JBDS). Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. *Diabetic Medicine* 2011;28(5):508-515*

This is the first edition of the national guideline for the management of DKA.

15. Lopez M-J, Fletcher T, Armstrong B, Genser B, **Dhatariya K**, Mondal D, Ducatman A, Leonardi G. Association of Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS) with age of puberty among children living near a chemical plant. *Environmental Science & Technology* 2011;45(19):8160-66

16. Gooday C, Panter K, **Dhatariya K**. Patients' perceptions of a shoe fitting service at a diabetic foot clinic. *Diabetic Foot Journal* 2011;14(1):33-38

17. *Daultrey H, Gooday C, **Dhatariya K**. Increased length of in-patient stay and poor clinical coding in people with diabetes with and without foot disease – a point prevalence study. *Journal of the Royal Society of Medicine Short Reports* 2011;2:83. DOI 10.1258/shorts.2011.011100*

These data showed that in-patients with diabetes were in hospital for longer than their counterparts without diabetes who had the same reasons for admission, but also that clinical coding was poor.

18. Murray NJ, Abadi S, Blair A, Dunk M, Sampson MJ, On behalf of the **Norfolk Diabetes Prevention Study Group**. The importance of type 2 diabetes prevention: The Norfolk Diabetes Prevention Study. *British Journal of Diabetes & Vascular Disease* 2011;11(6):308-13

19. Curtis P, Sampson M, Potter J, **Dhatariya K**, Rimm EB, Kroon PA, Cassidy A. Chronic ingestion of flavan-3-ols and isoflavones improves insulin sensitivity and lipoprotein status and attenuates estimated 10-year CVD risk in medicated postmenopausal women with type 2 diabetes: a one year double-blind randomized controlled trial. *Diabetes Care* 2012;35(2):226-32

20. ***Dhatariya K, Levy N, Kilvert A, Watson B, Cousins D, Flanagan D, Hilton L, Jairam C, Leyden K, Lipp A, Lobo D, Sinclair-Hammersley M, Rayman G. NHS Diabetes guideline for the peri-operative management of the adult patient with diabetes. *Diabetic Medicine* 2012;29(4):420-433***

This is the first edition of the national guideline for the peri-operative management of adult patients with diabetes undergoing surgery.

21. *Evans NR, Richardson L, **Dhatariya KK, Sampson MJ. Diabetes specialist nurse telemedicine: admissions avoidance, costs and casemix. *Practical Diabetes* 2012;29(1):25-28***

22. Bharathy K, Bachmann MO, Murray N, **Dhatariya K**, Fenech M, John WG, Scarpello TJ, Sampson MJ. Use of haemoglobin A_{1c} to detect impaired fasting glucose or Type 2 diabetes in a United Kingdom community based population. *Diabetes Research and Clinical Practice* 2012;96(2):211-216

23. *Evans NR, **Dhatariya KK. Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. *Clinical Medicine* 2012;12(2):137-139***

These data showed that in an unselected cohort of emergency medical admissions glucose concentrations on admission were significantly related to outcomes – length of hospital stay, 28 day readmission rates and mortality at 28 days.

24. Chitale A, Musonda P, McGregor AM, **Dhatariya K**. Determining the utility of the 60 minute cortisol measurement in the short synacthen test. *Clinical Endocrinology* 2013;79(1):14-19
25. Rudd B, Levy N, Patel K, **Dhatariya K**. A Survey of the implementation of the NHS Diabetes Guidelines for management of Diabetic Ketoacidosis in the Critical Care Units of the East of England. *Journal of the Intensive Care Society* 2013;14(1):60-64

These data showed that many intensive care units across the East of England had not yet adopted the national DKA guideline.

26. Gooday C, Hallam C, Sieber C, Mtariswa L, Turner J, Schelenz S, Murchison R, Messenger G, Morrow D, Hutchinson R, Williams H, **Dhatariya K**. The development of an antibiotic formulary for a tertiary care foot clinic: Admission avoidance using intramuscular antibiotics for the treatment of borderline foot infections in people with diabetes. *Diabetic Medicine* 2013;30(5):581-589

These data challenged the accepted wisdom of the Infectious Diseases Society of America that there were only a limited number of categories to define severity of infection, and at the same time creating a new treatment paradigm to promote admissions avoidance for patients with moderate-to-severe diabetes related foot infection.

27. Rutter C, Jones C, **Dhatariya K**, James J, Irvine L, Wilson EC, Singh H, Walden E, Holland R, Harvey I, Bradley C, Sampson MJ. Determining UK in-patient diabetes treatment satisfaction – The DIPSat programme. *Diabetic Medicine* 2013;30(6):731-738

These data used the newly validated diabetes in-patient treatment satisfaction questionnaire to assess what patients felt their treatment was like.

28. **Dhatariya K**. Should in-patient hyperglycaemia be treated? *BMJ* 2013;346:f134

This paper went through the evidence to show that hyperglycaemia in hospitalised in-patients is associated with harm (however that is measured), but also highlighted the lack of data to show that 'normalising' glucose concentrations was associated with any reduction in harm.

29. Curtis PJ, Potter J, Kroon PA, Wilson P, **Dhatariya K**, Sampson MJ, Cassidy A. Vascular function and atherosclerosis progression following 1 year flavonoid intake in statin treated postmenopausal women with type 2 diabetes: a double-blind randomized controlled trial. *American Journal of Clinical Nutrition* 2013;97(5):936-942
30. Murchison R, Gooday C, **Dhatariya K**. The development of a Charcot foot after significant weight loss in people with diabetes – 3 cautionary tales. *Journal of the American Podiatric Medical Association* 2014;104(5):522-525
31. **Dhatariya K**. Diabetes related emergencies. *Student BMJ* 2013;21:f3825

32. **Dhatariya K.** Admission avoidance using intramuscular antibiotics for the treatment of borderline foot infections in people with diabetes in a tertiary care foot clinic. *BMJ Quality Improvement Reports* 2013;2:1
33. Gooday C, Murchison R, **Dhatariya K.** Assessing the economic impact of a podiatrist – analysis of clinic activity after temporary loss of 50% of the podiatrists from a tertiary specialist foot clinic *Diabetic Foot and Ankle* (<http://diabeticfootandankle.net/index.php/dfa/article/view/21757>)

This paper showed the importance of specialist diabetes podiatrists in admissions avoidance, and that a single podiatrist can pay for themselves by preventing just one amputation per year.

34. Howieson A, Brunswicker A, **Dhatariya K.** An assessment of current perioperative practice and a review of the literature of patients with diabetes undergoing knee replacement surgery. *Journal of the Royal Society of Medicine Open* 2014;5(2):1-6
35. Gooday C, Murchison R, **Dhatariya K.** Complex relationships requiring long-term follow-up: Obesity, bariatric surgery-induced diabetic remission, and the diabetic foot. *Diabetic Foot Journal* 2014;17(1):20-24
36. Swafe L, Narmani V, Stavrika C, **Dhatariya K.** How frequently are bedside glucose levels measured in hospital in-patients on glucocorticoids? *Clinical Medicine* 2014;14(3):327-328

These are the first data to show the prevalence of in-patient corticosteroid use and how infrequently bedside or laboratory glucose concentrations are measured.

37. **Dhatariya K.** In-patient glucocorticoid use – Beneficence Vs. Nonmaleficence. *British Journal of Hospital Medicine* 2014;75(5):252-256
38. Challis BG, Harris J, Sleigh A, Issac I, Orme SM, Seevaratnam N, **Dhatariya K**, Simpson HL, Semple RK. Familial adult onset hyperinsulinism due to an activating glucokinase mutation: Implications for pharmacological glucokinase activation. *Clinical Endocrinology* 2014;81(6):855-861
39. Gooday C, Murchison R, **Dhatariya K.** Complex relationships requiring long-term follow-up: Obesity, bariatric surgery-induced diabetic remission, and the diabetic foot. *Diabetes in Practice* 2014;3(2):59-67
40. Geiker,N, Myint KS, Heck P, **Dhatariya K**, Larsen S, Andersen M, Stender S, Torp-pedersen C, Finer N, Astrup A. Effect of intentional weight loss on physical and cardiac performance in obese patients with ischaemic heart disease: A two centre intervention trial. *Journal of Food and Nutrition* 2014;1(1):3
41. Murchison R, Gooday C, **Dhatariya K.** Is septic arthritis arising from a diabetic foot wound a diagnosis that we should consider more often? *Diabetic Foot Journal* 2015;18(1):14-18
42. Srinivas V, **Dhatariya K.** Hypoglycaemia in the elderly. *GM2* 2015;45(4):17-19

43. Haddadin F, Clark A, Evans N, **Dhatariya K**. Admission blood glucose helps predict one year, but not two year, mortality in an unselected cohort of acute general medical admissions. *International Journal of Clinical Practice* 2015;69(6):643-648

These data build on previous work to show that that in an unselected cohort of emergency medical admissions glucose concentrations on admission were strongly related to outcomes at 1 year.

44. Scott A, on Behalf of the **Joint British Diabetes Societies (JBDS) for In-patient Care**. Management of hyperosmolar hyperglycaemic state in adults with diabetes. *Diabetic Medicine* 2015;32(6):714-724

This is the first edition of the national guideline for the management of HHS.

45. Gu Y, Kokar C, Gooday C, Morrow D, **Dhatariya K**. A 5-year follow-up study to assess clinical outcomes of patients with diabetes undergoing lower limb angiography for significant peripheral artery disease. *Diabetes Therapy* 2015;6(4):481-493
46. Barker P, Creasey PE, **Dhatariya K**, Levy N, Lipp A, Nathanson MH, Penfold N, Watson B, Woodcock T. Perioperative management of the surgical patient with diabetes 2015. *Anaesthesia* 2015;70(12):1427-1440
47. English E, Smith G, Idris I, Dhatariya K, John WG, Kilpatrick E. The effect of anaemia on HbA_{1c} analysis: A systematic review. *Diabetologia* 2015;58(7):1409-1421
48. **Dhatariya K**. Oral versus intravenous antibiotics for moderate infections in diabetic foot wounds: what are the considerations? *Diabetic Foot Journal* 2015;18(4):198-202
49. Rollins KE, Varadhan KK, **Dhatariya K**, Lobo D. Systematic review of the impact of HbA_{1c} on outcomes following surgery in patients with diabetes mellitus. *Clinical Nutrition* 2016;35(2):308-316

These authors systematically reviewed the relationship between peri-operative HbA_{1c} and surgical outcomes showing that it was relatively poor, but very likely due to the heterogeneity of studies and the way the data were collected.

50. **Dhatariya K**, Nunney I, Iceton G. Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. *Diabetic Medicine* 2016;33(2):269-270

These were the first data collected on a national basis on what facilities individual diabetes team had to management adult patients presenting with DKA.

51. **Dhatariya K K**, Nunney I, Higgins K, Sampson MJ, Iceton G. A national survey of the management of diabetic ketoacidosis in the UK in 2014. *Diabetic Medicine* 2016;33(2):252-260

This was the largest national survey ever conducted on the management of adult patients presenting with DKA

52. Baxter M, Gooday C, **Dhatariya K**. The effect of radiological contrast media on renal function and inflammatory markers in people with diabetes – a clinical study and review. *British Journal of Diabetes and Vascular Disease* 2015;15(4):187-191
53. Zeun P, Gooday C, Nunney I, **Dhatariya K**. Predictors of outcomes in diabetic foot osteomyelitis treated initially with conservative (non-surgical) medical management – a retrospective study. *The International Journal of Lower Extremity Wounds* 2016;15(1):19-25
54. Stark C, Murray T, Gooday C, Nunney I, Loveday D, **Dhatariya K**. 5 year retrospective follow-up of new cases of Charcot neuroarthropathy – a single centre experience. *Foot and Ankle Surgery* 2016;22(3):176-180
55. *Vasilopoulos T, Morey TE, Dhatariya K, Rice MJ. Limitations of significance testing in clinical research: A review of multiple comparison corrections and effect size calculations with correlated measures. Anesthesia and Analgesia* 2016;122(3):825-830
56. Beaney A, Nunney I, Gooday C, **Dhatariya K**. Factors determining the risk of diabetes foot amputations – a retrospective analysis of a tertiary diabetes foot care service. *Diabetes Research Clinical Practice* 2016;114:69-74
57. **Dhatariya K**, Gooday C, Franke B, Piling T, Flanagan A, Zeidan L. An open, non-comparative, multi-centre investigation to evaluate the performance and safety of Mepilex® Transfer Ag on diabetic foot ulcers. *Journal of Wound Care* 2016;25(5):256-265
58. *Edge JA, Nunney I, Dhatariya K. Diabetic ketoacidosis in an adolescent and young adult population in the UK in 2014; national survey comparison of the management in paediatric and adult settings. Diabetic Medicine* 2016;33(10):1352-1359
- These data looked at the on the management of adolescent and young adult patients presenting with DKA used the same methodology for the adult national survey.
59. Essackjee Z, Gooday C, Nunney I, **Dhatariya K**. Indicators of prognosis for admissions from a specialist diabetic foot clinic: A retrospective service improvement exercise. *Journal of Wound Care* 2017; 26(1):40-45
60. Clokie M, Greenway AL, Harding K, Jones NJ, Vedhara K, Game F, **Dhatariya K**. New horizons in understanding of the causes and management of diabetic foot disease. Report from a 2017 Diabetes UK Annual Professional Conference Symposium. *Diabetic Medicine* 2017;34(3):305-315
61. *Charlton R, Murchison R, Gooday C, Dhatariya K. Implementation of a new foot assessment tool for people with diabetes in hospital. Diabetic Foot Journal* 2017;20(1):24-28
62. *Varadarajan M, Patel M, Kakkar N, Li Ping Wah-Pun Sin E, Maxey D, Nunney I, Dhatariya K. Are the results from the 2014 national DKA survey applicable to individual centres? Diabetes Research Clinical Practice* 2017;127:140-146

63. Sudlow A, O'Connor HM, Narwani V, Swafe L, **Dhatariya K**. Assessing the prevalence of dexamethasone use and subsequent glucose measurements in an unselected cohort of patients undergoing surgery – a single centre study. *Practical Diabetes* 2017;34(4):117-122
64. Pournaras DJ, Photi ES, Barnett N, Challand CP, Chatzizacharias N, Dlamini N, Doulias T, Foley A, Hernan J, Kumar B, Martin J, Nunney I, Panagiotopoulou I, Shivakumar O, Sengupta N, Sinclair P, Stather P, Than MM, Wells AC, Xanthis A, **Dhatariya K**. Assessing the quality of primary care referrals to surgery of patients with diabetes in the East of England: A multi-centre cross-sectional cohort study. *International Journal of Clinical Practice*. DOI: 10.1111/ijcp.12971
65. **Dhatariya K**, Skedgel C, Fordham R. The cost of treating diabetic ketoacidosis in the UK: a national survey of hospital resource use. *Diabetic Medicine*. DOI:10.1111/dme.13427

Miscellaneous

1. Stanisstreet D, Walden E, Jones C, Graveling A, Amiel S, Crowley C, **Dhatariya K**, Frier B, Malik R. The hospital management of hypoglycaemia in adults with diabetes mellitus. JBDS on behalf of NHS Diabetes. March 2010
This is the first edition of the national guideline for the management of hypoglycaemia.
2. Savage MW, Sinclair-Hammersley M, Rayman G, Courtney H, **Dhatariya K**, Dyer P, Edge J, Evans P, Greenwood M, Hallahan G, Hilton L, Kilvert A, Rees R. Joint British Diabetes Societies In-patient Care Group. The Management of Diabetic Ketoacidosis in Adults. March 2010
This is the first edition of the national guideline for the management of DKA.
3. **Dhatariya K**, Nagi D, Jones TH. ABCD position statement on the management of hypogonadal males with type 2 diabetes. *Practical Diabetes International* 2010;27(9):408-412
4. **Dhatariya K**, Flanagan D, Hilton L, Kilvert A, Levy N, Rayman G, Watson B, Cousins D, Jairam C, Leyden K, Lobo D, Sinclair-Hammersley M. Joint British Diabetes Societies In-patient Care Group. 2011 Management of adults with diabetes undergoing surgery and elective procedures: improving standards.
This is the first edition of the national guideline for the management of adult patients undergoing surgery.
5. Grimsdell R, **Dhatariya K**, Levy N. Management of the surgical patient with diabetes: the role of the ODP. *Technic: The Journal of Operating Department Practice*. Online CPD August 2011.

6. Flanagan D, Watkinson M, **Dhatariya K**, Kilvert A, Cox A, Jenkins C, Baker E, Worthington J, Lamén L, Leivesley K, Balian L, Burke M, Fairburn P, O'Brien S, Davies H, Jacques N, James S. Self-management of diabetes in hospital. Joint British Diabetes Societies for In-patient Care Group. NHS Diabetes. 2012
7. Lobo D, **Dhatariya K**, Levy N, Kilvert A, Watson B, Rayman G, Flanagan D, Hilton L, Cousins D, Jairam C, Leyden K, Sinclair-Hammersley M. The peri-operative management of the adult patient with diabetes. *Issues in Professional Practice*. Association of Surgeons of Great Britain and Ireland Available at http://www.asgbi.org.uk/en/publications/issues_in_professional_practice.cfm
8. Roberts A, Penfold S, Ashton-Cleary S, Banerjee M, Berkeley H, Brooks C, Bruce D, **Dhatariya K**, Dinning L, Eaglesfield B, Gregory S, Hughes T, Kar P, Oyibo S, Robinson N, Sinclair A, Voigt D, Wessels L, Williams J, Rilstone S, Oliver L, Davies H, Hughes S, Jacques N. Glycaemic management during the in-patient enteral feeding of stroke patients with diabetes. Joint British Diabetes Societies (JBDS) for In-patient Care Group. NHS Diabetes. 2012
9. Scott A, Claydon A, Brennan G, Carey P, **Dhatariya K**, Hammersley M, Hanson P, Ritchie S, Savage M, Sinclair A. The Management of the Hyperosmolar Hyperglycaemic State (HHS) in Adults with diabetes. Joint British Diabetes Societies (JBDS) for In-patient Care Group. NHS Diabetes. 2012
10. Ryder REJ, McKnight J, Blann AD, **Dhatariya K**, Gregory R, Robinson AM, Rowles S, Sharp P, Winocour P, Walton C, on behalf of the Association of British Clinical Diabetologists (ABCD). ABCD position statement on GLP-1 based therapies and pancreatic damage. *Practical Diabetes* 2013;30(9):388-391
11. Pintilie H, Petchey W, **Dhatariya K**, Karim M. A collapse with hypertension and hypokalaemia. *BMJ* 2014;349:g6582
12. Dashora U, Gallagher A, **Dhatariya K**, Winocour P, Gregory R. ABCD position statement on the risk of diabetic ketoacidosis with the use of Sodium-Glucose Cotransporter-2 inhibitors. *British Journal of Diabetes* 2016;16(4):206-210

Editorials (* peer reviewed)

1. ***Dhatariya K**. Type 2 diabetes is cardiovascular disease. *Journal of the Royal Society of Medicine* 2003;96(8):371-372
2. ***Dhatariya K**. Is there a role for dehydroepiandrosterone replacement in the intensive care population? *Intensive Care Medicine* 2003;29(11):1877-1880
3. **Dhatariya K**. Androgen replacement in women. *Endocrine News* 2005;30(1):11-12
4. ***Dhatariya K**. Diabetic ketoacidosis. *BMJ* 2007;334(7607):1284-1285

This editorial was the reason I was first invited to be involved in the JBDS guideline on the management of DKA and argues that 0.9% sodium chloride solution should be the fluid replacement of choice in DKA.

5. **Dhatariya K, Kilvert A.** *The new NHS Diabetes guidelines on the peri-operative management of people with diabetes. Practical Diabetes 2011;28(5):200-201*
6. **Dhatariya K.** *Enteral feeding and keeping glucose levels at target. Practical Diabetes 2012;29(4):132*
7. ***Dhatariya K.** *Peri-operative management of adults with diabetes: why do we need guidance? British Journal of Hospital Medicine 2012;73(7):366-367*
8. ***Dhatariya K.** *Does dexamethasone induced hyperglycaemia contribute to post-operative morbidity and mortality? British Journal of Anaesthesia 2013;110(5):674-675*
9. **Dhatariya K.** *Admissions avoidance in diabetes – Guidance from the Joint British Diabetes Societies In-patient Care Group. Practical Diabetes. 2014;31(1):6-7*
10. ***Dhatariya K.** *The use of point of care blood ketone monitors in the management of diabetic ketoacidosis in adults. Annals of Clinical Biochemistry. 2014;51(5):525-527*
11. **Dhatariya K, Fox M.** *Should patients with active foot ulcers be non-weight bearing or take exercise to improve cardiovascular fitness? Diabetic Foot Journal 2014;17(3):92-9*
12. **Srinivas V, Kazmi K, Dhatariya K.** *Hypoglycaemia: Patient inconvenience or serious cardiovascular risk? British Journal of Cardiology 2014;21(4):128-130*
13. **Dhatariya K.** *The evolution of DKA management. British Journal of Diabetes and Vascular Disease 2015;15(1):31-33*
14. **Dhatariya K.** *Pharmacotherapy for type 2 diabetes in very elderly patients: Practicing nihilism or pragmatism? Age and Ageing 2015;44(4):540-542*
15. **Dhatariya K.** *The management of diabetic ketoacidosis in the UK in 2014 – results of a national survey. Journal of Diabetes Nursing 2016;20(4):124-126*
16. ***Dhatariya KK, Wiles MW.** *Pre-operative testing guidelines: a NICE try but not enough. Anaesthesia 2016;71(12):1403-1407*
17. ***Kumar CM, Seet E, Eke T, Joshi GP, Dhatariya K.** *Glycaemic control during cataract surgery – a growing problem and we are none the wiser. British Journal of Anaesthesia 2016;117(6):687-691*
18. ***Dhatariya K, Umpierrez GE.** *Guidelines for management of diabetic ketoacidosis: Time to revise? Lancet Diabetes and Endocrinology 2017;5(5):321-323*

Reviews (* peer reviewed)

1. **Dhatariya K**, Watkins PJ. Signs of diabetic neuropathy. *General Practitioner* 3rd September 1999:48
2. **Dhatariya K**, Watkins PJ. Complications in diabetes. *General Practitioner* 10th September 1999:42
3. **Dhatariya K**, Harris PE. Ectopic ACTH – A Brief Overview. *CME Bulletin in Endocrinology and Diabetes* 2001;3(3):83-5
4. ***Dhatariya K**, Nair KS. Dehydroepiandrosterone – is there a role for replacement? *Mayo Clinic Proceedings* 2003;78(10):1257-1273
5. ***Dhatariya K**, Hall GM, Levy N. *The impact of hyperglycemic variability on the surgical patient. Current Opinion in Anesthesiology* 2016;29(3):430-437
6. *Levy N, Penfold NW, **Dhatariya K**. Perioperative management of the patient with diabetes requiring emergency surgery. *British Journal of Anaesthesia – Education* 2017;17(4):129-136
7. *Stubbs DJ, Levy N, **Dhatariya K**. The rationale and the strategies to achieve perioperative glycaemic control. *British Journal of Anaesthesia – Education*. 2017;17(6):185-193
8. *Stubbs DJ, Levy N, **Dhatariya K**. Diabetes medication pharmacology. *British Journal of Anaesthesia – Education*. 2017;17(6):198-207
9. ***Dhatariya KK**. Up-to-date management of neuroarthropathic joints. *Diabetic Foot Journal Middle East* 2017;3(1):6-9
10. ***Dhatariya K**. Blood ketones – measurement, interpretation, limitations and utility in the management of diabetic ketoacidosis. *Review of Diabetic Studies* 2016;13(4):217-225
11. ***Dhatariya K**, Vellanki P. Treatment of Diabetic Ketoacidosis (DKA) / Hyperglycemic Hyperosmolar State (HHS): Novel Advances in the Management of Hyperglycemic Crises (UK Versus US). *Current Diabetes Reports* 2017;17:33-39

Book Chapters (* peer reviewed)

1. **Dhatariya K**, Nair KS. Amino acid metabolism in disease – Diabetes Mellitus. Metabolic & therapeutic aspects of amino acids in clinical nutrition. Second edition. Cynober L (Ed): CRC Press. November 2003. ISBN 0849313821
2. **Dhatariya K**. Hospital in-patient diabetes management and diabetic emergencies. pp732-750. In: *Oxford Handbook of Endocrinology and Diabetes*. Third Ed. Edited by

John Wass, Katherine Owen. 2014 Oxford University Press, Oxford, UK. ISBN 9780196944438

3. ***Dhatariya K.** Chapter 20. The pathobiology of neuropathy. In: The diabetic foot: Evidence-based management. Ed by Hinchliffe R, Thompson M, Schaper N, Tripathi R and Timaran C. JP Medical Publishers. 2014. ISBN: 1907816623
4. **Dhatariya K, Matfin G.** *Emergent Perioperative Hyperglycemia Management. In: Endocrine and Metabolic Medical Emergencies: A Clinician's Guide.* Ed Matfin G. Endocrine Press, Chevy Chase, MD. ISBN: 978-1-936704-77-4
5. **Dhatariya K, Savage MW, Sampson MJ, Matfin G, Scott A.** *Severe Hyperglycemia, Diabetic Ketoacidosis, and Hyperglycemic Hyperosmolar State. In: Endocrine and Metabolic Medical Emergencies: A Clinician's Guide.* Ed Matfin G. Endocrine Press, Chevy Chase, MD. ISBN: 978-1-936704-77-4
6. Corsino L, **Dhatariya K, Umpierrez GE.** Management of diabetes and hyperglycemia in hospitalized patients. <http://www.endotext.org/chapter/diabetes-treatment-strategies/management-of-the-hospitalized-diabetic-patient/>
7. **Dhatariya K.** Diabetic ketoacidosis and hyperosmolar crisis. *Medicine.* 2014;42(12):723-726
8. ***Dhatariya K, James J.** Chapter 34. In-hospital treatment and surgery in patients with diabetes. In *Textbook of Diabetes. 5th edition.* Ed. Richard Holt, Allan Flyvbjerg, Barry Goldstein and Clive Cockram. Wiley Blackwell ISBN 978-1-118-91202-7
9. Allan B, **Dhatariya K, Walden E, Jairam C, Sampson M.** In-patient diabetes care and admissions avoidance in older people with diabetes. *Diabetes in Old Age 4th edition.* Ed Alan Sinclair, Trisha Dunning, Leocadio Rodriguez Manas, Medha Munshi. Wiley Blackwell ISBN 978-1-118-95459-1
10. **Dhatariya K.** Chapter 1. Perioperative management for the elective outpatient and hospitalized inpatient with diabetes mellitus. In: *Surgical Reconstruction of the Diabetic Foot and Ankle, 2nd Edition.* Ed Thomas Zgonis. Wolters Kluwer / Lippincott Williams and Wilkins
11. Levy N, **Dhatariya K.** Metformin (Glucophage). In: *Essence of Anesthesia Practice, 4th Edition.* Ed by Lee Fleisher, Michael Roizen, and Jeffrey Roizen. Elsevier Health Sciences ISBN 978-0-323-39497-0
12. Levy N, **Dhatariya K.** Oral hypoglycaemics. In: *Essence of Anesthesia Practice, 4th Edition.* Ed by Lee Fleisher, Michael Roizen, and Jeffrey Roizen. Elsevier Health Sciences ISBN 978-0-323-39497-0
13. **Dhatariya KK, Sampson MJ.** In-patient Management of type 1 diabetes, with a focus on older people. In: *IDF Type I Diabetes Guideline for Adults.* Ed Alan Sinclair & Trisha Dunning

Admissions Avoidance

Title of paper:

Gooday C, Hallam C, Sieber C, Mtariswa L, Turner J, Schelenz S, Murchison R, Messenger G, Morrow D, Hutchinson R, Williams H, **Dhatariya K** (2013); An antibiotic formulary for a tertiary care foot clinic: admission avoidance using intramuscular antibiotics for borderline foot infections in people with diabetes. Diabetic Med 30: 581-589

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

I led the group that developed the antibiotic formulary. I then had the initial idea that there should be an economic analysis of its use. I did the literature searches and I developed what factors should be included in the analysis. I analysed the results and I wrote the initial and final drafts of the manuscript.

Background to the paper

The diabetic foot remains the most common 'diabetes specific' reason for an acute hospital admission for people with diabetes [101]. An acute infection is the most commonly encountered diabetic foot problem. The most important guideline used to determine the management of diabetes related foot infections is that from the Infectious Diseases Society of America (IDSA) [102]. This guideline divides foot infections into 'not infected', 'mild', 'moderate', or 'severe'. These categories are shown in shown in Table 1. Similarly, the guideline from the International Working Group for the Diabetic Foot (IWGDF), uses the PEDIS grade (perfusion, extent/size,

depth/tissue loss, infection, and sensation), with an wound classified as ‘uninfected’ according to the IDSA, corresponds to a PEDIS grade of 1; a mildly infected wound according to IDASA is a PEDIS grade 2, moderate is 3 and severely infected according to IDSA criteria is PEDIS grade 4 [102].

Each of these categories has a suggested management plan associated with it. For example, the guideline says that a mildly infected wound (PEDIS grade 2) can be treated with narrow spectrum antibiotics according to local microbiological sample trends, or that people with severely infected wounds (PEDIS grade 4) should be admitted to hospital for treatment with appropriate intravenous antibiotics. However, in the moderately infected category (PEDIS grade 3), the IDSA guideline also advocates acute hospital admission for intravenous antibiotic treatment.

As a specialist diabetic foot team we initially had no rational antibiotic policy for what agents to give and to whom or for how long. In addition we felt that there were a significant minority of individuals who fell into the IDSA category of ‘moderate’ infection but who were not ill enough to warrant acute hospital admission, or for those whom hospital admission would have an immediate serious and significant impact on their lives or livelihood. Thus we set out to a) rationalise our antibiotic use and b) to develop an admission avoidance category, by subdividing the ‘moderate’ category and adding a subcategory of ‘moderate infection – borderline admission’. This is shown in Table 2. This generated a specific diabetic foot antibiotic prescribing guideline shown in Table 3. This allowed consistency within the clinical team to ensure that whoever saw the patient would follow the same antibiotic prescribing rules. It also prevented potentially avoidable acute hospital admissions that,

according to the best known global guidelines, would have necessitated one. This was done by advocating the use of intramuscular antibiotics given once daily in the community by either the primary care nurses or by the district nurses. We then ran this protocol for several months and did an economic analysis of the change in antibiotic regimen and also of the outpatient intramuscular antibiotic regimen.

Objectives of the study

To assess the impact of empirical intramuscular antibiotic use in the treatment of 'severe – borderline admission' foot infections. In particular to assess the impacts of admissions avoidance and any cost savings achieved. In addition, to analyse the outcomes and costs associated for those individuals who were treated with the intramuscular and oral antibiotic regimen and compared them to those who were admitted directly with severe infections for intravenous treatment.

What this study added to the literature

Whilst the objective of this study was not to consider rationalising an antibiotic protocol for the diabetic foot infections that presented to a specialist foot service, it was the first study to consider a specific 'admissions avoidance' strategy. It also showed that by rationalising our antibiotic prescribing we did not increase the costs. With respect to the intramuscular antibiotic regimen, we halved the rates of hospital admission for those who previously would have been admitted. Furthermore, those who were admitted had a significantly shorter length of hospital stay if they had had a course of intramuscular antibiotics prior to admission. We showed that our regimen led to significant cost savings.

What changed as a result of the paper?

These data are now referenced as an admission avoidance scheme in other, related, documents from the Joint British Diabetes Societies for In-patient Care Group [103], as well as by the National Institute for Health and Care Excellence [104]. As a result of this work, the specialist diabetes foot clinic that I lead won the 'Admissions avoidance' category in the 2012 national Quality in Care Awards, and was runner up in 'Diabetes Team of the Year' category at the 2013 BMJ awards.

In 2017, the proposed update for the management of diabetic foot infections from the IDSA added a new category to their classification, now dividing 'moderate' infections into 'Class A' and Class B'. Those with 'Class A' infections were, like our classification, not unwell enough to be admitted to hospital, but had infection of sufficient severity to warrant parenteral antibiotics given as an outpatient [105]. Those with 'Class B' would be admitted for intravenous antibiotics. Thus our work has had an influence on international policy.

In retrospect, what should have been done differently in this study?

Looking back at this work, we had relatively few patients who were given intramuscular antibiotics, and even though we had sufficient numbers to show statistical significance in terms of cost savings, a larger number would have made the argument stronger. Prior statistical advice would have also allowed us to power the study more appropriately.

Future work as a result of this publication

With the advent of a change in microbiological personnel, and an update on sensitivities, as well as a change in the availability of outpatient delivered intravenous antibiotics, our policy is currently in the process of being updated. We will then again look at the economic impact of this change.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

<http://onlinelibrary.wiley.com/doi/10.1111/dme.12074/abstract>

Clinical Description	IDSA	IWGDF (PEDIS)
No symptoms or signs of infection	Uninfected	1
Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). If erythema, must be >0.5 cm to ≤2 cm around the ulcer.	Mild	2
Local infection (as described above) with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis), and no systemic inflammatory response signs (as described below)	Moderate	3
Local infection (as described above) with the signs of systemic inflammatory response syndrome (SIRS), as manifested by ≥2 of the following: <ul style="list-style-type: none"> • Temperature >38°C or <36°C • Heart rate >90 beats/min • Respiratory rate >20 breaths/min or PaCO₂ <32 mm Hg • White blood cell count >12 000 x 10⁶ or <4000 cells/μL or ≥10% immature (band) forms 	Severe	4

Table 1 – Classification for the severity of diabetes related foot disease, taken from the Infectious Diseases Society of America (IDSA) and the International Working Group for the Diabetic Foot [102,106].

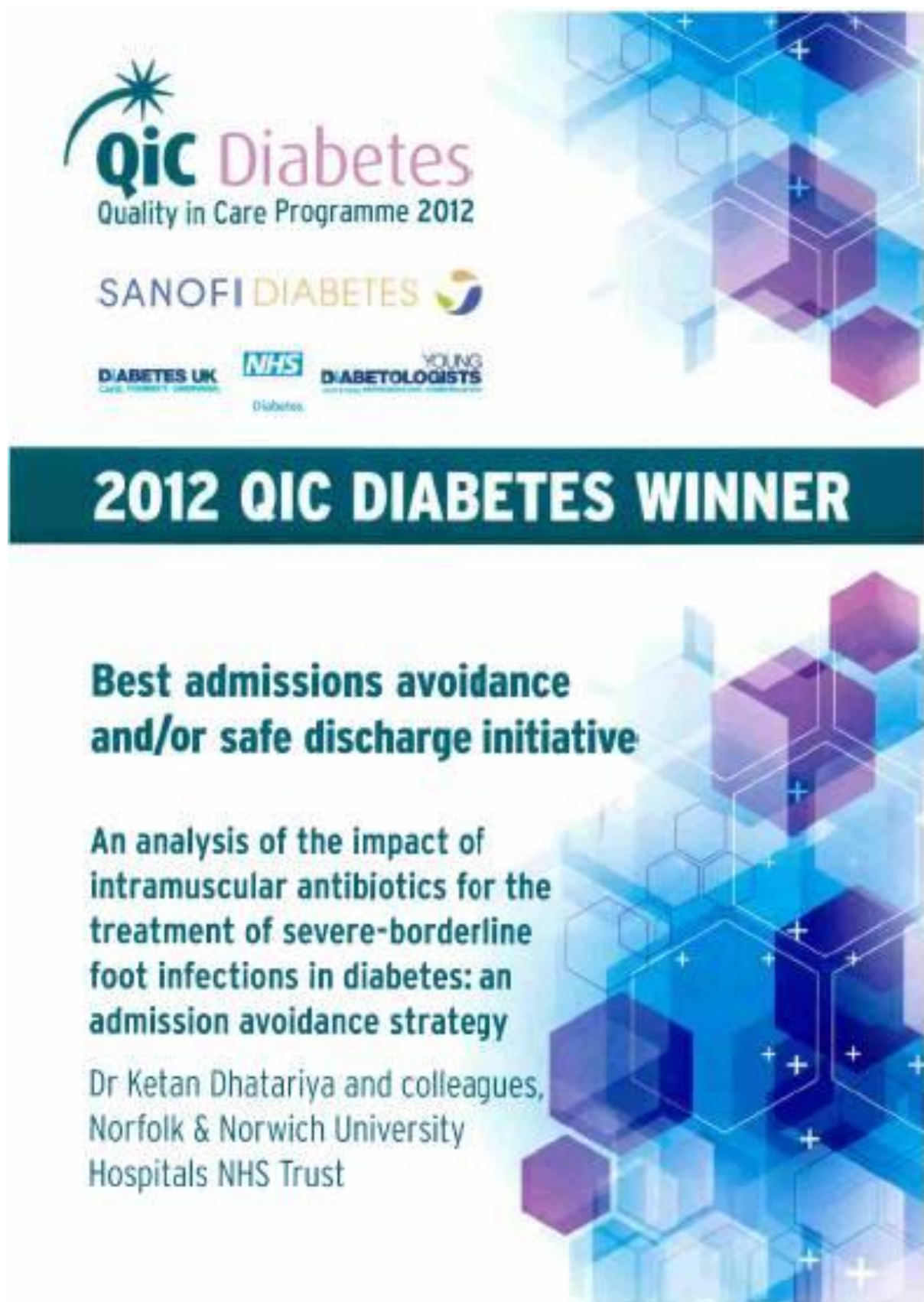
Clinical Description	IDSA	IWGDF
No symptoms or signs of infection	Uninfected	1
Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). If erythema, must be >0.5 cm to ≤2 cm around the ulcer.	Mild	2
Local infection (as described above) with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis), and no systemic inflammatory response signs (as described below)	Moderate	3
Cellulitis > 2 cm around the ulcer associated with lymphangitis or foot failing to respond to oral antibiotics alone and not systemically unwell	Moderate infection - borderline admission	
Local infection (as described above) with the signs of SIRS, as manifested by ≥2 of the following: <ul style="list-style-type: none"> • Temperature >38°C or <36°C • Heart rate >90 beats/min • Respiratory rate >20 breaths/min or PaCO₂ <32 mm Hg • White blood cell count >12 000 x10⁶ or <4000 cells/μL or ≥10% immature (band) forms 	Severe	4

Table 2 – Our modified severity classification, including the admissions avoidance category ‘Moderate infection – borderline admission’ [107].

	FIRST CHOICE		PENICILLIN ALLERGY		DURATION
	PARTIAL OR FULL THICKNESS	EXTENDING TO UNDERLYING SOFT TISSUE/ BONE	PARTIAL OR FULL THICKNESS	EXTENDING TO UNDERLYING SOFT TISSUE/ BONE	
MILD	Co-amoxiclav 625mg tds PO	Co-amoxiclav 625mg tds PO	Clarithromycin 500mgs bd PO	Clarithromycin 500mgs bd PO Metronidazole 400mgs tds PO	Review after 1-2 weeks. May require an additional 1-2 weeks of treatment
MODERATE	Co-amoxiclav 625mgs tds PO If co-amoxiclav has previously been used with no success then consider using Clindamycin 150mg-300mg qds PO instead	Co-amoxiclav 625mgs tds PO +/- Ciprofloxacin 500mgs bd PO If co-amoxiclav has previously been used with no success then consider using Clindamycin 150mg-300mg qds PO instead of co-amoxiclav	Clindamycin 150mg - 300mg qds PO	Clindamycin 150mg-300mg qds PO +/- Ciprofloxacin 500mgs bd PO	2-4 weeks
MODERATE INFECTION BORDERLINE ADMISSION	Ceftriaxone 1-2g od IM* Ciprofloxacin 500mgs bd PO Metronidazole 400mg tds PO If MRSA positive use teicoplanin in place of ceftriaxone		Ceftriaxone 1-2g od IM* Ciprofloxacin 500mgs bd PO Metronidazole 400mg tds PO Teicoplanin IM* 400mg od Ciprofloxacin 500mg bd PO Metronidazole 400mg tds PO		2-4 weeks
SEVERE NEEDS ADMISSION	Tazocin 4.5g tds IV If polymicrobial infection suspected with MRSA then add in vancomycin 1g bd IV to the above		Clarithromycin 500mg bd IV Metronidazole 500mg tds IV Ceftazidime 1g tds IV (2g tds IV if very severe). Substitute with Ciprofloxacin 500mg bd PO in true penicillin allergy. If polymicrobial infection suspected with MRSA then add in vancomycin 1g bd IV to the above regimen (omitting clarithromycin)		2-4 weeks
OSTEOMYELITIS	Co-amoxiclav 625mg tds PO (+ sodium fusidate 500mg tds PO if no evidence of healing after 4 weeks and a sodium fusidate sensitive staph aureus identified). Consider ciprofloxacin 500mg bd + metronidazole 400mg tds PO if a gram negative organism identified or no evidence of improvement after 4 weeks		Clindamycin 300mg qds PO Consider ciprofloxacin 500mg bd + metronidazole 400mg tds PO if a gram negative organism identified or no evidence of improvement after 4 weeks		4-6 weeks

Table 3 – Award winning diabetic foot antibiotic prescribing guideline generated from our modification of the IDSA guideline [107].

QIC award certificate

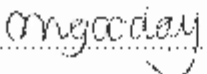


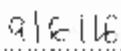
To whom it may concern

This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Gooday C, Hallam C, Sieber C, Mtariswa L, Turner J, Schelenz S et al. An antibiotic formulary for a tertiary care foot clinic: admission avoidance using intramuscular antibiotics for borderline foot infections in people with diabetes. Diabetic Med. 2013;30:581-9

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he directly supervised the team who carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed..........

Date..........

Catherine Gooday

Principal Podiatrist, Elsie Bertram Diabetes Centre

Norfolk and Norwich Hospital

Title of paper:

Gooday C, Murchison R, **Dhatariya K** (2013); An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic Foot & Ankle 4: 21757

Impact factor of the journal

Unavailable – not listed. However, according to Google Scholar (accessed 1st October 2017) this paper has been cited twice.

My contribution to this peer reviewed publication

I lead the multidisciplinary foot clinic at the Norfolk and Norwich University Hospital. The immediate impact of the loss of the podiatrists led to me having the initial idea that there should be an economic analysis of their loss. I did the literature searches and I developed what factors should be included in the analysis. I analysed the results and I wrote the initial and final drafts of the manuscript.

Background to the paper

The ideal multidisciplinary foot team is made up of the podiatrists, the diabetes doctor, the orthopaedic and vascular surgeons, the microbiologist, radiologist, orthotist, and diabetes specialist nurse. In the diabetic foot clinic at the Norfolk and Norwich University Hospitals that I lead I am very pleased that over the 8 years that I have led the team, we have every one of these groups represented. At the start of the list were the podiatrists. This is because they do the bulk of the work and are the 'gate keepers' for who needs to be seen by the consultants, and in which speciality clinics they need to be seen in (medical,

vascular or orthopaedic). They also work daily on the wards, assessing new cases of diabetes related foot disease that have either been admitted as a result of the foot disease, or an individual that has been found to have a diabetes related foot problem in addition to the primary cause for their admission.

Much of this work is done as part of their 'day-to-day' activity and does not generate any income for the acute Trust, and thus, in the past they have been deemed as an 'expense' rather than revenue generating to the teams responsible for fiscal accountability.

In 2010, due to an entirely unforeseeable set of circumstances, we lost 50% of our specialist podiatry staff in a very short time. This led to an immediate reduction, and in some cases cessation, of some aspects to the service delivered by the foot clinic. This study was an opportunistic way of assessing the economic impact – or worth – of podiatrists in a specialist diabetic foot clinic. We looked at clinic activity ('income generation'), as well as hospital admission rates, amputation rates, and hospital length of stay for patients ('cost') with diabetes related foot disease for the time prior to the loss of staff, during that time, and for the 6 months after the full complement was re-established.

Objectives of the study

To assess the economic impact of a loss of half of our specialist podiatrists by undertaking a formal review of our in-patient and outpatient activity before and after a 7-month interruption of normal service. We also compared the number of admissions due to diabetic foot complications and looked at the number of overall 'bed days', i.e. number of days per year that a bed at our institution was occupied by someone with a diabetic foot

problem. In addition, we looked at the length of stay of hospital in-patients admitted with foot problems before and during the period of staff shortage.

What this study added to the literature

For the first time, we were able to show that podiatrists save a lot of money. The acute Trust, and the Primary Care Trust did not replace the missing members of staff (other than occasional non-specialist podiatrists from the community) for over seven months. During that time length of stay went up, the number of expected amputations rose, and the delay in getting urgent referrals meant a larger number of 'excess' acute hospital admissions during that time. In addition, because the team had to focus on the more complex feet, those with less need were discharged into the community, thus generating less income as well as increasing costs. These data showed that the income generated went down by 23% (£407,285 the year before the loss of staff to £214,006 for the year during which there was the staff absence), with an increased expenditure of almost £90,000 due to the factors mentioned.

A full time band 7 specialist diabetes podiatrist at that time cost at that time was £35,184.

What changed as a result of the paper?

We used this economic data to successfully argue to the Primary Care Trust and the Acute Trust that the short term saving they felt they had achieved by not employing replacement podiatrists had led to a significant escalation in overall costs within other parts of the hospital. This was because of the rise in admissions due to diabetes foot disease that could have very easily been managed in the outpatient clinic. These data

have been used by other Trusts across the UK to justify employing specialist podiatrists as part of an overall 'admission's avoidance' strategy.

In retrospect, what should have been done differently in this study?

The set of circumstances that led to the halving of the numbers of podiatrists was unforeseeable, and unexpected. We had tried for a long time to justify why employing podiatry staff was economical, but without 'proof of worth' the funders of the service felt we had just been trying to promote our own service. These data show that we were not. However, it took us several months to go through the data to show what effect this loss of staff had had. If we had collected the activity, admission, amputation data etc., in real time as part of routine clinical work then it would have taken us less time to gather the evidence we needed to convince the Primary Care Trust and the Acute Trust to adequately fund the service, and of course fewer individuals would have lost their legs. As a result of this episode we now collect this data as a matter of routine.

Future work as a result of this publication

This paper represented the chance to conduct an opportunist, stand alone, piece of work. It was not anticipated, and thus currently no further work will need to be repeated (one hopes).

Confirmation of authorship

This is shown.

External link to the paper on the journal website

<http://www.tandfonline.com/doi/full/10.3402/dfa.v4i0.21757>

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Gooday C, Murchison R, Dhatariya K. An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic Foot & Ankle 2013;4:21757

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he directly supervised the team who carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed.....*cmgooday*.....

Date.....*9/6/16*.....

Catherine Gooday

Principal Podiatrist, Elsie Bertram Diabetes Centre
Norfolk and Norwich Hospital

General Management of Patients in Hospital with Diabetes

Title of paper:

Daultrey H, Gooday C, **Dhatariya K** (2011); Increased length of in-patient stay and poor clinical coding: audit of patients with diabetes. J R Soc Med Sh Rep 2: 83

Impact factor of the journal

Unknown. This is currently not a 'listed' journal. Google Scholar reports that this paper has been cited sixteen times [accessed 1st October 2017]

My contribution to this peer reviewed publication

I lead the multidisciplinary foot clinic at the Norfolk and Norwich University Hospital. I had the initial idea to try and get our own institutions' data on length of stay for our patients admitted with diabetes related foot disease. I supervised the medical student who did the data collection. I did the literature searches and I analysed the results and I wrote the initial and final drafts of the manuscript.

Background to the paper

People with diabetes have longer hospital stay than those without diabetes [10]. In addition, the most frequent cause of an acute diabetes specific hospital admission is the 'diabetic foot' [101]. It has been well recorded that clinical coding is done poorly, with patients with diabetes also being affected by this [108].

Since the split in 1991 of the health service into 'providers' and 'purchasers', secondary care institutions need to bill primary care funders for the services they provide. The amount needed to bill is dependent on knowing what to bill for. There is a fixed cost associated with each diagnosis that a patient could have. These diagnoses and

associated costs are derived from Healthcare Resource Group (HRG) codes [109]. These HRG's are translated by clinical coding at each hospital from the data written on the discharge summary from each individual patient that is sent to the general practitioner. If there are incorrect diagnoses, then the hospital may get paid less than it should be for the work that it has done. The amount received is according to the corresponding HRG code for that diagnosis. In addition, for every diagnosis that is not included (i.e. just the primary admission diagnosis is listed on the discharge summary and no other pre-existing co-morbidities) then, again, the hospital gets paid less that it could otherwise have been.

The discharge summary is thus the mechanism by which a hospital generates a lot of its income. However, this important document is often filled out by the most junior member of the medical team who often has little or no idea of the importance of the discharge summary – the Foundation Year doctor.

This study looked at discrepancies between those people known to have diabetes related foot disease on a particular day in the hospital and looking at the discharge summaries 1 year later, how often that was recorded on the discharge summary, and also whether length of hospital stay was longer for those known to have diabetes, compared to those who did not.

Objectives of the study

To establish if patients with diabetes and foot problems were in hospital for longer than the national average length of stay, as stated by the Hospital Episode Statistics database. Another objective was to identify the accuracy of clinical coding within the Norfolk and Norwich University Hospital (NNUH), establishing its reliability for future research. This

was the first such piece of work at the NNUH looking at patients with diabetes and foot problems.

What this study added to the literature

It confirmed what had previously been known. A) That diabetes was poorly recorded on the discharge summary, even when it was the primary cause for admission, and when having diabetes in addition to any other diagnosis increased the tariff associated with a hospital admission. B) That patients with diabetes stay in hospital for longer than those who do not have the condition

What changed as a result of the paper?

We have tried to ensure that discharge summaries are prioritised by our junior staff. They are started at the time of hospital admission, and all known diagnoses are listed, not just the condition for which the patient was admitted.

In retrospect, what should have been done differently in this study?

This was a cross sectional study taken on 1 day only. Clearly this has some limitations, but is similar in nature to the data collection exercise conducted as part of the National Diabetes In-patient Audit [101]. To get a better idea, a longer study over time would have been better, and information technology systems now allow this to be done.

Future work as a result of this publication

These data need to be repeated to see if any improvements have been made, although, to date, this has not been done.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

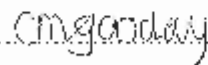
<http://journals.sagepub.com/doi/full/10.1258/shorts.2011.011100>

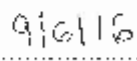
To whom it may concern

This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Daultrey H, Gooday C, Dhatariya K. Increased length of inpatient stay and poor clinical coding: audit of patients with diabetes. J.R.Soc.Med.Sh.Rep. 2011;2:83

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he directly supervised the student who carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed..........

Date..........

Catherine Gooday

Principal Podiatrist, Elsie Bertram Diabetes Centre

Norfolk and Norwich Hospital

Title of paper:

Narwani V, Swafe L, Stavraka C, **Dhatariya K** (2014); How frequently are bedside glucose levels measured in hospital in-patients on glucocorticoids? *Clinical Medicine* 14: 327-328

Impact factor of the journal

1.63

My contribution to this peer reviewed publication

I had the initial idea to try and find out what the prevalence of glucocorticoid use was in hospital in-patients, and then to find out how many of them had glucose concentrations measured. I supervised the medical students who did the data collection. I did the literature searches and I analysed the results and I wrote the initial and final drafts of the manuscript.

Background to the paper

In November 2013 I attended the Autumn Meeting of the Association of British Clinical Diabetologists. At that time I was a member of the executive committee, and was the meetings secretary. During the event I discussed the possibility of producing a guideline on steroid induced hyperglycaemia with a few other attendees. This idea was warmly received. However because of the resistance that I had encountered when trying to disseminate the findings of the Joint British Diabetes Societies for In-patient Care (JBDS) group national guideline on the perioperative management of patients with diabetes undergoing surgery from the anaesthetists and surgeons, I felt that we may get a similar degree of resistance from those medical specialities who were high prescribers of glucocorticoids.

As one of the writing group of the JBDS guideline on the management of Hyperglycaemic Hyperosmolar Syndrome [110], and as someone who relatively frequently came across patients admitted with hyperglycaemia a few days after starting glucocorticoids I felt this was an important issue. However, I was also aware from previous conversations with colleagues from the gastroenterology, dermatology, rheumatology, chest and oncology departments, they did not feel that glucocorticoid induced hyperglycaemia was an issue. They all acknowledged that glucocorticoid use was associated with hyperglycaemia, but they did not know how often it occurred. Looking at the literature it was clear that there was evidence for frequent glucocorticoid use in the community [111,112]. However, what was not known was the prevalence of glucocorticoid use in hospital. Thus we undertook this point prevalence survey to see how common glucocorticoid use was at the Norfolk and Norwich University Hospital.

Objectives of the study

The objective was to assess the prevalence of glucocorticoid use in a large university teaching hospital. Furthermore, what were the indications for use and finally, to determine how many individuals on glucocorticoids were having regular blood glucose concentrations measured. We also wanted to know if blood glucose testing was more frequent in people with a previous diagnosis of diabetes mellitus.

What this study added to the literature

This is the first study that looked at the prevalence of glucocorticoid use in hospital in-patients. We found that 12.8% (n=120) of all in-patients were on some form of glucocorticoid, but that of those, only 20.8% of these (n=25) had any evidence of blood

glucose testing. Of these, 13 were known to have pre-existing diabetes. Thus we showed that glucose testing in people in hospital receiving glucocorticoids was very poor.

What changed as a result of the paper?

These data were included in the JBDS guideline on the management of hyperglycaemia and steroid (glucocorticoid) therapy that was launched in 2014 [113]. This has also fed into other work that I have done, but not mentioned in this thesis on the impact of giving dexamethasone as part of an anaesthetic regimen [114].

In retrospect, what should have been done differently in this study?

This work was done by an enthusiastic group of medical students over a weekend. It would have been better to have a longer assessment period, with regular assessments of prevalence. In addition, it would have then been possible to see if the outcomes for people on glucocorticoids was different (e.g. length of hospital stay, or mortality) to those not on the drugs.

There are further potential differences between those receiving glucocorticoids as part of treatment for a long term medical condition, (gastroenterological, respiratory, oncology, dermatological, or rheumatological), as opposed to a short (even single) dose as part of e.g. a peri-operative regimen. These differences would need to be explored, but as stated in other work I have done (that is not mentioned in this thesis), to assess the impact of harm associated with e.g. peri-operative dexamethasone use, the numbers needed would need to be very large [115]. To look at differences in peri-operative outcomes for those given peri-operative steroids, looking at the prevalence of diabetes in the community, the risk of developing post-operative hyperglycaemia with a dose of steroid, the risk of

developing post-operative complications as a result of that hyperglycaemia and then aiming for a statistically significant difference, the sample size is estimated at over 15,000 people. This would require a multi-centre collaborative trial.

Future work as a result of this publication

This work has led to collaborations with the department of surgery and anaesthesia in Vanderbilt University School of Medicine in Tennessee where they have a very large database of over 200,000 patients who have undergone surgery, with over 75% of them having received glucocorticoids as part of their anaesthetic regimen. This should give us sufficient numbers to assess differences in outcomes between those who did receive them and those that did not.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

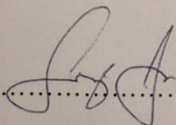
<http://www.clinmed.rcpjournal.org/content/14/3/327.full?sid=76515a90-721d-464f-9e2d-a7990219baab>

To whom it may concern

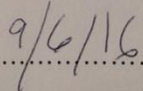
This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Swafe L, Narwani V, Stavrika C, Dhatariya K. How frequently are bedside glucose levels measured in hospital inpatients on glucocorticoids? Clinical Medicine 2014;14:327-8

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he directly supervised the team who carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed..........

Dr Leyla Swafe

Date..........

Outcomes of In-patient Hyperglycaemia

Title of paper:

Evans NR, **Dhatariya KK** (2012); Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. Clin Med JRCPL 12: 137-139

Impact factor of the journal

1.63

My contribution to this peer reviewed publication

I had the initial idea to try and find out what the relationship was between admission glucose concentrations and outcomes. I supervised the junior doctor who did the data collection. I did the literature searches and I analysed the results and I wrote the initial and final drafts of the manuscript.

Background to the paper

Hyperglycaemia is common in patients presenting to emergency departments. This is either due to the presence of pre-existing diabetes, or due to the transient hyperglycaemia of acute illness – ‘stress hyperglycaemia’ [63,116]. Previous work had looked at the impact of glucose concentrations at initial presentation, and subsequent outcomes in specific disease areas, e.g. pneumonia, stroke or acute coronary syndrome [117-119]. Work looking at ‘all comers’ had previously been done, but in the USA, which showed a relationship between admission blood glucose and outcomes [64]. All of these studies showed that high glucose concentrations on initial presentation was associated with poorer outcomes, using whatever measure chosen to determine ‘outcomes’, e.g. longer length of hospital stay, increased mortality and so forth.

However, because of the large differences in the way that health care provision was delivered in the USA, it was unclear whether those findings could be directly translated to the UK. On this background we undertook this study that looked at all admissions to the Acute Medical Unit (AMU) at the Norfolk and Norwich University Hospital for one month in February 2010 (n=1502) and found those who had blood glucose concentrations measured (n=893). We used outcome measures that had been previously published by others to ensure that our data were comparable.

Objectives of the study

The objective was to investigate the relationships between dysglycaemia and length of stay, short-term mortality and readmission in an unselected AMU population. The follow-up rate of hyperglycaemia in individuals without diabetes was also measured.

What this study added to the literature

These data show that in an unselected UK population presenting to an AMU that high glucose concentrations at the time of admission were strongly correlated to increased length of hospital stay, increased 28 day readmission rates, and higher 28 day mortality. There were no differences depending on age, gender or admission speciality. These data were the first of their kind to show this in the UK.

These data add to the wealth of evidence to suggest that glucose should be measured on all patients presenting to an Emergency Department

What changed as a result of the paper?

Many other authors have now repeated this exercise and shown the same results. As of October 2017, according to Google Scholar, this paper has been cited 30 times. The authors of many these other papers, have used our data as a starting point from which to develop strategies to a) diagnose diabetes / stress hyperglycaemia at an earlier stage b) to develop algorithms and decision tools for use in the emergency department to reduce length of hospital stay [120].

In retrospect, what should have been done differently in this study?

Because we were able to show what we set out to, within a relatively short time frame, we were successful in our goal. In addition, these data have been the springboard for a number of other pieces of work that have aimed to improve the outcomes of people presenting to emergency departments. Thus, I feel that we did what we had to do, and I would do nothing different.

Future work as a result of this publication

We used the same dataset to assess if the single glucose measurement taken at the time of the acute hospital admission predicted outcomes at one and two years after this admission – this work is presented later in this thesis.

In addition, these data have also been part of the more recent conversations surrounding the important issue of diagnosing new diabetes in adults during hospital admissions. Indeed there is a new guideline from the Joint British Diabetes Societies for In-patient Care Group dealing with this issue due for publication in Autumn 2017.

Confirmation of authorship

This is shown.

External link to the paper on the journal website


<http://www.clinmed.rcpjournal.org/content/12/2/137.full?sid=76515a90-721d-464f-9e2d-a7990219baab>

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Evans NR, Dhatariya KK. Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. Clin.Med.JRCPL 2012;12:137-9

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he directly supervised me, when I carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed.....

Dr Nicholas Evans

Date.....07/06/2016

Title of paper:

Haddadin F, Clark A, Evans N, **Dhatariya K** (2014); Admission blood glucose helps predict 1 year, but not 2 years, mortality in an unselected cohort of acute general medical admissions. *Int J Clin Pract* 69: 643-648

Impact factor of the journal

2.57

My contribution to this peer reviewed publication

I had the initial idea to try and find out what the long terms relationship was between admission glucose concentrations and 2 year outcomes. I supervised the junior doctors who did the data collection. I did the literature searches and I wrote the initial and final drafts of the manuscript.

Background to the paper

Previous work had been done elsewhere looking at the relationships of blood glucose concentrations at the time of hospital admission and short term outcomes in selected cohorts of patients [117-119]. These data showed that the higher the admission glucose concentration, the greater the likelihood of an adverse event – longer length of hospital stay, greater risk of death, etc. We had previously looked at the relationship between 28-day outcomes in terms of length of hospital stay, readmission rates and mortality according to the admission blood glucose concentrations of all patients presenting to the Acute Medical Unit of the Norfolk and Norwich University Hospital during February 2010. These data have been presented earlier in this thesis. Those data showed, in agreement with the previous work, that high admission glucose concentrations were associated with

clinically significant and statistically significantly poorer outcomes when compared to those admitted with normal glucose values.

Objectives of the study

Using the data that we had collected from a previous study presented elsewhere in this thesis, we wanted to see whether that single admission glucose concentration also helped to predict longer term outcomes, in particular one and two year mortality. We used that initial cohort and then looked to see who was alive at one year and two years later, and if there was a correlation between risk of death and glucose concentrations on admission to hospital.

What this study added to the literature

This dataset was the first time that a longer term assessment of the relationship between a single blood glucose concentration taken at the time of an acute hospital admission and the relationship between that glucose and the risk of death in the next 2 years.

What changed as a result of the paper?

As is explained in the section on the commentary piece in the British Medical Journal discussed later in this thesis, whilst this data adds to the wealth to show that a high glucose concentration during hospital admission is associated with increased risk of harm, there are currently no data (other than in cardiac and liver transplant surgery) to show that normalising glucose concentrations is associated with a reduction in that risk. Thus this paper adds to the information to show that the risks are not limited to the current hospital admission, but can help to predict future risk of premature death.

In retrospect, what should have been done differently in this study?

As part of this data collect we were limited to knowing which specialist they were triaged to. In our institution, we have a 'speciality triage system;' all patients are assessed in the Acute Medical Unit and then triaged to the appropriate speciality. What we did not have at the time of writing is to see what the individuals died of, and to see if there were any correlations with that. It is likely however, that even with almost a thousand people, of whom a large proportion died, that the number of people who died from any particular cause of death with a particular glucose concentration would have been small to be able to make any clear correlations possible. Much larger numbers would have been needed.

Future work as a result of this publication

Currently, this work has fed into the work in the surgical arena. There are very similar data to show that in surgical admissions, high pre and post-operative glucose concentrations are related to an increased risk of complications and death. However, most of the data looking at complication rates are limited to 30 day post-operative outcomes. These data suggest that we should also be looking a longer timeframes. I am currently leading a project being planned that will involve conducting a large multicentre study see if there is a relationship between random glucose and HbA_{1c} values taken at the pre-operative assessment clinic and 30 day outcomes. However, as part of this, it is planned to also look at one and two year outcomes.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

<http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12574/full>

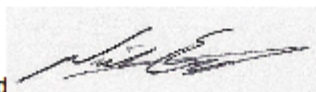
To whom it may concern

This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Haddadin F, Clark A, Evans N, Dhatariya K. Admission blood glucose helps predict 1 year, but not 2 years, mortality in an unselected cohort of acute general medical admissions. Int.J.Clin.Pract. 2014;69:643-8

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he directly supervised the team who carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed



Dr Nicholas Evans

Date 08/06/2016

Title of paper:

Dhatariya K (2013); Should in-patient hyperglycaemia be treated? Br Med J 346: f134

Impact factor of the journal

19.97

Background to the paper

As one of the senior members of the steering group of the Joint British Diabetes Societies for In-patient Care Group, and as one of the senior co-authors, or lead authors on most of the guidelines that the group has produced I had read a lot of material on the impact of high glucose concentration in hospital in-patients. These data are best summarised by the statement that “high glucose concentrations in hospitalised in-patients significantly increases their risk of harm – however that harm may be defined”. In many respects this is the same situation as general outpatient diabetes care was up to the early 1990’s – that “high glucose concentrations over a period of many years in people with diabetes significantly increases the risk of micro and macrovascular complications”. It was only with the publication of the two seminal intervention trials in diabetes – the Diabetes Control and Complications Trial (DCCT) for people with type 1 diabetes [4], and the United Kingdom Prospective Diabetes Study (UKPDS) [5,68] that it became clearer that lowering glucose concentrations reduced the risk of developing complications. In the world of in-patient diabetes, as mentioned, we have a lot of data to show that high glucose concentrations are associated with harm, but as yet, we have very little data to show that intervention makes a difference in reducing that harm. This ‘uncertainties’ page in the BMJ outlines this point. That whilst there are very good theoretical arguments for lowering blood glucose concentrations, there are almost no data (other than in cardiac or liver transplant surgery)

to show that these interventions make any difference to outcomes, other than by increasing the risk of harm due to severe hypoglycaemia.

Objectives of this peer reviewed paper

I wanted to summarise the data that had been published to date. In particular to state that whilst there was a great deal of evidence to show that hyperglycaemia in hospital in-patients was associated with harm, and poorer outcomes, there was very little consistent data (except, possibly in cardiac and liver transplant surgery) to show that intervening, and lowering glucose concentrations made a difference. Thus, to practice 'evidence based medicine', when there is no evidence of benefit, I questioned should it be done?

What this study added to the literature

This commentary put into words one of the great fears that I had been having over the time that I have been a senior member of the Joint British Diabetes Societies for In-patient Care Group. Almost all of the guidelines advocate aiming for an ideal glucose concentration of 6.0 to 10.0mmol/L, with a range of 4.0 to 12.0mmol/L being acceptable. However, these targets have all been consensus based, with no evidence at all for these recommendations. In addition, for many people, achieving these targets in hospital would require being on insulin, a drug known to be one of the most frequent causes of severe harm in hospitalised patients [79,121,122]. It enunciated the argument between being seen to address a recognised problem, but without any evidence to justify the actions we were promoting. If one were a 'purist' who followed only evidence based medicine, then given there is no evidence of benefit, should hyperglycaemia in hospitalised in-patients be treated? However, with the lack of evidence that treating high glucose concentrations is associated with benefit, but is very definitely associated with an increased risk of harm

from hypoglycaemia, should the risk of potential harm vs no potential benefit be taken into account?

What changed as a result of the paper?

This piece had brought the subject of in-patient hyperglycaemia to greater prominence than it had previously. In particular it has highlighted the importance of looking for diabetes or hyperglycaemia in the hospitalised population.

A national survey was undertaken in 2012 by my colleague Professor Mike Sampson, chair of the Joint British Diabetes Societies for In-patient Care Group. In that he asked every specialist diabetes team in the UK a number of questions on what they thought about the guidelines that the group had produced up to that time [123]. That showed that the vast majority of specialist diabetes teams found the JBDS guidelines useful and rated them as 'very good' or 'excellent'. The data also found that, other than the peri-operative guideline, most acute Trusts had either adopted or adapted the JBDS guidelines, suggesting that despite the lack of hard evidence that glucose lowering made a difference to outcomes, that teams felt ('intuitively'?) that normalising glucose concentrations was the correct course of action. The JBDS suite of guidelines 'allowed' them to do this (or rather almost gave them a license to do so), but also to do it across the UK in a consistent manner. Thus whilst the 'Uncertainties' piece was deliberately meant to be provocative, the overwhelming answer from practicing clinical teams to the question "Should in-patient hyperglycaemia be treated?" was "Yes!"

In retrospect, what should have been done differently?

The original version of the manuscript was almost three times longer than that which was eventually published. I regret not being able to have the whole version published because that made the arguments clearer with more examples. However, due to constraints placed on me by the journal, it was limited to the document eventually published.

Future work as a result of this publication

This is ongoing. The clear message that came across from this, and from other work done prior to the publication of this manuscript – and subsequently, is that more high quality work needs to be done to gather the evidence to show that treating high glucose concentrations in the in-patient population safely results in better outcomes for patients.

Confirmation of authorship

Not needed because I was the sole author.

External link to the paper on the journal website

<http://www.bmj.com/content/346/bmj.f134>

The Benefits of a Diabetes In-patient Specialist Nurse

Title of paper:

Sampson MJ, Dozio N, Ferguson B, **Dhatariya K** (2007); Total and excess bed occupancy by age, speciality and insulin use for nearly one million diabetes patients discharged from all English Acute Hospitals. *Diabetes Res Clin Pract* 77: 92-98

Impact factor of the journal

2.54

My contribution to this peer reviewed publication

I was involved in the discussions about what outcomes should be measured and what analysis should be undertaken. I was also involved in the discussions about the manuscript preparation and revisions undertaken.

Background to the paper

Data from surveys undertaken in individual hospitals had shown that patients with diabetes spent longer in hospital than those without diabetes with the same condition or under the same admitting team. It had also been shown in data from the US that patients with diabetes had a longer length of hospital stay than those without diabetes admitted for the same condition and that this had significant economic consequences [124]. However, similar data was not available on a national basis in the UK.

Objectives of the study

This study was an ambitious attempt to collect data based on discharge summaries that make up the Hospital Episode Statistics (HES) data to look at length of hospital stay

depending on the speciality of the admitting consultant, broken down by medical and acute surgical sub-specialities.

What this study added to the literature

These data showed that, in agreement with the US data, patients with diabetes had longer lengths of hospital stay regardless of their admission speciality, accounting for up to 24% excess bed days. Whilst the increase length of stay was modest – rarely greater than 1 day – in total, because people with diabetes accounted (at that time) approximately 10% of all in-patients, this still equated to a very large number of excess bed days. The data looked at the spread of these excess bed days across age and speciality and showed that excess length of stay decreased with age, with those with diabetes over the age of 75 years having much the same length of stay as those without diabetes of the same age.

What changed as a result of the paper?

These data provided diabetes teams across the UK, and further afield, with sufficient information to convince hospital management that investing in in-patient diabetes services should be a priority. Furthermore, to show that fairly simple service redesigns could help to reduce in-patient bed usage, reduce length of stay, reduce medication use, mealtime and insulin errors, improve day case listing rates, reduce admissions, and be associated with higher satisfaction scores.

In retrospect, what should have been done differently in this study?

These data compared the discharge data for 943,613 people recorded as having diabetes compared to 10,724,414 people without diabetes over the four years that the study analysed. Other work presented earlier in this thesis has shown that coding data is

relatively poor, and thus in an ideal world, better quality data would have been used – i.e. individual patient data. However, discharge codes (and subsequent costs charged by hospitals to funders) are highly reliant on these documents. They are often lacking in sufficient detail. Individual patient notes could be looked at to ensure that the coding was correct – or at least ask individual hospitals to do an audit of the coding inaccuracies with their own institutions and then make the adjustments on the data based on their findings. Diabetes is often not reported in discharge summaries, and thus its impact is likely to be underestimated.

Future work as a result of this publication

These data have provided the foundation for further work on all aspects of in-patient diabetes – in terms of admissions avoidance and many other strategies to help reduce the length of stay. There have been attempts made to try and analyse where the delays occur in discharging patients and to quantify the economic impact of this excess length of stay.

[8]

Confirmation of authorship

This is shown.

External link to the paper on the journal website

[http://www.diabetesresearchclinicalpractice.com/article/S0168-8227\(06\)00455-4/pdf](http://www.diabetesresearchclinicalpractice.com/article/S0168-8227(06)00455-4/pdf)

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper:

Sampson MJ, Dozio N, Ferguson B, Dhatariya K. Total and excess bed occupancy by age, speciality and insulin use for nearly one million diabetes patients discharged from all English Acute Hospitals. Diabetes Res.Clin.Pract. 2007;77:92-8

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed.....

Professor Mike Sampson MD FRCP

Consultant in diabetes and Honorary Professor of Medicine, Norwich Medical School

Date.....

Title of paper:

Sampson MJ, Brennan C, **Dhatariya K**, Jones C, Walden E (2007); A national survey of in-patient diabetes services in the United Kingdom. *Diabetic Med* 24: 643-649

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

I was involved in the initial discussions on the questionnaire development. I was also involved in the discussions about what outcomes should be measured and what analysis should be undertaken. I was also involved in the discussions about the manuscript preparation and revisions undertaken.

Background to the paper

As the prevalence of diabetes in the general population was rising, it was becoming more apparent that the numbers of hospital in-patients with diabetes was also increasing. However, it was also clear that the vast majority of patients with diabetes were not admitted *because* of a diabetes specific problem; rather they were admitted *with* diabetes being an additional diagnosis. This meant that these patients' diabetes was being looked after by non-specialists. With the advent of new drug classes, new data on glycaemic targets, and new standards of care, it was becoming clearer that there was an increasing risk of harm – or rather, inappropriate management for patients in hospital.

Objectives of the study

This study was a survey of all diabetes teams across the UK to assess what provisions for in-patients with diabetes were available.

What this study added to the literature

This was the first national survey of national in-patient diabetes services available in the UK. It was very representative, because 91.2% of all UK specialist diabetes teams responded. It showed that whilst most hospitals had a guideline for diabetic ketoacidosis, one third of all UK hospitals did not have a co-ordinated guideline for the management of the most common cause for an acute diabetes related hospital admission – the diabetic foot. Similarly, only a minority of hospitals had guidelines in place for managing hypoglycaemia or peri-operative diabetes care. Only 20.4% of responding hospitals had guidelines for all 10 conditions asked about. Furthermore, only 42.2% of hospitals had an in-patient podiatry service, and 58.3% of respondents said they had access to a dietitian able to see in-patients. Of more concern, however, was that despite the evidence for the benefits of an in-patient diabetes nurse service, only 51.4% of hospitals had one. Their workload and case mix was described. This was the first time that such an in-depth study of in-patient services had been carried out.

What changed as a result of the paper?

These data have set much of the ground work for part of the National Diabetes In-patient Audit (NaDIA). This national audit has been carried out annually since 2011 (except for 2014). This audit expanded the data collected to include more data on individual patient harms as well as staffing levels. The NaDIA data now forms a central part of the Care Quality Commission (CQC) pre-inspection packs. As a result of discussions between the

Joint British Diabetes Societies for In-patient Care Group and the CQC – I am one of those involved in these discussions – in-patient diabetes is one of the very few ‘condition specific’ quality indicators that the CQC ask about – the others being standards of care for people with dementia and for those with learning difficulties. The CQC now has a number of ‘key lines of enquiry’ around the care of people in hospital with diabetes. As of April 2017, these are as follows:

Evidence required: Prior to the inspection, and in discussion with Trust senior management, does the provider:

- Participate in the annual NaDIA programme.
- Have a credible and overarching written strategy for in-patient diabetes care across the entire Trust as part of an approved Trust governance framework.
- Have a written policy for the safe prescribing and administration of insulin, linked to direct or online mandatory training of all staff, with evidence of adoption of national guidance on in-patient diabetes care and insulin use [101,125,126], and programmes to review improvement in outcomes.
- Have a dedicated in-patient diabetes specialist service as one of their core services, with routine and planned access to this service for all in-patients with diabetes, not just emergency admissions [127].
- Have a foot multidisciplinary team (MDT) for in patients with acute diabetic foot problems and /or high risk feet while in-patients.
- Have a robust system in place to identify all current in-patients with a known diabetes diagnosis, with evidence of a rapid referral system to the specialist in-patient diabetes team for those experiencing diabetes management problems.

- Collect annually, and review, the in-patient experience of diabetes care, and the key issues raised, positive and negative.

Intelligence: If the inspection team feels there is little evidence of the above elements of a good in-patient diabetes service in place, then review:

- Severe in-patient hypoglycaemia rate by quartile against comparator Trusts (NaDIA data)
- Insulin prescription error and management errors per year by quartile against comparator Trusts (NaDIA data)
- Hospital acquired foot lesions against comparator Trusts (NaDIA data)
- Access to the in-patient diabetes specialist team
- Evidence of adoption, or adaption, of national insulin and in-patient diabetes management guidelines, and uptake of mandatory training in insulin management among all relevant staff.
- Sample insulin prescription chart(s): Is the insulin correctly prescribed
- Action taken at Trust and ward level for patients when glucose readings are at the extremes (very high or very low) – what action is taken, and by whom?

During the inspection

- The inspection team should ask ward managers and patients with diabetes about the specific issue of timing of insulin in relation to meals, and quality of meals and snacks
- The inspection team should check that a foot assessment has been documented for all patients with diabetes during the current in-patient episode

- The inspection team should examine the insulin prescription chart. Is the name and dose of insulin correct? Is the timing of insulin correct? Is 'unit' written in full on the prescription? Is correct insulin administration equipment used.
- The inspection team should ask junior doctors and nurses whether they have had training in insulin prescription and management at this Trust? Are they confident in insulin prescription and management?

The start of the process – i.e. the publication of the initial paper – has led directly to the inclusion of diabetes as part of the CQC inspections for all Acute Hospitals

In retrospect, what should have been done differently in this study?

The very large changes that these data have resulted in over the years suggest that they are very robust. Thus, in retrospect, I do not feel that anything could have or should have been done differently at the time.

Future work as a result of this publication

NaDIA started in 2011 and has continued to be carried out annually since then, under the leadership and stewardship of Professor Gerry Rayman in Ipswich. In 2014 there was insufficient funding to enable NaDIA to be carried out nationally, but as a result of the data being part of the CQC inspection, it is now almost guaranteed to be funded from now on.

The data generated from NaDIA continues to form the basis of much ongoing service improvement work in individual hospitals.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

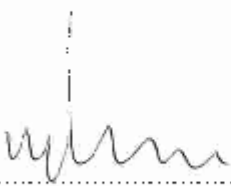
<http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2007.02156.x/abstract>

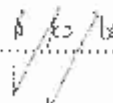
To whom it may concern

This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper:

Sampson MJ, Brennan C, Dhatariya K, Jones C, Walden E. A national survey of in-patient diabetes services in the United Kingdom. Diabetic Med. 2007;24:643-9

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed 

Date 

Professor Mike Sampson MD FRCP

Consultant in diabetes and Honorary Professor of Medicine, Norwich Medical School

Title of paper:

Sampson MJ, Crowle T, **Dhatariya K**, Dozio N, Greenwood, R, Heyburn PJ, Jones C, Temple RC, Walden E (2006); Trends in bed occupancy for in-patients with diabetes before and after the introduction of a diabetes in-patient specialist nurse service. Diabetic Med 23: 1008-1015

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

I was involved in the discussions about what outcomes should be measured and what analysis should be undertaken. I was also involved in the discussions about the manuscript preparation and revisions undertaken.

Background to the paper

It had been recognised for many years that people with diabetes in hospital experienced problems with excess morbidity, prolonged length of stay and extreme dissatisfaction. These issues were long standing, systemic, and well described. However, there were few data available on what interventions made a difference to these findings. The background to this was the appointment to our hospital of one of the country's first diabetes in-patient specialist nurse (DISN). At the time of her appointment in 2003/2004, the prevalence of in-patient diabetes was much less than it currently is at 9.7%, compared to 17% in 2016 [2]. These data showed that a simple service redesign based around a dedicated in-patient diabetes specialist nurse team had been shown to reduce length of stay, reduce medication use, mealtime and insulin errors, improve day case listing rates, reduce

admissions, and be associated with higher satisfaction scores. However, it has been shown from the NaDIA data and older national surveys commissioned by the Association of British Clinical Diabetologists presented earlier in this thesis, that about one third of UK Trusts (particularly smaller Trusts) lacked this very simplest of service models. There was little incentive for Acute Trusts to improve or change, and it was felt that much of this poor quality practice (and acceptance of poor outcomes) had become embedded as part of 'normal' Trust care.

Objectives of the study

The objective of the study was to provide accurate data for excess diabetes bed occupancy, and examine evidence of benefit for a diabetes in-patient specialist nurse (DISN) service model locally and nationally.

What this study added to the literature

The data presented in this paper helped to provide individual Trusts with the information to show that a small amount of investment could lead to substantial improvements in care, as well as significant cost savings. It was the first time that an accurate analysis of bed usage had been carried out showing the benefits of a diabetes in-patient specialist nurse.

What changed as a result of the paper?

Other authors have also shown the benefits of an in-patient service [128]. These data, and those from NaDIA, show that the numbers of referrals to the DISN teams have been increasing year on year. However, despite the very strong evidence base supporting their use only two thirds of all acute hospitals now have a DISN available [101]. In addition,

there are not enough of them to see everyone, with the DISN's themselves reporting that they are only being able to see two thirds of those they feel they ought to be seeing [101].

As mentioned, many other teams across the UK and other parts of the world have seen the value of appointing in-patient nurses. The appointment of the DISN's led to the formation of the UK DISN group, a founding partner in the JBDS Group. The original DISN appointed who was the centre of the paper, Esther Walden, has been the chair of the UK group since its inception. The JBDS group has published a large number of national guidelines for the management of in-patients with diabetes, with all of these having substantial input from the DISN's. Thus this study had had direct impact on millions of in-patients across the UK and the world.

In retrospect, what should have been done differently in this study?

This paper was amongst the first ever published to show the benefits of a dedicated in-patient diabetes specialist nurse. The only thing that could have been done differently is perhaps doing it earlier. The reason it was not, is that it took a great deal of persuasion to convince our hospital of the potential value of such a nurse. That there was no data to support their appointment proved to delay them being put into place.

Future work as a result of this publication

The DISN group continue to play an integral role in the development and writing of all JBDS in-patient guidelines.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

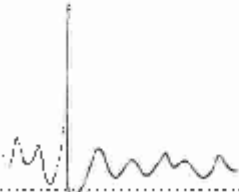
<http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2006.01928.x/abstract>

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper:

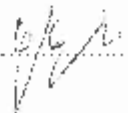
Sampson MJ, Crowle T, Dhatariya K, Dozio N, Greenwood RH, Heyburn PJ et al. Trends in bed occupancy for inpatients with diabetes before and after the introduction of a diabetes inpatient specialist nurse service. *Diabetic Med.* 2006;23:1008-15

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signature.....

Professor Mike Sampson MD FRCP

Consultant in diabetes and Honorary Professor of Medicine, Norwich Medical School

Date.....

The Diabetes In-patient Treatment Satisfaction Study (DIPSat)

Title of paper:

Sampson MJ, Singh H, **Dhatariya KK**, Jones C, Walden E, Bradley C (2009);

Psychometric validation and use of a novel diabetes in-patient treatment satisfaction questionnaire. Diabetic Med 26: 729-735

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

I was a co-applicant on this Diabetes UK funded research project. I was involved in the discussions when submitting the grant application. I attended most of the steering group meetings and actively participated in the discussions about what outcomes should be measured and what analysis should be undertaken. I was also involved in the discussions about the manuscript preparation and revisions undertaken.

Background to the paper

Having diabetes is associated with an almost doubling of risk for hospital admission for people with the condition, compared to those without diabetes who have the same condition [9]. The management of diabetes is often complex and the underlying medical condition that has necessitated hospital admission can change the day-to-day needs of the person with diabetes. This poses challenges for patients and their caregivers, because even in people who correctly self-manage their own diabetes, several things can change during the time of an acute illness that may influence glycaemic control. These include (but are not limited to), change of environment, change of diet and altered levels of intake, differing levels of physical activity, and the direct effects of the physical illness (e.g. being

nil by mouth before or after an operation, or post-operative nausea and vomiting). Added to this, it is well recognised that the doctors most frequently in contact with the patients – junior medical staff – have low levels of confidence and competence when dealing with diabetes [83]. Taken together, in the unfamiliar and often frightening atmosphere of an acute hospital admission, it was unknown how patients with diabetes felt about their care, and importantly what aspects of their care were most important in determining their levels of treatment satisfaction as an in-patient.

On this background, funding was sought and awarded from Diabetes UK, to develop and validate a self-completed questionnaire that would appropriately assess the satisfaction of care provided to hospital in-patients with diabetes.

Objectives of the study

To develop the first psychometrically validated diabetes treatment satisfaction questionnaire for hospital in-patients.

What this study added to the literature

Prior to the publication of this paper there has been a lot of work done to assess patient satisfaction in people with diabetes with the treatment they had received as outpatients, or with other diabetes related complications [129-132]. However, nothing had been done to look at hospital in-patients with diabetes. This paper looked at the modification of existing outpatient questionnaires and added some questions to make them suitable for in-patient use. At the time of publication, it was a novel approach to an understudied subject in an increasing large proportion of hospital in-patients.

What changed as a result of the paper?

The number of hospital in-patients with diabetes is rising – the 2016 data from the National Diabetes In-patient Audit (NaDIA) showed that the range prevalence of diabetes across UK hospitals was a mean of 17%, and a range of 4% to over 35% [2]. The publication of this paper has led to an increased awareness of the importance of treating people with diabetes who are in hospital correctly. In particular the major issues surrounding the availability – in terms of timing and choice – of hospital food, as a source of major dissatisfaction in this population.

In retrospect, what should have been done differently in this study?

At the time that this study was first thought of and conducted, this was a novel idea. The use of other validated diabetes treatment satisfaction questionnaires was already established, and the validation of this tool for in-patients was the next obvious step. It was planned as a series of work that were all carried out. Thus, in retrospect, I do not believe that anything different should have been done.

Future work as a result of this publication

The next step was the production of a validated diabetes treatment satisfaction questionnaire in 5 South Asian languages. This work was done, and completed, and has been submitted for publication.

Confirmation of authorship

This is shown.

External link to the paper on the journal website


<http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2009.02754.x/abstract>

To whom it may concern

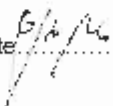
This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper.

**Sampson MJ, Singh H, Dhatariya KK, Jones C, Waldon E, Bradley C.
Psychometric validation and use of a novel diabetes in-patient treatment
satisfaction questionnaire. Diabetic Med. 2009;26:729-35**

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed 

Professor Mike Sampson MD FRCP

Date 

Consultant in diabetes and Honorary Professor of Medicine, Norwich Medical School

Title of paper:

Rutter CL, Jones C, **Dhatariya KK**, James J, Irvine L, Wilson EC, Singh H, Walden E, Holland R, Harvey I, Bradley C, Sampson MJ (2013); Determining in-patient diabetes treatment satisfaction in the UK—the DIPSat study. *Diabetic Med* 30: 731-738

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

I was a co-applicant on this Diabetes UK funded research project. I was involved in the discussions when submitting the grant application. I attended most of the steering group meetings and actively participated in the discussions about what outcomes should be measured and what analysis should be undertaken. I was also involved in the discussions about the manuscript preparation and revisions undertaken.

Background to the paper

Having diabetes is associated with an almost doubling of risk for hospital admission for people with the condition, compared to those without diabetes who have the same condition [9]. The management of diabetes is often complex and the underlying medical condition that has necessitated hospital admission can change the day-to-day needs of the person with diabetes. This poses challenges for patients and their caregivers, because even in people who correctly self-manage their own diabetes, several things can change during the time of an acute illness that may influence glycaemic control. These include (but are not limited to), change of environment, change of diet and altered levels of intake, differing levels of physical activity, and the direct effects of the physical illness (e.g. being

nil by mouth before or after an operation, or post-operative nausea and vomiting). Added to this, it is well recognised that the doctors most frequently in contact with the patients – junior medical staff – have low levels of confidence and competence when dealing with diabetes [83]. Taken together, in the unfamiliar and often frightening atmosphere of an acute hospital admission, it was unknown how patients with diabetes felt about their care, and importantly what aspects of their care were most important in determining their levels of treatment satisfaction as an in-patient. This has always been a strong theme in patient comments and complaints, raised repeatedly by Diabetes UK over the last decade. In-patients with diabetes are very vulnerable (particularly those on insulin) to variable meal times and meal quality, to nil by mouth policies and insulin management, and to the tendency of inexperienced clinical staff to take over insulin management and blood glucose monitoring, from often very experienced patients.

This study was a follow on, a natural progression, from the development of the validated questionnaire described previously. This used the Diabetes In-patient Treatment Satisfaction Questionnaire to assess what insulin treated patients with diabetes felt about the care they received in hospital.

Objectives of the study

To use the first psychometrically validated diabetes treatment satisfaction questionnaire for hospital in-patients to examine what determinants of in-patient diabetes care were associated with treatment satisfaction or dissatisfaction.

What this study added to the literature

This was the first time that patients has been surveyed to assess their perceptions of the quality of diabetes care, using a validated instrument, in such large numbers (n=1,319). The findings were novel, if not unsurprising, that in-patients with diabetes in hospital in the UK have high levels of dissatisfaction with their diabetes care. Many people were satisfied with their diabetes care in hospital, but there were very high levels of dissatisfaction with the timings and choice of available meals, with 23% saying they would rarely or never chose to eat the food they were offered in hospital, and that 20% of people reported having high glucose concentrations during their in-patient stay, and 7% has episodes of hypoglycaemia. 26% of respondents reported at least one episode of a glucose that was so low they required rescue treatment from a third party. All of these factors were associated with lower satisfaction scores.

What changed as a result of the paper?

Prior to the publication of this paper, what patients with diabetes thought about their care whilst in hospital has not been deemed to be particularly important. Subsequently, other authors have cited this work in an attempt to raise this issue – and how it impacts on the overall patient experience and thus outcomes [133,134]. In addition, in-patient treatment satisfaction is now a prominent feature in the National Diabetes In-patient Audit (NaDIA) with the 2015 data showing that 34% of patients reported that their hospital sometimes, rarely or never provided the right choice of food to manage their diabetes [101].

In retrospect, what should have been done differently in this study?

Due to logistical difficulties of using the questionnaires, and to try and keep the patient population sampled as 'homogenous' as possible, only those patients on insulin who were

seen by a Diabetes In-patient Specialist Nurse were approached to take part in the study. These represent a minority of diabetes patients – 35.6% of all patients with diabetes in the 2015 NaDIA dataset [101], with the vast majority being on diet or oral hypoglycaemic agents only. These latter patients may have different experiences, but given the complexity of the study and the cost restraints, it was deemed not possible to be able to survey them.

Future work as a result of this publication

The next step was to develop a version of the Diabetes In-patient Treatment Satisfaction Questionnaire for five South Asian Languages, Hindi, Urdu, Bengali, Punjabi and Gujarati. Then to administer the questionnaire and compare the outcomes of in-patient diabetes treatment between people who described themselves at 'White British', those people who were of South Asian origin but said that English was their first language and those who used one of the 5 South Asian languages as their first language. This was done and the study completed. It has been submitted for publication.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

<http://onlinelibrary.wiley.com/doi/10.1111/dme.12095/abstract>

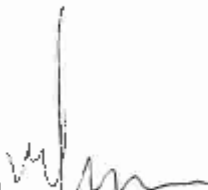
To whom it may concern

This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper:


Rutter CL, Jones C, Dhatariya KK, James J, Irvine L, Wilson EC et al.

Determining in-patient diabetes treatment satisfaction in the UK—the DIPSat study. Diabetic Med. 2013;30:731-8

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed 

Professor Mike Sampson MD FRCP

Date 

Consultant in diabetes and Honorary Professor of Medicine, Norwich Medical School

The Management of Diabetic Ketoacidosis

Title of paper:

Dhatariya KK (2007); Diabetic ketoacidosis. Br Med J 334: 1284-1285

Impact factor of the journal

17.4

Background to the paper

Prior the publication of the Diabetes Control and Complications Trial (DCCT) [4] and the United Kingdom Prospective Diabetes Study (UKPDS) [5] it had been recognised that long terms poorly controlled diabetes was associated with an increased risk of developing the microvascular and macrovascular complications of diabetes. What had not been demonstrated until those studies were published, was that if glycaemic control was improved, would it make a difference to the risk of developing complications. Both of these studies showed that good glycaemic control achieved early after the diagnosis of diabetes and then maintained for 6-7 years led to significant reductions in the risk of developing complications. These benefits were maintained many years later, even when the trials had stopped, and the glycaemic control in the intensive treatment arm had deteriorated once the trials had stopped – so called ‘metabolic memory’ [135,136].

The management of hyperglycaemia in hospital in-patients reflects this history for outpatients with diabetes – there are currently plenty of data to suggest that in-patients with high glucose concentrations experience a variety of harms, but there are currently very few data to show that intervening makes a difference to outcomes.

In 2006 I was at event where one of the other guests was a local intensivist. Over the following hours we had a robust discussion. The main tenant of their argument was ‘why do physicians insist on using 0.9% sodium chloride solution (“normal saline”) as the fluid resuscitation of choice when treating DKA?’ Their vociferous argument went on for quite some time, and I was unable to counter the argument at that time, other than by saying ‘this is how it has always been done, and there seems to be little evidence of harm’. As a result of this encounter I undertook a literature review of the arguments and was able to formulate this paper, which was eventually published in the BMJ.

Objectives of the paper

To argue the case (by providing evidence) for continued use of 0.9% sodium chloride solution as the fluid replacement of choice for people presenting with DKA. In addition, to argue against the use of alternative fluids, such as Hartmann’s solution.

What this study added to the literature

For many years there had been a debate about what was the best fluid to use in replacing the losses seen in patients presenting with DKA. There had been very few randomised controlled trials comparing the use of 0.9% sodium chloride solution with other crystalloids, e.g. Hartmann’s solution or Ringer’s lactate solution. This editorial explained the arguments for why most diabetologists have safely used 0.9% sodium chloride solution for many decades. It also argued why other solutions were not suitable because of the potential risks. This debate had not occurred in print for many years prior to this editorial being published.

What changed as a result of the paper?

Within a few days of the editorial being published I began to get a lot of correspondence – predominantly from anaesthetists – personally and as ‘rapid reviews’ telling me (in no uncertain terms) that “I didn’t know what I was talking about”. The editorial has been cited 23 times (accessed 1st October 2017), and has been cited in at least one subsequent randomised controlled trial comparing the use of different crystalloid solutions in this situation [137]. On a broader level, this paper opened up the discussion again about what is the best way of replacing fluids in this group of sick individuals. On reflection, it is now widely acknowledged, that there is no single ‘physiologically correct’ solution that currently exists that adequately replaces the fluid and electrolytes lost during an episode of acute DKA.

On a personal level what changed for me is that this manuscript was read by the members of the JBDS DKA guideline writing group who at the time were in the earliest stages of formulating the guidance. They invited me to join the group and I have been a senior member of the JBDS steering group since then, where I have either been the lead co-author, or a co-author on most of the guidelines written by the group.

In retrospect, what should have been done differently?

On reflection, I feel that I would have done nothing differently at that time. Diabetologists had used 0.9% sodium chloride solution safely for decades with no apparent evidence of harm, yet its use was consistently challenged by intensivists and anaesthetists, again, with no evidence of benefit for the alternatives they put forward. That the argument was opened up, that more work has been done subsequently, that the majority of specialist

diabetes teams across the UK continue to use 0.9% sodium chloride solution as first line fluid replacement of choice suggests that my argument has been supported.

Future work as a result of this publication

For me, this editorial was the start of the process that has got me deeply involved in a) collecting the data to show the harms associated with in-patient hyperglycaemia, and b) to allow me to work on projects to show that intervening will make a difference to outcomes.

Confirmation of authorship

Not needed because I was the sole author.

External link to the paper on the journal website

<http://www.bmj.com/content/334/7607/1284>

Title of paper:

Savage MW, **Dhatariya KK**, Kilvert A, Rayman G, Rees JA, Courtney CH, Hilton L, Dyer PH, Hammersley MS (2011); Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. *Diabetic Med* 28: 508-515

And the main document from which this paper was derived:

Dhatariya K, Savage M, Kelly T, Sampson M, Walton C, Claydon A, Dyer P, Evans P, Khan A, Kilvert A, Leech N, Levy N, Rayman G, Rees A, Sinclair-Hammersley M (2013) Joint British Diabetes Societies In-patient Care Group. The management of diabetic ketoacidosis in adults. Second edition. Update: September 2013

Impact factor of the journal

3.12. Furthermore, in 2014, this paper was the 4th most downloaded manuscript from the Wiley online website (<http://onlinelibrary.wiley.com>) globally, and in 2015, it was the 3rd most downloaded manuscript from the website [data given to me verbally from 2 Associate Editors of the journal].

My contribution to this non-peer reviewed publication

I was a senior member of the writing group. I attended all of the meetings and the teleconferences. I was actively corresponding by email to all of the other co-authors. I was involved in writing the first edition of the guideline. For the second edition, I was the person who co-ordinated the updates, and wrote the final draft of the guideline. It was not peer reviewed, because as the editor of the journal said to me when he received it 'the

writing group is made up of enough experts in the field in the UK that it has already been peer reviewed in the writing process’.

Background to the paper

Despite their having been a progression of publications on the way DKA should be treated, in the early 1980’s there remained an appreciable mortality and morbidity [33]. This was despite using a regimen similar to the one used by many diabetes teams – low dose intravenous insulin infusion, aggressive fluid replacement and correction of electrolyte disturbances. However, what there seemed to be lacking was a formal definition of DKA and a standardised approach to exactly how much insulin, what fluid replacement and at what rate, and what electrolytes should or should not be replaced, and if they were to be replaced, how fast.

Because there were no data about many of these unanswered questions, the JBDS group asked for a copy of the DKA guidelines from hospitals across the UK. They received dozens of these and they were all carefully analysed by the writing group for areas of commonality highlighted but also, more importantly, areas of differences in practice. The writing group then had several face to face meetings, and emails to thrash out what should evolve from these many documents. Over this iterative process, the first edition of the national guideline was written. It was acknowledged that this was a consensus document, which cited the evidence where it existed, but used a pragmatic, consensus based approach for where areas of controversy were apparent.

However, within a few weeks of the first version of this guideline being published newer data were emerging, on the use of the protocol in ‘real world’ clinical practice and other

data, e.g. the differences between outcomes using 0.9% sodium chloride solution and Hartmann's solution [138]. Soon after the publication of the first edition of these national guidelines, several abstracts were presented in local, regional and national meetings with a variety of messages. It became apparent that there were changes that needed to be made and these were outlined in the updated document.

Objectives of the guideline

To harmonise the management of DKA in different hospitals across the UK.

What this study added to the literature

This paper was the first national guideline for the management of DKA. The writing group were not aware of any other country that had produced such a guideline. I am still unaware of any other country in the world that has what we have in the UK – a standardised approach to the management of DKA for non-specialists. The paper also included a 1 page, easy-to-read and easy-to-follow guide on how DKA should be managed.

In addition, the updated version of the guideline allowed further advertising and dissemination of the guideline by the bodies who make up the Joint British Diabetes Societies – i.e. Diabetes UK, The Association of British Clinical Diabetologists and the Diabetes In-patient Nurse Group. The data included in this updated online version made no formal changes to the management of patients with DKA, but gave more references as to why things had changed from the way things 'used to be done'.

What changed as a result of the paper?

New words and abbreviations were added to the diabetes vocabulary as a result of this paper. In particular 'VRIII' – variable rate intravenous insulin infusion, and 'FRIII' – fixed rate intravenous insulin infusion. The former National Clinical Director for Diabetes, Dr Rowan Hillson, should be credited with this change.

Other things that changed quite substantially in the management of patients with DKA were the continuation of long acting subcutaneous insulin in those already on it as well as their FRIII / VRIII. In addition, the guideline advocates that arterial blood gas measurements are not necessary because the differences between arterial and venous blood are not sufficiently large enough to change management [39]. In addition, venous blood gas measurements are associated with less morbidity than arterial blood gas sampling. Finally, the writing group strongly advocated the use of 0.9% sodium chloride solution as the fluid replacement of choice in DKA.

One of the major concerns that I had as a result of the first and subsequent versions of the guideline was whether it worked – were patients benefitting from its use? Previous work had shown that the first version of the guideline was being used and was well received. A survey was sent out by the chair of JBDS, Professor Mike Sampson in autumn 2012 to all secondary care diabetes teams. 105 replies were received, with over 90% of respondents rated the first version of the JBDS DKA guidelines as 'Excellent' or 'Good' (Figure 1).

However, as a result of this difficulty of knowing whether the guideline worked I carried out a survey on the management of DKA across the UK. Those data are discussed later in this thesis.

This work and the work that has arisen from it was part of the reason that I was shortlisted for the 2017 Royal College of Physicians Excellence in Patient Care Awards.

In retrospect, what should have been done differently in this study?

On balance, at the time I think that the writing group made every effort to ensure that the final document was as comprehensive as possible, and as evidence based as it could be. However, more efforts could have been made to engage other groups of people who were involved in the care of these ill patients, in particular to have anaesthetic input from an intensive care perspective. This was done for the second edition. Also, greater input from acute medicine would have been appreciated; however, one of the authors (Dr PH Dyer) was predominantly an acute physician at the time and did have that perspective when the document was written.

In retrospect, I believe that the second version of the guideline was timely and showed that the JBDS group were 'dynamic'. That we understood that times changed, and the evidence base changed, and thus we needed to be seen to be 'proactive' in our approach. I believe that this has been one of the strengths of the JBDS Group. The peri-operative guideline that I led the writing group for (discussed elsewhere in this thesis) also went through this process. Further updates of the DKA guideline and the peri-operative guidelines are due in 2017/2018.

Future work as a result of this publication

The work discussed later in this thesis shows that the second edition of this guideline was written because more evidence came out on why we made the recommendations that we

did. It was clear that changes needed to be made quite quickly, not only because of feedback from specialist diabetes teams across the UK, who were very quick to adopt or locally adapt the guidelines, but also because of new data that had been published.

In addition, as a result of this difficulty of knowing whether the guideline worked I carried out a survey on the management of DKA across the UK. That data is discussed in a subsequent section. This is the largest national survey on the management of DKA ever carried out.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

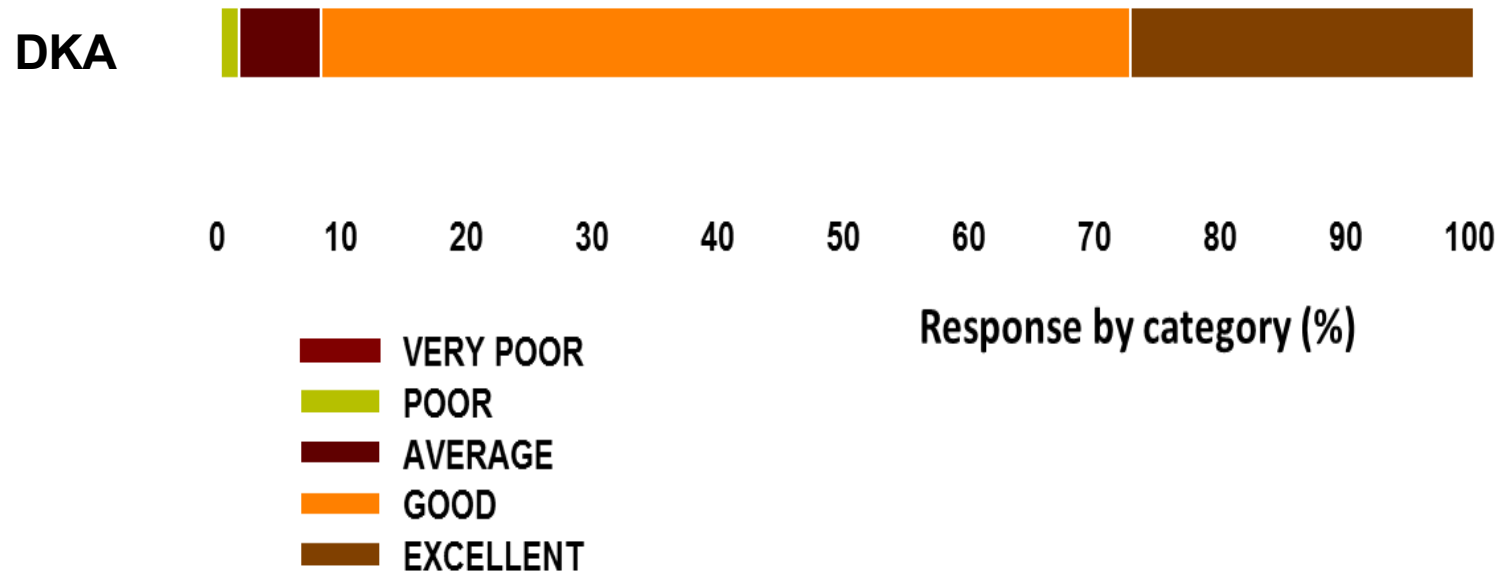
<http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2011.03246.x/abstract>

External link to the guidelines on the website of the Association of British Clinical Diabetologists

http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_DKA_Adults.pdf

http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_DKA_Adults_Revised.pdf

Figure 1 – Data from Mike Sampson. Feedback from 104 hospitals – first shown at Diabetes UK March 2013





HEALTHY COMMUNITIES AND
WORLD CLASS HEALTHCARE

CARING PASSIONATE TRUSTWORTHY

Medical Services
PO Box 126
BENDIGO VIC 3552
P (03) 5454 7554
F (03) 5454 7504

To whom it may concern:

This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper:

Savage MW, Dhatariya KK, Kilvert A, Rayman G, Rees JA, Courtney CH et al. Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. *Diabetic Med.* 2011;28:508-15

I can confirm that Dr Dhatariya was involved in several aspects of this work. He was a senior member of the writing group, and led the writing group of the second edition of this guideline. He had substantial input into the preparation of the work prior to publication.

Signed

Date

8/6/16

A/Prof Mark W Savage MB ChB MD FRCP(London) FRACP

Director of Medicine and Clinical Dean, Consultant Endocrinologist and General Physician, Medical Services, Bendigo Health, PO Box 126 Bendigo Victoria 3552, Australia

Adjunct Clinical A/Prof, Monash University, School of Rural Health, Bendigo

Bendigo Health Care Group
PO Box 126, Bendigo Victoria 3552

General enquiries P 03 5454 5000
ABN 26 875 445 912

www.bendigohealth.org.au
www.newbandigehospital.org.au



Medical Services
PO Box 126
BENDIGO VIC 3552
F (03) 5454 7564
F (03) 5454 7504

To whom it may concern


This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper:

Dhatariya, K, Savage, M, Kelly, T, Sampson, M, Walton, C, Claydon, A, Dyer, P, Evans, P,
Khan, A, Kilvert, A, Leech, M, Levy, N, Rayman, G, Rees, A, and Sinclair-Hammersley, M.

**Joint British Diabetes Societies Inpatient Care Group. The management of diabetic
ketoacidosis in adults. Second edition. Update: September 2013.**

<http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm>. 2013

I can confirm that Dr Dhatariya was involved in several aspects of this work. He was a senior member of the writing group, and led the writing group of this, the second edition of this guideline. He had substantial input into the preparation of the work prior to publication

Signed 

Date 8/6/16

Director of Medicine and Clinical Dean, Consultant Endocrinologist and General Physician,
Medical Services, Bendigo Health, PO Box 126 Bendigo Victoria 3552, Australia
Adjunct Clinician/Prof, Monash University, School of Rural Health, Bendigo

Bendigo Health Care Group
PO Box 126 Bendigo Victoria 3552

General enquiries P.03 5454 6000
ABN 26 375 415 911

www.bendigohalth.org.au
www.monash.edu.au/ruralhealth

Title of paper:

Rudd B, Patel K, Levy N, **Dhatariya K** (2013); A survey of the implementation of the NHS diabetes guidelines for management of diabetic ketoacidosis in the intensive care units of the East of England. *Journal of the Intensive Care Society* 14: 60-64

Impact factor of the journal

Unknown. This is currently not a 'listed' journal. Google Scholar reports that this paper has been cited six times [accessed 1st October 2017]

My contribution to this peer reviewed publication

I was involved with the initial discussions about what should be involved in the data collection and what analyses should be done. I also helped write the final version of the submitted manuscript.

Background to the paper

With the publication of the first edition of the JBDS guidelines on the management of DKA in 2011 local, regional and national data – usually published in abstract form from individual secondary care diabetes teams – suggested that they had a high level of acceptance, with the majority of teams either adopting them or adapting them for their own use. This was confirmed by a national survey carried out by Professor Mike Sampson, Chair of JBDS and presented at Diabetes UK Annual Professional Conference in 2013 [123]. In the US and in the UK, it is strongly recommended that patients presenting with moderate or severe DKA be cared for in a high dependency unit (HDU) or intensive care unit (ITU) [20,42]. However, in the UK only a minority of patients presenting with DKA are looked after in these, level 2 (HDU), or level 3 (ITU) environments. Partly because of the

relative unavailability of HDU/ITU beds in the UK [139]. However, many intensive care units are 'closed' units. This means that they are run predominantly by teams who specialise in intensive care. This approach has been known to improve patient outcomes for over 20 years [140]. Thus, this approach does rely on the intensive care team to stay up to date with all aspects of critical illness. With the best will in the world, it is hard to keep up to date with the developments in all areas of ones' speciality. This study aimed to look at the knowledge of, uptake and utilisation of the JBDS DKA guideline 18 months after the initial edition had been published, in 13 ITU's across the East of England.

Objectives of the study

To audit critical care units within hospitals in the East of England and find out whether they had changed their DKA guidelines and adopted the '*gold standard*' recommendations from the JBDS. In particular focussing on the introduction of weight based fixed rate intravenous insulin infusions, use of ketone meters, choice of resuscitation fluid, and continuation of basal long-acting insulin analogues.

What this study added to the literature

The data confirm that most units had their own DKA protocols but that most had not adopted or adapted the JBDS guidelines. Almost all of the units were run by anaesthetists and as such over half used Hartmann's solution as their preferred resuscitation fluid; over half did not use the recommended fixed rate intravenous insulin infusion and 4 of the 13 units had not updated their DKA guidelines since 2010 (with a further 2 not being sure or data unavailable). In addition, only 3 units had changed their practice to continue long acting subcutaneous insulin in addition the intravenous insulin infusions. The data also

suggested that there was either a lack of knowledge about the guideline or that there was resistance to its use.

What changed as a result of the paper?

There was a concerted push to make more ITU teams know about the JBDS guideline after publication of this paper in the main UK ITU journal – published by the UK Intensive Care Society. In addition, my lead co-author, Dr Nicholas Levy has been instrumental in bringing the guidelines to ITU teams across the East of England and more widely by his frequently run anaesthetic conferences at the Association of Anaesthetists of Great Britain and Ireland (AAGBI).

In retrospect, what should have been done differently in this study?

It is clear that one of the reasons for the lack of uptake of the first edition of the guidelines is that no anaesthetists were involved in the writing group. There had been very little attempt to engage with other teams that were involved in the management of DKA, in particular the acute physicians. This changed with the second edition, where we had anaesthetic input at the very start as part of the writing group, and the document had endorsement from the Intensive Care Society

Future work as a result of this publication

It is hoped that this survey can be repeated to see if things have changed since the publication of the second edition.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

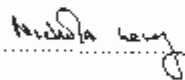
<http://journals.sagepub.com/doi/pdf/10.1177/175114371301400112>

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was a senior author on the following paper:

Rudd B, Patel K, Levy N, Dhatariya K. A survey of the implementation of the NHS diabetes guidelines for management of diabetic ketoacidosis in the intensive care units of the East of England. JICS 2013;14:60-4

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he was involved in the discussions around the conduct of the study, and he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed 

Date: 12/6/2014

Nicholas Levy

Consultant Anaesthetist

West Suffolk Hospital

Title of paper:

Dhatariya KK, Nunney I, Higgins K, Sampson MJ, Iceton G (2016); A national survey of the management of diabetic ketoacidosis in the UK in 2014. *Diabetic Med* 33: 252-260

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

I conceived the idea of the national survey. I wrote the data collection tool. I wrote to all diabetes teams in the UK and collected all the data. I helped analyse the data and came up with the interpretations. I wrote the initial and final drafts of the manuscript.

Background to the paper

It was a common anecdotal experience as a trainee that when one changed to a new hospital as a diabetes registrar to be asked to 're-write the DKA guideline'. There was often no justification to do so, other than to ensure that the most up-to-date literature was incorporated. However, there was little data to show that any particular version of a guideline actually worked. The history and evolution of the management of DKA is discussed at the start of this thesis, but in the 1980's when a standardised regimen of low dose intravenous insulin infusion, aggressive fluid replacement and correction of electrolyte disturbances had been established, there was still a significant mortality [33]. There had been little data collected in the UK on outcomes of DKA, except for a notable paper in 1993 describing the persisting mortality associated with the condition [141]. It was against this background of small variations in care between hospitals, and no assessment of their outcomes that the first version of the national guideline was published. The second

edition incorporated new data and further justification for the suggested changes in 'accepted dogma'. However, what had not been done was an assessment of whether the guideline actually worked. Thus I created the 5 page questionnaire, and with the help of the mailing lists from JBDS, Diabetes UK, ABCD and the DISN group, I invited every secondary care diabetes team to submit data on the next 5 patients looked after in their Trust with a diagnosis of DKA. This questionnaire is listed as an appendix in the published paper. However, the questions asked are listed in Tables 1-5 in the paper.

220 teams were invited to submit data, and 283 forms were received from 72 hospitals between May and November 2014

Objectives of the study

To examine outcomes of adult patients presenting with DKA in 2014, mapped against accepted the UK national guidance.

What this study added to the literature

Several new things were shown in the data.

- The median time from admission to diagnosis was 35.5minutes
- That the time to starting 0.9% sodium chloride solution was 6 minutes later and the time taken to start an intravenous insulin infusion was 60 minutes after admission
- The data showed that more than 80% of UK hospitals were using the JBDS guideline.
- Median time to biochemical resolution of DKA was 18.77 hours
- 8% of all cases of DKA were in existing hospital in-patients
- Unlike previous data that suggested between 25-30% of all cases of DKA were newly presenting cases of type 1diabetes [142-147], our data showed that newly diagnosed

type 1 diabetes only accounted for 6.1% of cases, with infection and non-compliance accounting for most cases

- Hypoglycaemia (glucose $<4.0\text{mmol/l}$) occurred in 27.6% and hypokalaemia ($<4.0\text{mmol/l}$) occurred in 67% of the patients. These data are similar to the rates seen in single centre studies recently reported [148,149]
- The guidelines were often not followed with respect to the use of a VRll, potassium replacement and the introduction of 10% glucose at the appropriate time
- During the study, only 1 person died, but that was several months after the initial admission for DKA, and the cause of death was listed as osteomyelitis

What changed as a result of the paper?

The data were only published in February 2016, but as of 1st October 2017 the paper had been cited 20 times. In addition, these data have been presented by me at several national and international meetings, in particular to discuss the significance of the hypoglycaemia and hypokalaemia. A possible reason for this could be the continuing fixed rate intravenous insulin infusion that continues even when glucose concentrations drop until ketone concentrations come down. This will continue to drive potassium concentrations down. The arguments are that either insulin infusion rates reduce when glucose concentrations drop, or the rate of potassium replacement should be increased. However both of these solutions have potential problems.

If the insulin infusion rate were to decrease (e.g. from 0.1unit/Kg/hr to 0.05unit/Kg/hr), then there is a risk that the time taken for the DKA to resolve would lengthen and thus the patient would stay in hospital for longer.

If the potassium infusion rate were to be increased, this would necessitate a central venous catheter, and the patient would need to be in a monitored bed in a level 2 (HDU) or level 3 (ITU) environment. In the UK it has recently been reported that we have the lowest number of ITU beds in Europe [139].

When I have presented these data there has been discussion in open fora on whether these guideline should be changed. There has been overwhelming feeling that they should remain unchanged because many of these findings may represent the guidelines not being followed, rather than them being wrong.

This work and the work that has arisen from it was part of the reason that I was a finalist for the 2017 Royal College of Physicians Excellence in Patient Care Awards.

In retrospect, what should have been done differently in this study?

The main piece of data that was not collected was the change in glucose over time. In addition, it was only after the data collect finished and the data published that I realised that it could be used to generate an analysis on how much it costs to treat an episode of DKA. This work has now been done, and has been accepted for publication. However, the major strengths of that paper are that it is a 'bottom-up' approach using individual patient care data, but despite this, several assumptions have had to be made.

Future work as a result of this publication

As the data were being collected, I was contacted by Dr Julie Edge, a consultant paediatrician from Oxford, who is a world expert on paediatric DKA. She wanted to conduct a very similar survey for adolescents presenting with DKA using the same

questionnaire, but adapted for an adolescent patient group. This data was collected in 2014/2015 and is presented elsewhere in this thesis.

Furthermore, as mentioned work has been done and submitted for publication on an economic analysis of DKA admissions. Now that this work has been completed for the adult population, it will be repeated for the adolescent dataset.

One of the next pieces of work that has been done is to see if the results from a national survey are applicable to individual hospitals. Thus I have supervised 3 medical students who have collected data on 51 consecutive admissions with DKA to the Norfolk and Norwich University Hospitals NHS Foundation Trust using the same data collection form for the national dataset. These data have recently been published [150], and whilst they would fit well in this thesis, they are not included. They show very similar findings in most areas or care, suggesting that the national survey findings are indeed, applicable to individual hospitals.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

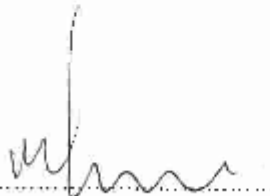
<http://onlinelibrary.wiley.com/doi/10.1111/dme.12875/abstract>

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Dhatariya KK, Nunney I, Higgins K, Sampson MJ, Iceton G. A national survey of the management of diabetic ketoacidosis in the UK in 2014. Diabetic Med. 2016;33:252-60

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he wrote the questionnaire, he carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed.....

Date.....

Professor Mike Sampson MD FRCP

Consultant in diabetes and Honorary Professor of Medicine, Norwich Medical School

Title of paper:

Dhatariya K, Nunney I, Iceton G (2016); Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. *Diabetic Med* 33: 269-270

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

I conceived the idea of the national survey. I wrote the data collection tool. I wrote to all diabetes teams in the UK and collected all the data. I helped analyse the data and came up with the interpretations. I wrote the initial and final drafts of the manuscript.

Background to the paper

I led the writing group for the second edition of the national DKA guideline. However, as part of this I wanted to know whether the guidelines actually worked. In addition, in my role as a senior member of the JBDS, and one of the few people who had been co-authors on all of the guidelines published to that point, I was often asked whether some form of work could be done to help teams assess how they were doing compared with others. Thus I carried out the world's largest national survey on the management of DKA. This consisted of two parts, one part is presented earlier in this thesis, on individual patient management, but the other part, presented here, was a single page of questions assessing the factors that may have limited teams from delivering the care that they may have wished to when treating patients admitted with DKA. Whilst there are overarching data from the National Diabetes In-patient Audit (NaDIA) [101], there are very few individual institutional data

such as this available. Of the 220 UK diabetes secondary care teams invited to participate, 67 hospitals returned the questionnaire. Data were collected on glucose meter availability, ketone meter availability and personnel availability. In addition, the questionnaire asked whether teams regularly reviewed their cases of DKA, and whether regular education was held for medical and nursing staff.

Because JBDS had published guidance on diabetes self-management in hospitalised in-patients [151], there were also questions asking whether this was possible in their Trust.

Objectives of the study

To examine the services provided by and facilities available to diabetes specialist teams and the institutional factors involved in the ability to provide comprehensive care for adult patients presenting with DKA in 2014.

What this study added to the literature

There were almost no data of a similar nature ever previously published, thus this is a way of documenting where secondary care diabetes teams in the UK are with respect to recommendations from national bodies. In addition, because the JBDS guidelines are in many ways 'aspirational', i.e. 'This is what we believe a good diabetes service should have', then more teams will hopefully be able to use these data to enable improvements in their own services.

What changed as a result of the paper?

As of 1st October 2017, these data have been cited three times, but the data were only published in February 2016.

This work and the work that has arisen from it was part of the reason that I was a finalist in the 2017 Royal College of Physicians Excellence in Patient Care Awards.

In retrospect, what should have been done differently in this study?

That only 30% of all UK hospitals replied was a little disappointing. Thus, there was always the risk of reporting bias. I am aware, having filled out the forms myself that they were time consuming. There was no funding available to carry out this work, and thus teams did so out of good will. If future work were to be carried out, then I would have sought funds to allow teams to have been compensated for their time. This may have increased the return rate, thus increasing the generalisability of the work.

Future work as a result of this publication

This work needs to be repeated in the next 5 years or so. As the numbers of people with diabetes continue to rise, it is very likely that the numbers of people admitted with DKA will also continue to rise. The correct management of these individuals is of paramount importance, and the availability of appropriately educated staff and equipment is key. I would hope that the data presented in this paper serves as a start so that changes over time can be monitored.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

<http://onlinelibrary.wiley.com/doi/10.1111/dme.12877/full>

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was the senior author on the following paper:

Dhatariya K, Nunney I, Icceton G. Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. Diabetic Med. 2016;33:269-70

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he directly supervised the team who carried out the study and was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed.....*I. Nunney*.....

Date.....*8/6/2016*.....

Ian Nunney

Statistician

Norfolk and Norwich University Hospitals NHS Foundation Trust & University of East

Anglia

Title of paper:

Edge JA, Nunney I, **Dhatariya KK** (2016); Diabetic ketoacidosis in an adolescent and young adult population in the UK in 2014: a national survey comparison of management in paediatric and adult settings. *Diabetic Med* 33:1352-1359

Impact factor of the journal

3.12

My contribution to this peer reviewed publication

Dr Julie Edge conceived the idea of the national survey based on the work I had done in adults. I co-wrote the data collection tool. I collected all the data. I helped analyse the data and came up with the interpretations with Dr Edge. I helped write the initial and final drafts of the manuscript.

Background to the paper

I had led the writing group for the second edition of the national guideline on the management of adult patients with diabetic ketoacidosis (DKA) produced under the auspices of the Joint British Diabetes Societies for In-patient Care group. As mentioned elsewhere in this thesis, whilst I was aware that these guidelines had been well received and widely used [123], I had no idea whether they actually worked. This uncertainty is what led to me conducting the national survey that was discussed earlier in this thesis.

The survey was initially designed to be carried out in the adult population, however, I was contacted by Dr Julie Edge, consultant paediatric endocrinologist in Oxford, and one of the world's foremost authorities on paediatric DKA to ask if she could adapt and use the form

that I had created for the adult survey to conduct a similar one in the adolescent population. This led to the development of the questionnaire is given as an appendix in the published paper.

Part of the reason for this, was to find out if there were differences in the way adolescents were treated compared to adults. Part of this lies in the reason why the JBDS adopted the weight based, fixed rate intravenous insulin infusion rate, something that was a change from what had previously been done in adults which was to use a fixed rate intravenous insulin infusion (FRIII) at ~6 unit per hour (or something similar) that varied depending on where you worked. The weight based regimen had been advocated for use in children for many years [152], based on work done in the 1970's [153]. The question that the adult writing group had asked was 'when does a child become an adult?' Thus when should one move from the weight based FRIII to a non-weight based, empirical FRIII? The adult writing group could not decide, because we had all seen 14 year old children who were fully grown in adult stature, and also 18 year olds who were physically tiny. Thus, for the adult guideline one of the major shifts in the treatment paradigm had been the move to using the weight based, FRIII [42].

Similar to the reason for why I conducted the adult survey, Dr Edge wanted to see if the guidelines used across the UK actually worked. The guidelines most commonly used were those from the International Society for Pediatric and Adolescent Diabetes and the British Society for Paediatric Endocrinology and Diabetes [154,155].

Objectives of the study

The aim of this joint survey was to examine the quality of management of young people (under the age of 22 years) against the JBDS guidelines in adult services [42], and the BSPED guidelines for paediatric services [155], and study the differences in management and outcomes.

What this study added to the literature

This study was the first of its kind – a nationwide survey of clinical practice in these patients. The data showed that most units used the BSPED guidelines, and that there were several similarities in the care received by the 14-22 year olds who presented with DKA, than those patients who were in the adult survey. These similarities included a significant proportion of patients treated using the guidelines developed either hypoglycaemia, or hypokalaemia. These would suggest that either the guidelines were not being followed, or the guidelines are wrong. Currently, when the data collected in the adult and adolescent surveys suggest that the guidelines are not being appropriately followed, then it is difficult to justify changing the guidelines

What changed as a result of the paper?

Whilst the paper was accepted for publication in February 2016, it was only published in the paper edition of the journal in September 2016, thus it has not had enough time for any change to have been implemented since publication.

In retrospect, what should have been done differently in this study?

Currently it is too early to know if anything should have been done differently. It is the first national survey of its kind in the world, and thus sets the benchmark for other countries to do something similar.

Future work as a result of this publication

I have been working with the paediatric department at the Norfolk and Norwich University Hospitals NHS Foundation Trust to look at the management of DKA in children – i.e. from 1 to 17 years, admitted with the condition between 2012 and 2014 (n=99). These found that a significant proportion of those with suspected DKA did not fulfil the BSPED criteria. In addition – as with the adult and adolescent surveys – there were significant areas where guideline adherence and management was suboptimal. However, even when the guidelines were adhered to, there was still a high incidence of hypokalaemia and hypoglycaemia, suggesting that the 2009 guidelines were insufficient at preventing possible harm. As of October 2017 these data have been revised and re-submitted for publication.

More work has also been done looking at the utility of ketone measurements in the diagnosis of DKA in children. This work has looked at all admissions with suspected DKA and plotted the pH with plasma ketone concentrations and glucose concentrations. This work has shown that the sensitivity and specificity to be able to diagnose DKA is greatest when the ketone concentrations are 4.4 mmol/l, not at the 3.0 mmol/l that the current ISPAD and BSPED guidelines recommend. As of October 2017 these data are being prepared for submission for publication.

In addition, I am now part of the discussions taking place to look at the care of those aged between 16 and 18 years old. These adolescents will most often be under the outpatient care of the paediatricians / transition team, but if they are admitted to hospital then they

are most often under the care of the adult diabetes team. The JBDS guideline is for 18 years old and above, yet if admitted, 16-18 year olds should be treated using the BSPED guideline which most adult teams do not use or know about. Thus there is a move to try and unify the guidelines for this age group. This is a work in progress.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

<http://onlinelibrary.wiley.com/doi/10.1111/dme.13065/full>

To whom it may concern

This is to confirm that Dr Ketan Dhatariya was an author on the following paper:

Edge JA, Nunney I, Dhatariya KK (2016); Diabetic ketoacidosis in an adolescent and young adult population in the UK in 2014: a national survey comparison of management in paediatric and adult settings. Diabetic Med 33; 1352-1359

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he conceived the study, he wrote the initial questionnaire upon which the questionnaire used in the adolescent population in the current paper was based, he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Signed 

Date 19/09/2016

Ian Nunney

Statistician

Norfolk and Norwich University Hospitals NHS Foundation Trust & University of East

Anglia

Peri-operative Diabetes Care

Title of paper:

Dhatariya K, Levy N, Kilvert A, Watson B, Cousins D, Flanagan D, Hilton L, Jairam C, Leyden K, Lipp A, Lobo D, Sinclair-Hammersley M, Rayman G (2012); NHS Diabetes guideline for the perioperative management of the adult patient with diabetes. *Diabetic Med* 29: 420-433

And the main document from which this paper was derived:

Dhatariya K, Flanagan D, Hilton L, Kilvert A, Levy N, Rayman G, Watson B, Cousins D, Jairam C, Leyden KM, Lobo DN, Sinclair-Hammersley M (2015) Management of adults with diabetes undergoing surgery and elective procedures: Improving standards. Revised September 2015

Impact factor of the journal

3.12. Furthermore, in 2014, this paper was the 5th most downloaded manuscript from the Wiley online website (for website see below) globally, and in 2015, it was the 4th most downloaded manuscript from the website [data given to me verbally from 2 Associate Editors of the journal].

My contribution to this non-peer reviewed publication

I was a senior member of the writing group. I attended all of the meetings and the teleconferences. I was actively corresponding by email to all of the other co-authors. I was involved in writing the first edition of the guideline. For the second edition, I was the person who co-ordinated the updates, and wrote the final draft of the guideline. It was not peer reviewed, because as the editor of the journal said to me when he received it 'the

writing group is made up of enough experts in the field in the UK that it has already been peer reviewed in the writing process’.

Background to the paper

There have been several studies showing that hyperglycaemia in the post-operative period is associated with harm. These include (but are not limited to) general surgery [11,71], cardiac surgery [156], vascular surgery [157,158], neurosurgery [159], orthopaedic surgery [160,161], colorectal surgery [162], trauma [163], breast surgery [164], liver transplantation [165], hepato-biliary and pancreatic surgery [166], cholecystectomy [167], and foot and ankle surgery [168]. These harms include wound infection, length of time in hospital, acute kidney injury, myocardial infarction, time spent on Intensive Care Unit or on a ventilator and death. The perioperative mortality rate is up to 50% higher than the non-diabetes population [11]. Because of these factors, and the data to show that people with diabetes are less likely to be offered day case surgery and are more likely to have emergency surgery, have longer lengths of stay following admission and have a higher rate of 28 day readmissions following surgery [90], it would seem sensible to optimise glycaemic control prior to surgery and around the time of the operation. However, this optimisation would require a great deal of co-ordination between all the people involved in the care of the person with diabetes. In addition, as discussed elsewhere in this thesis, these data show that whilst there is evidence to show that high peri-operative glucose concentrations are associated with harm (using whatever measure of harm chosen), there are no data (other than in cardiac and liver transplant surgery) to show that correction of glucose concentrations is associated with improved outcomes. However, despite this lack of evidence it was felt that the approach that should be taken was that of ‘the absence of evidence does not mean the absence of effect’. Thus the Joint British Diabetes Societies

for In-patient Care Group formed a writing group to create these guidelines. I was the lead of this group, and the subsequent lead author on the guideline.

Objectives of the study

To harmonise the perioperative care of adult patients with diabetes undergoing surgery or procedures across the UK.

What this study added to the literature

For the first time, a document had appeared that ensured that glycaemic control was high on the agenda of surgeons and anaesthetists. Despite the huge amount of data to show that high glucose concentrations peri-operatively were associated with harm, it was a common finding for anaesthetists to allow 'permissive hyperglycaemia' to ensure that patients were not hypoglycaemic whilst under anaesthetic. In addition, it was clear that there was no accountability for the glucose amongst surgical or anaesthetic teams. In one of the documents published by the Royal College of Surgeons in 2011 entitled "The Higher Risk General Surgical Patient: towards improved care for a forgotten group", the word 'diabetes' appears only once, and the term 'hyperglycaemia' does not appear at all [169].

This ground-breaking guideline covered the entire patient journey from the time of referral from primary care through to discharge home. Each section has the aims of needed to be achieved at each of the seven steps (referral from primary care, surgical outpatient, pre-operative assessment clinic, hospital admission, theatres and recovery, post-operative care and discharge). In addition, each section has aims and recommendations.

The guideline also had sections covering the factors that lead to adverse outcomes, and also a section on standards of care (these came with defined audit standards). There was, as with many of the other JBDS guidelines, a section on controversial areas. This is because, for many of the recommendations there was no trial evidence and many of them were based on consensus. There were also several appendices that included how to manipulate oral and injectable glucose lowering agents on the day prior to surgery and on the day of surgery to ensure that patients with diabetes could be admitted on the day of surgery – something that had previously been shown to be lacking for patients with diabetes [8].

What changed as a result of the paper?

Several things have changed since this guideline was published. In 2013 my colleague Professor Mike Sampson, chair of the JBDS-IP Group presented data from a national survey of all diabetes teams across the UK to see what they felt about the JBDS guidelines [123]. That showed that the peri-operative guideline had been the one that had been the hardest to implement. This is because it involved many different specialities – primary care, surgeons, anaesthetists, pre-operative assessment clinic nurses and so on. People who do not usually have diabetes care in the forefront of their minds when looking after their patients. However, more recently, the Association of Anaesthetists of Great Britain and Ireland formed a working party on this subject, that I was a part of, and produced their own version of the guideline that was recently published in their main journal [170]. In addition, because of this, glycaemic control is to be included in the 2017 edition of the Guidelines for the Provision of Anaesthetic Services (GPAS) produced by the Royal College of Anaesthetists.

Furthermore, the National Institute for Health and Care Excellence, have recently produced an updated a guideline for pre-operative tests [171]. This states that all patients known to have diabetes should have an HbA_{1c} measured within 3 months of their procedure, although I have argued that NICE have missed out on an opportunity to do more good [172].

In retrospect, what should have been done differently in this study?

I believe that this guideline has been revolutionary for the care of patients with diabetes undergoing surgery. It is an evolving document, and has taken into account the appearance of new drug classes since it was first published, as well as taking into consideration new safety data with some of these drugs. Given the slow pace of change in the UK National Health Service generally, I am aware that embedding glycaemic control into the culture of surgeons will take time, but this has been the start. Thus I do not feel I would have done anything differently.

Future work as a result of this publication

A lot of work has taken place and is planned as a result of this guideline. In 2016, the Health Technology Assessment Programme put out a call (HTA Number 16/25: Poorly Controlled Diabetes and Outcome in Elective Surgery). However, I wrote to them telling them, that on the basis of the most up-to-date evidence they were asking the wrong question. This was because most of the data now showed that those people who were known to have diabetes did relatively well compared to those who had previously undiagnosed diabetes / hyperglycaemia who did the worst. The plan should have been firstly to identify those who had previously undiagnosed diabetes / hyperglycaemia and see what their post-operative outcomes were compared to those who did not have

diabetes or were normoglycaemic. Secondly, if the first dataset showed a difference in outcomes, then to design an intervention to show an improvement. This work is currently in its early stages, and I am leading a group of interested individuals from across the UK to set up and run a multi-centre large trial with a sample size of 15,350. This sample size is based on several sources of evidence:

a) The mean length of stay for all patients with diabetes admitted to the Norfolk and Norwich during 2015 was, on average 1.8 days longer than for those without diabetes. If 'zero length of stay' patients were excluded (i.e. day cases) then the mean LOS was 2.7 days longer than those without diabetes (SD~12 days).

b) My colleague Professor Mike Sampson is running the worlds' largest diabetes prevention study. He has now screened over 10,000 people who are at risk of getting diabetes – i.e. >40 years old, or BMI>30Kg/m², or previous history of gestational diabetes or family history of diabetes. He has shared his (as yet unpublished) data with me, and he has found that the current prevalence of previously undiagnosed diabetes in this cohort is 4.6%. There are some limitations with his data – i.e. this is a predominantly Caucasian population, and is selected to increase the chance of getting the population he needs for his study. Being white means that the prevalence is likely to be an underestimate compared to the UK average, but directing the recruitment to those at risk, will increase the prevalence. We have also looked at the Public Health England estimates, which suggest a prevalence of undiagnosed diabetes of 2.3% (95%CI 2.1, 2.6) and non-diabetic hyperglycaemia prevalence of 10.7% (95%CI 10.2, 11.1).

If we use length of stay as our outcome, looking at these data he has calculated a sample size required would be 600 in each group. Thus if the prevalence is ~4.5% and this is 600,

then the target recruitment size will need to be 15,350 or so (allowing for a 15% drop out). That would give us sufficient number of people with diabetes, those with non-diabetic hyperglycaemia, and a large number of people without either with whom to compare.

In addition, we have recently completed a study that looked at the quality of GP referral letters to all surgical specialities across 10 hospitals across the East of England and used the suggested referral form in the guideline as the template. These data were recently accepted for publication (Pournaras DJ, Photi ES, Barnett N, Challand CP, Chatzizacharias N, Dlamini N, Doulias T, Foley A, Hernan J, Kumar B, Martin J, Nunney I, Panagiotopoulou I, Shivakumar O, Sengupta N, Sinclair P, Stather P, Than MM, Wells AC, Xanthis A, Dhatariya K. Assessing the quality of primary care referrals to surgery of patients with diabetes in the East of England: A multi-centre cross-sectional cohort study. *International Journal of Clinical Practice*. DOI: 10.1111/ijcp.12971).

Finally, the National Confidential Enquiry in Patient Outcomes and Death (NCEPOD) took up peri-operative care as one of their major themes during 2017 – 2019. I am part of the steering group for that work. It is due to look at a number of factors in the care of adult patients (over 16 years old) undergoing surgery – elective or emergency. This is still a work in progress.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

<http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2012.03582.x/full>

External link to the guideline on the website of the Association of British Clinical Diabetologists


http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_Surgical_Guideline_2015_Full.pdf

To whom it may concern

This is to confirm that Dr Kelvin Dhatariya was the senior author on the following paper:

Dhatariya K, Levy N, Kilvert A, Watson B, Cousins D, Flanagan D et al. NHS Diabetes guideline for the perioperative management of the adult patient with diabetes. Diabetic Med. 2012;29:420-33

I can confirm that Dr Dhatariya was involved in several aspects of this work. He was a senior member of the writing group, and co-led the writing group of the second edition of this guideline. He had substantial input into the preparation of the work prior to publication.

Signed 

Date 12/6/16

Nicholas Levy

Consultant Anaesthetist

West Suffolk Hospital

Title of paper:

Rollins KE, Varadhan KK, **Dhatariya K**, Lobo DN (2016); Systematic review of the impact of HbA_{1c} on outcomes following surgery in patients with diabetes mellitus. Clin Nutr 35: 308-316

Impact factor of the journal

4.49

My contribution to this peer reviewed publication

I was involved in the discussions about what questions should be asked by the systematic review prior to it starting. I was then involved in the discussions with the authors on each draft of the manuscript on how the data should be presented and what they meant. I helped to write the final version of the manuscript

Background to the paper

As I led the writing group for the national guideline written by the JBDS-IP group on the peri-operative management of patients with diabetes undergoing surgery or procedures it became clear as the various papers were being reviewed that there were differences in what different authors thought of as 'glycaemic control'. This could be thought of as referring to glucose concentrations, either pre or post-operatively, or they may refer to glycated haemoglobin (HbA_{1c}) concentrations. For many (non-specialist) authors this seems to be a relatively minor distinction. However, with the recommendation that the group made – that HbA_{1c} concentrations should be less than 69mmol/mol (8.5%) prior to elective surgery (where it could be safely achieved) – it was felt important to look at the differences in the outcomes if glucose were considered, or if HbA_{1c} was considered when

looking at post-operative outcomes. Thus this systematic review emerged looking at all of the data that had been published in a large number of surgical specialities where HbA_{1c} concentrations had been measured and outcomes assessed.

Objectives of the study

Using a systematic review of published work, to assess the relationship between long-term preoperative glycaemic control (as measured by HbA_{1c}) and risk of developing postoperative complications.

What this study added to the literature

This was the first time that such a systematic review had been carried out, and although the results were not in keeping with the findings of high glucose concentrations – i.e. that high pre-operative HbA_{1c} concentrations were associated with poorer outcomes – the authors came to the conclusion that the reason they did not see this was because the studies included were relatively heterogeneous, predominantly retrospective, and often contained small patient numbers. Thus it was difficult to make any firm recommendations.

What changed as a result of the paper?

The JBDS guidelines still recommend that for elective surgical patients, HbA_{1c} should be <69mmol/mol (8.5%) where it can be safely achieved. This is broadly in line with observational data from a large single centre cohort from the USA who showed that post-operative harm was much more likely to occur if HbA_{1c} values were >64mmol/mol (8.0%) [173]. I am aware that with the Association of Anaesthetists of Great Britain and Ireland and the Royal College of Anaesthetists becoming more aware of the importance of peri-operative glycaemic control, that the findings of the systematic review, far from making

them less enthusiastic about controlled peri-operative HbA_{1c} and glucose concentrations has made them more determined to collect the evidence using larger studies.

In retrospect, what should have been done differently in this study?

This was a systematic review, and thus the authors were entirely reliant on collecting the published literature, which was done very methodically. Thus they review process, which followed the PRISMA checklist [174].

Future work as a result of this publication

As mentioned elsewhere in this thesis, work is currently in progress to set up a large multi-centre study recruiting 15,350 people due to undergo surgery to assess the relationship between pre-operative glucose and HbA_{1c} concentrations and 30 day post-operative outcomes. This proposed study will help to answer the question set by the systematic review.

Confirmation of authorship

This is shown.

External link to the paper on the journal website

[http://www.clinicalnutritionjournal.com/article/S0261-5614\(15\)00082-5/pdf](http://www.clinicalnutritionjournal.com/article/S0261-5614(15)00082-5/pdf)



The University of
Nottingham

UNITED KINGDOM • CHINA • MALAYSIA

1 February 2017

Faculty of Medicine and Health Sciences

School of Medicine

Nottingham Digestive Diseases Centre

E Floor, West Block

Nottingham University Hospitals,

Queen's Medical Centre

Nottingham NG7 2UH, UK

Tel: +44-115-8231149

Fax: +44-115-8231160

E-mail: Dileep.Lobo@nottingham.ac.uk

To whom it may concern

Dileep N Lobo, MS, DM, FRCS, FACS, FRCPE

Professor of Gastrointestinal Surgery &

Deputy Head of Division

This is to confirm that Dr Ketan Dhatariya was a contributing author on the following paper:

Rollins KE, Varadhan KK, Dhatariya K, Lobo DN. Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus. Clin.Nutr. 2016;35:308-16

I can confirm that Dr Dhatariya was involved in all aspects of this research. In particular he was involved in the discussions around the conduct of the study, and he was involved in the analysis of the outcomes and in the discussions surrounding the findings. He had substantial input into the preparation of the work prior to publication.

Dileep N Lobo

Summary and Conclusions

I started this thesis by stating my hypothesis: That because of the work I have published, the management of in-patients with diabetes has improved. Whilst I can offer no absolute 'proof' that my contributions have directly helped improve the care of people in hospital with diabetes, there are other direct markers of care that may help to make this inference.

Firstly, there are the data from the most recent most recent (2016) National Diabetes In-patient Audit that showed several areas where, over the last few years, care has changed – often improving, but not always.

Since 2010, the National Diabetes In-patient Audit has tracked the care of hospital in-patients with diabetes. The data from the 2016 audit carried out amongst 209 hospital sites across the UK was that the prevalence of diabetes amongst in-patients continued to rise and was, on average, 17%, this figure has risen from 15% in 2011 [2]. Several other statistics were of direct interest to this thesis:

Hospital stay:

The 2011 NaDIA showed that only 58% of in-patients were seen by a member of the diabetes team. This had risen to 69% in 2016. Unfortunately, 28% of hospitals still do not have in-patient diabetes specialist nurses. These two statements are relevant because of the data published, and presented in this thesis looking at the impact of the DISN

Hypoglycaemia:

The prevalence of all hypoglycaemic episodes decreased from 26% in 2011 to 20% in 2016. Looking more closely, the rates of mild (self-treated) hypoglycaemia fell from 23% in

2011 to 18% in 2016, and the rate of severe hypoglycaemia (i.e. requiring third party assistance) fell from 11% to 8% between those years. Within the latter category, the prevalence of severe hypoglycaemia requiring injectable rescue treatment fell from 2.2% in 2011 to 1.7% in 2016. These two statements are relevant because of the guideline published, but not presented in this thesis, on the management of hypoglycaemia in hospital in-patients [175]. I was a contributor on those guidelines.

DKA and HHS:

Disappointingly, 4% of in-patients with type 1 diabetes developed DKA during their hospital stay, a rise from 3% in 2011. This statement, although very disappointing, is relevant because of the work I have done on DKA. Some of this work is presented in this thesis. The incidence of HHS in in-patients with type 2 diabetes remained unchanged since 2015, at 0.2%. This statement, although very disappointing, is relevant because of the guideline published, but not presented in this thesis, on the management of HHS [54]. I was a contributor on those guidelines.

Other findings may not have been directly related to the work I have published. These include:

Intravenous insulin:

The 2016 NaDIA data showed that there were fewer people on intravenous insulin infusions – 11% in 2011 and 8% in 2016. In addition, fewer people were on what was felt to be excessively long intravenous insulin infusions – 8% in 2011 to 6% in 2016. Finally, it was felt by the teams filling out the audit forms that the transfer from intravenous to subcutaneous insulin was better, with errors falling from 19% in 2011 to 14% in 2016.

These are relevant because there has been a guideline published on this [176]. I was a contributor on those guidelines.

Medication errors:

Despite the increasing use of electronic prescription charts, a proportion of drug charts still had at least one medication error. However, the rate decreased from 40% in 2011 to 38% in 2016. However this still means that almost two out of five in-patient drug charts had a drug error recorded. Drug chart errors were more likely to occur for patients on surgical wards – 41% – compared to patients on a medical ward – 37%. Prescription errors were less likely to occur if in-patients were treated in a hospital that used an electronic prescription chart – 19% – compared to hospitals that did not use have electronic charts – 25%.

The care of in-patients with diabetes is far from ideal and a lot of work remains to be done. I was involved in writing one of the first national training modules for insulin safety, however, this was initially free (or made available to individual Trusts at minimal cost) but then when the price for these modules rose significantly, alternative training modules were developed [177]. I was a reviewer for this new module. Insulin prescribing has a direct relationship to this thesis because it addresses patient safety, in particular because insulin errors (prescribing, dispensing and administering) have been denoted as ‘Never Events’ by NHS England [122].

In addition, other authors have developed regular staff training on all aspects of diabetes care [178]. However, despite some authors putting in a huge amount of work into specific

aspects of in-patient diabetes care, it does not always show evidence of improved outcomes [133,179,180].

However, to date there has been little incentive for Trusts to become actively involved in the management of in-patients with diabetes. The issue has in the past been thought to be 'too big' to appear on Trust management 'radars' when dealing with the consequences of poorly controlled diabetes, because of the lack of a cohesive way of measuring harm. However, this may soon change.

Since 2013 I have been part of a small group of people from the JBDS who have lobbied the Care Quality Commission (CQC) to highlight the plight of in-patients with diabetes. From many 'corridor conversations' I have had in the last few years, it is clear that most senior managers are not engaged with the concerns that the diabetes specialist teams have regarding the care received by this group of in-patients. One of the very few national organisations who have the 'teeth' – i.e. the power to sanction and make a case for real change within Trusts is the CQC.

Some of the senior JBDS team have been CQC inspectors, and with their help and guidance, the JBDS have designed a 'Brief Guide' and a series of Key Lines of Enquiry for use by CQC inspectors. This is for Acute Trusts and Care Homes. These developments make diabetes one of the very few 'disease specific' areas upon which Trusts will be judged (the others being learning difficulties and dementia). Trusts will need to provide CQC inspectors as part of the pre-inspection documentation, their NaDIA data and the evidence of a number of things:

1. That the Trust participates in the annual national diabetes in-patient audit (NaDIA) programme
2. That the Trust has a credible and overarching written strategy for in-patient diabetes care across the entire Trust as part of an approved Trust governance framework
3. That the Trust has a written policy for the safe prescribing and administration of insulin, linked to direct or online mandatory training of all staff, with evidence of adoption of national guidance on in-patient diabetes care and insulin use, and programmes to review improvement in outcomes
4. That the Trust has a dedicated in-patient diabetes specialist service as one of their core services, with routine and planned access to this service for all in-patients with diabetes, not just emergency admissions
5. That the Trust has a foot multidisciplinary team (MDT) for in patients with acute diabetic foot problems and /or high risk feet while in-patients
6. That the Trust has a robust system in place to identify all current in-patients with a known diabetes diagnosis, with evidence of a rapid referral system to the specialist in-patient diabetes team for those experiencing diabetes management problems
7. That the Trust collect annually, and review, the in-patient experience of diabetes care, and the key issues raised, positive and negative

The CQC is a recognised independent arbiter of quality and should an institution fail to meet their exacting standards, then the CQC has the power to 'name and shame' but also impose sanctions on the failing institution. However, until this is rolled out across the UK and has been in place for two-three years with regular NaDIA returns, it will be difficult to assess their impact.

Further evidence that the work I have contributed to has helped to change the care for in-patients with diabetes is by looking at the numbers of abstracts presented at regional, national and international conferences where the JBDS guidelines in particular form the basis for local service evaluations and audits. That this work is being carried out suggests that individual diabetes teams see the JBDS audit standards as something to aspire to and benchmark themselves against. Not only do many of these abstracts show the scale of the problem, but also offer innovative and novel approaches to managing such patients.

An (unpublished) example of this is the work done by the surgical and anaesthetic team in Northampton General Hospital, led by Dr Karen Leyden, who audited their peri-operative pathway in 2013 and found that 7.1% of their surgical patients had diabetes. They reduced the number of people with diabetes on a VRIII from 45% in 2009 to 24% in 2013 – in 95% of these cases it was deemed that it was the 'correct' strategy. They found that the number of people who could be managed by simple manipulation of their diabetes medication rose from 55% in 2009 to 76% in 2013, with 94% of patients maintaining a pre-operative glucose of between 4-12 mmol/L, up from 79% in 2009. They found that prior to the introduction of the JBDS peri-operative guideline only 75% of patients had a capillary blood glucose concentration measured, and this rose to 89% after it had been introduced. These changes resulted in the rate of pre-operative hypoglycaemia (i.e. a blood glucose concentration of <4.0 mmol/L) falling from 8% to 1%, and the rate of hyperglycaemia (>12.0 mmol/L) falling from 13% to 5%. The use of the most appropriate fluid (0.45% NaCl/5% glucose/0.15% KCl) rose from 0% in 2009 to 82% in 2013, and the use of 5% dextrose fell from 89% to 4%. This was associated with no overall change in sodium concentrations, as opposed to a previous mean drop of 2.0 mmol/L. Thus this single

centre data suggests that making a change using a guideline I helped to write made a material difference to the care of hospital in-patients with diabetes.

Change is unlikely to come overnight, but knowing where we are is the start of the journey when one knows where one needs to get to. The question remains about whether the existence of a guideline makes a difference to the management of individual patients. All of the guidelines on which I have been an author or contributor need assessment – to see whether they work or not. So far, only one guideline has been surveyed [97,98]. Currently at least one other is currently being actively considered for national assessment. As the response to the data from the national DKA survey has shown there were several aspects of the guideline that diabetes teams felt was very valuable, but the fact that individuals were not following the guidelines meant that a significant proportion of patients developed hypoglycaemia and/or hypokalaemia. Thus more attention needs to be paid to staff education in order to ensure that people use the guideline correctly.

Thus there are some positive aspects to a management guideline [181]. Ideally they improve the quality of patient care and outcomes. In addition, they unify diagnostic criteria; reduce variations in care – discouraging the use of ineffective, dangerous, wasteful or out of date models of care; and they allow for retrospective and prospective audit of outcomes. They also improve clinical decision making by recommending specific care processes. However, they also may prevent the teams using them from seeing other points of view or critically appraise their need, or their utility. Indeed, a recent critique of the American Diabetes Association guideline on the management of DKA does just that [94]. Most importantly, the teams for whom the guidelines are based at should know that they exist, should like what they contain, have no barriers to their implementation, use

them when appropriate and follow their recommendations. These last requirements are, of course, the areas of guideline use that are most prone to being misused. However, as the guidelines are used more commonly, one hopes that their use becomes more embedded as routine in hospitals that treat in-patients with diabetes.

The prevalence of diabetes continues to rise unabated, and the consequence will be that more people with diabetes will be admitted to hospital – for the most part not because of diabetes, but they will have diabetes in addition to the condition that necessitated admission. As I have tried to describe throughout this thesis, patients with diabetes in hospital unfortunately come to greater harm than those without diabetes. However I hope that the work that I have done, or contributed to, has in some way mitigated these harms. Furthermore, that unifying practice across the UK and elsewhere, has improved the care for people in hospital with diabetes and that it will continue to improve from now on.

References

- [1] Diabetes UK. State of the nation 2016.
<https://www.diabetes.org.uk/Documents/Position%20statements/Diabetes%20UK%20State%20of%20the%20Nation%202016.pdf>. 2016. [Last accessed 17th August 2017]
- [2] NHS Digital. National Diabetes Inpatient Audit (NaDIA) - 2016.
<http://www.content.digital.nhs.uk/catalogue/PUB23539>. 2017. [Last accessed 17th August 2017]
- [3] Bruno A, Gregori D, Caropreso A *et al*. Normal glucose values are associated with a lower risk of mortality in hospitalized patients. *Diabetes Care* 2008; **31**(11):2209-2210.
- [4] The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Eng J Med* 1993; **329**(14):977-986.
- [5] UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; **352**(9131):837-853.
- [6] International Diabetes Federation. IDF diabetes atlas. 7th Edition.
<http://www.idf.org/diabetesatlas>. 2016. [Last accessed 17th August 2017]

- [7] Diabetes UK. Diabetes facts and stats. Version 3.
<http://www.diabetes.org.uk/Documents/About%20Us/Statistics/Diabetes-key-stats-guidelines-April2014.pdf>. 2014. [Last accessed 17th August 2017]
- [8] Kerr M. Inpatient care for people with diabetes: the economic case for change.
<https://www.diabetes.org.uk/upload/News/Inpatient%20Care%20for%20People%20with%20Diabetes%20%20The%20Economic%20Case%20for%20Change%20Nov%202011.pdf>. 2013. [Last accessed 17th August 2017]
- [9] Moghissi ES, Korytkowski MT, Dinardo MM *et al*. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care* 2009; **32**(6):1119-1131.
- [10] Sampson MJ, Dozio N, Ferguson B, Dhatariya K. Total and excess bed occupancy by age, speciality and insulin use for nearly one million diabetes patients discharged from all English Acute Hospitals. *Diabetes Res Clin Pract* 2007; **77**(1):92-98.
- [11] Frisch A, Chandra P, Smiley D *et al*. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care* 2010; **33**(8):1783-1788.
- [12] Holman N, Hillson R, Young RJ. Excess mortality during hospital stays among patients with recorded diabetes compared with those without diabetes. *Diabetic Med* 2013; **30**(12):1393-1402.
- [13] Draznin B, Gilden J, Golden SH, Inzucchi SE, for the PRIDE investigators. Pathways to quality inpatient management of hyperglycemia and diabetes: A call to action. *Diabetes Care* 2013; **36**(7):1807-1814.

- [14] Laios K, Karamanou M, Saridaki Z, Androutsos G. Aretaeus of Cappadocia and the first description of diabetes. *Hormones (Athens)* 2012; **11**(1):109-113.
- [15] Dreschfeld J. The Bradshawe lecture on diabetic coma. *Br Med J* 1886; **2**(1338):358-363.
- [16] Bliss M. The Discovery of Insulin - the 25th anniversary edition. University of Chicago Press, 2007.
- [17] Banting FG, Best CH, Collip JB, Campbell WR, Fletcher AA. Pancreatic extracts in the treatment of diabetes mellitus. *CMAJ* 1922; **12**(3):141-146.
- [18] Root HF. The use of insulin and the abuse of glucose in the treatment of diabetic coma. *JAMA* 1945; **127**(10):557-563.
- [19] Black AB, Malins JM. Diabetic ketoacidosis. A comparison of results of orthodox and intensive methods of treatment based on 170 consecutive cases. *Lancet* 1949; **253**(6541):56-59.
- [20] Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care* 2009; **32**(7):1335-1343.
- [21] Foster NB. The treatment of diabetic coma with insulin. *Am J Med Sci* 1923; **166**:699-709.
- [22] Smith K, Martin HE. Response of diabetic coma to various insulin dosages. *Diabetes* 1954; **3**(4):287-295.

- [23] Shaw CE, Hurwitz GE, Schmcker M, Brager SH, Bessman SP. A clinical and laboratory study of insulin dosage in diabetic acidosis: comparison with small and large doses. *Diabetes* 1962; **11**(1):23-30.
- [24] Sonksen PH, Tompkins CV, Nabarro JD. Growth-hormone and cortisol responses to insulin infusion in patients with diabetes mellitus. *The Lancet* 1972; **300**(7769):155-160.
- [25] Alberti KG, Hockaday TD, Turner RC. Small doses of intramuscular insulin in the treatment of diabetic 'coma'. *Lancet* 1972; **302**(7828):515-522.
- [26] Kidson W, Casey J, Kraegen E, Lazarus L. Treatment of severe diabetes mellitus by insulin infusion. *Br Med J* 1974; **2**(921):691-694.
- [27] Page MM, Alberti KG, Greenwood R *et al.* Treatment of diabetic coma with continuous low-dose infusion of insulin. *Br Med J* 1974; **2**(921):687-690.
- [28] Alberti KG, Page MM, Pyke DA, Watkins PJ. Comparison of different insulin regimens in diabetic ketoacidosis. *Lancet* 1976; **307**(7950):83-84.
- [29] Kitabchi AE, Ayyagari V, Guerra SM. The efficacy of low-dose versus conventional therapy of insulin for treatment of diabetic ketoacidosis. *Ann Intern Med* 1976; **84**(6):633-638.
- [30] Sacks HS, Shahshahani M, Kitabchi AE, Fisher JN, Young RT. Similar responsiveness of diabetic ketoacidosis to low-dose insulin by intramuscular injection and albumin-free infusion. *Ann Intern Med* 1979; **90**(1):36-42.
- [31] Fisher JN, Kitabchi AE. A randomized study of phosphate therapy in the treatment of diabetic ketoacidosis. *J Clin Endocrinol Metab* 1983; **57**(1):177-180.

- [32] Morris LR, Murphy MB, Kitabchi AE. Bicarbonate therapy in severe diabetic ketoacidosis. *Ann Intern Med* 1986; **105**(6):836-840.
- [33] Carroll P, Matz R. Uncontrolled diabetes mellitus in adults: Experience in treating diabetic ketoacidosis and hyperosmolar nonketotic coma with low-dose insulin and a uniform treatment regimen. *Diabetes Care* 1983; **6**(6):579-585.
- [34] Wolfsdorf JI, Allgrove J, Craig ME *et al.* Diabetic ketoacidosis and hyperglycemic hypersmolar state. *Pediatr Diabetes* 2014; **15**(Suppl 20):154-179.
- [35] Hockaday TD, Alberti KG. Diabetic coma. *Clin Endocrinol Meta* 1972; **1**(3):751-788.
- [36] American Diabetes Association. Urine glucose and ketone determinations. *Diabetes Care* 1992; **15**(Suppl 2):38.
- [37] Wallace TM, Meston NM, Gardner SG, Matthews DR. The hospital and home use of a 30-second hand-held blood ketone meter: guidelines for clinical practice. *Diabetic Med* 2001; **18**(8):640-645.
- [38] Dhatariya K. Blood ketones - measurement, interpretation, limitations and utility in the management of diabetic ketoacidosis. *Rev Diabet Stud* 2016; **13**(4):217-225.
- [39] Herrington WG, Nye HJ, Hammersley MS, Watkinson PJ. Are arterial and venous samples clinically equivalent for the estimation of pH, serum bicarbonate and potassium concentration in critically ill patients? *Diabetic Med* 2012; **29**(1):32-35.
- [40] Gokel Y, Paydas S, Koseoglu Z, Alparslan N, Seydaoglu G. Comparison of blood gas and acid-base measurements in arterial and venous blood samples in patients with uremic acidosis and diabetic ketoacidosis in the emergency room. *Am J Nephrol* 2000; **20**(4):319-323.

- [41] Ma OJ, Rush MD, Godfrey MM, Gaddis G. Arterial blood gas results rarely influence emergency physician management of patients with suspected diabetic ketoacidosis. *Acad Emerg Med* 2003; **10**(8):836-841.
- [42] Savage MW, Dhatariya KK, Kilvert A *et al.* Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. *Diabetic Med* 2011; **28**(5):508-515.
- [43] Foster B. Diabetic coma: Acetonaemia. *Br Med J* 1878; **1**:78-81.
- [44] Fitcher T. Diabetic coma, aetiology, symptoms, and treatment. *North New York Medical Journal* 1897; **66**:821-825.
- [45] Rosenbloom J. A form of diabetic coma, not due to the acetone bodies. *New York Medical Journal* 1915; **102**:294-296.
- [46] Warburg E. Some cases of diabetic coma complicated with uraemia, and some remarks on the previous history of the diabetic coma. *Acta Med Scand* 1925; **61**(1):301-334.
- [47] Marble A, Root HF, White P. Diabetic Coma. *N Eng J Med* 1935; **212**(7):288-297.
- [48] Root HF, Leech R. Diabetic coma and hyperglycemic stupor compared. *Med Clin North Am* 1946; **30**:1115.
- [49] De Graeff J, Lips JB. Hyponatraemia in diabetes mellitus. *Acta Med Scand* 2016; **1957**(157):1-71.
- [50] Sament S, Schwartz MB. Severe diabetic stupor without ketosis. *S Afr Med J* 1957; **31**(36):893-894.

- [51] Ungar G, Freedman L, Shapira S. Pharmacological studies of a new oral hypoglycaemic drug. *Proc Soc Exp Biol Med* 1957; **95**:190-192.
- [52] Gerich JE, Martin MM, Recant L. Clinical and metabolic characteristics of hyperosmolar nonketotic coma. *Diabetes* 1971; **20**(4):228-238.
- [53] Arieff AI, Carroll HJ. Hyperosmolar nonketotic coma with hyperglycemia: Abnormalities of lipid and carbohydrate metabolism. *Metab Clin Exp* 1971; **20**(6):529-538.
- [54] Scott A, on Behalf of the Joint British Diabetes Societies (JBDS) for Inpatient Care. Management of hyperosmolar hyperglycaemic state in adults with diabetes. *Diabetic Med* 2015; **32**(6):714-724.
- [55] Dhatariya KK, Vellanki P. Treatment of diabetic ketoacidosis (DKA) / hyperglycemic hyperosmolar state (HHS): Novel advances in the management of hyperglycemic crises (UK versus US). *Curr Diab Rep* 2017; **17**(5):33-39.
- [56] Levetan CS, Passaro MD, Jablonski KA, Ratner RE. Effect of physician specialty on outcomes in diabetic ketoacidosis. *Diabetes Care* 1999; **22**(11):1790-1795.
- [57] Sampson MJ, Crowle T, Dhatariya K *et al.* Trends in bed occupancy for inpatients with diabetes before and after the introduction of a diabetes inpatient specialist nurse service. *Diabetic Med* 2006; **23**(9):1008-1015.
- [58] James J, Gosden C, Winocour PH *et al.* Diabetes specialist nurses and role evolution: a survey by Diabetes UK and ABCD of specialist diabetes services 2007. *Diabetic Med* 2009; **26**(5):560-565.

- [59] Price H, Thomsett K, Newton I, Alderson S, Hillson R. Developing best practice tariffs for diabetic ketoacidosis and hypoglycaemia. *Pract Diab* 2013; **30**(1):6-8.
- [60] Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2014. <http://www.cdc.gov/diabetes/pubs/statsreport14.htm>. 2014. [Last accessed 17th August 2017]
- [61] American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. *Diabetes Care* 2013; **36**(4):1033-1046.
- [62] Desborough JP. The stress response to trauma and surgery. *Br J Anaesth* 2000; **85**(1):109-117.
- [63] Dungan KM, Braithwaite SS, Preiser J-C. Stress hyperglycaemia. *Lancet* 2009; **373**(9677):1798-1807.
- [64] Umpierrez GE, Isaacs SD, Bazargan N *et al*. Hyperglycemia: An independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab* 2002; **87**(3):978-982.
- [65] Bersoux S, Cook CB, Kongable GL, Shu J, Zito DR. Benchmarking glycemic control in U.S. hospitals. *Endocr Pract* 2014; **20**(9):876-883.
- [66] Kosiborod M, Inzucchi SE, Spertus JA *et al*. Elevated admission glucose and mortality in elderly patients hospitalized with heart failure. *Circulation* 2009; **119**(14):1899-1907.
- [67] Van den Berghe G, Wouters P, Weekers F *et al*. Intensive insulin therapy in the surgical intensive care unit. *N Eng J Med* 2001; **345**(19):1359-1367.

- [68] UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998; **352**(9131):854-865.
- [69] Evans NR, Dhatariya KK. Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. *Clin Med JRCPL* 2012; **12**(2):137-139.
- [70] Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: A systematic overview. *Stroke* 2001; **32**(10):2426-2432.
- [71] Kwon S, Thompson R, Dellinger P *et al.* Importance of perioperative glycaemic control in general surgery: A report from the surgical care and outcomes assessment program. *Ann Surg* 2013; **257**(1):8-14.
- [72] Joint British Diabetes Societies Inpatient Care Group. Guidelines for the management of inpatient diabetes. <http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm>. 2014. [Last accessed 17th August 2017]
- [73] Dhatariya K, Levy N, Kilvert A *et al.* NHS Diabetes guideline for the perioperative management of the adult patient with diabetes. *Diabetic Med* 2012; **29**(4):420-433.
- [74] Hamblin PS, Topliss DJ, Chosich N, Lording DW, Stockigt JR. Deaths associated with diabetic ketoacidosis and hyperosmolar coma. 1973-1988. *Med J Aust* 1989; **151**(8):441-442.
- [75] Cullinane M, Gray AJ, Hargraves CM *et al.* Who Operates When? II The 2003 report of the national confidential enquiry into perioperative deaths.

<http://www.ncepod.org.uk/pdf/2003/03full.pdf>. 2003. [Last accessed 17th August 2017]

- [76] Cuthbertson BH, Amiri AR, Croal BL *et al.* Utility of B-type natriuretic peptide in predicting medium-term mortality in patients undergoing major non-cardiac surgery. *Am J Cardiol* 2007; **100**(8):1310-1313.
- [77] O'Brien MM, Gonzales R, Shroyer AL *et al.* Modest serum creatinine elevation affects adverse outcome after general surgery. *Kidney Int* 2010; **62**(2):585-592.
- [78] Lee TH, Marcantonio ER, Mangione EJ *et al.* Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; **100**(10):1043-1049.
- [79] National Patient Safety Agency. Insulin safety. Reducing harm associated with the unsafe use of insulin products.
<http://www.patientsafetyfirst.nhs.uk/Content.aspx?path=/interventions/relatedprogrammes/medicationsafety/insulin/>. 2010. [Last accessed 17th August 2017]
- [80] Jhanji S, Thomas B, Ely A *et al.* Mortality and utilisation of critical care resources amongst high-risk surgical patients in a large NHS trust. *Anaesthesia* 2008; **63**(7):695-700.
- [81] Pearce RM, Harrison DA, James P *et al.* Identification and characterisation of the high-risk surgical population in the United Kingdom. *Critical Care (London)* 2006; **10**(3):R10.

- [82] Sampson MJ, Brennan C, Dhatariya K, Jones C, Walden E. A national survey of inpatient diabetes services in the United Kingdom. *Diabetic Med* 2007; **24**(6):643-649.
- [83] George JT, Warriner D, mcGrane DJ *et al.* Lack of confidence among trainee doctors in the management of diabetes: the Trainees Own Perception of Delivery of Care (TOPDOC) Diabetes Study. *QJM* 2011; **104**(9):761-766.
- [84] Rollins KE, Varadhan KK, Dhatariya K, Lobo DN. Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus. *Clin Nutr* 2016; **35**(2):308-316.
- [85] Dhatariya K. Should inpatient hyperglycaemia be treated? *Br Med J* 2013; **346**:f134.
- [86] Yudkin JS, Lipska KJ, Montori VM. The idolatry of the surrogate. *BMJ* 2011; **343**:d7995.
- [87] National Institute for Health and Care Excellence. Type 2 diabetes in adults: management. NICE guideline NG28. <http://www.nice.org.uk/guidance/ng28>. 2015. [Last accessed 17th August 2017]
- [88] Inzucchi SE, Bergenstal RM, Buse JB *et al.* Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia* 2012; **55**(6):1577-1596.

- [89] National Diabetes Information Service. NHS atlas of variation in healthcare for people with diabetes. www.rightcare.nhs.uk/index.php/atlas/diabetes/. 2012. [Last accessed 17th August 2017]
- [90] Yorkshire and Humber Public Health Observatory. Variation in Inpatient Activity: Diabetes. <http://www.yhpho.org.uk/resource/view.aspx?RID=105866>. 2012. [Last accessed 17th August 2017]
- [91] Holman N, Young RJ, Jeffcoate WJ. Variation in the incidence of amputation of the lower limb in England. *Diabetologia* 2012; **55**(7):1919-1925.
- [92] Public Health England. The NHS atlas of variation in healthcare. http://fingertips.phe.org.uk/documents/Atlas_2015%20Compendium.pdf. 2016. [Last accessed 17th August 2017]
- [93] Francis R. Report of the Mid Staffordshire NHS Foundation Trust Public Inquiry. Volume 1: Analysis of evidence and lessons learned (part 1). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/279115/0898_i.pdf. 2013. [Last accessed 17th August 2017]
- [94] Dhatariya KK, Umpierrez GE. Guidelines for management of diabetic ketoacidosis: time to revise? *Lancet Diabetes and Endocrinology* 2017; **5**(5):321-323.
- [95] Savage MW, Kilvert A. ABCD guidelines for the management of hyperglycaemic emergencies in adults. *Pract Diab Int* 2006; **23**(5):227-231.
- [96] Dhatariya K, Savage M, Kelly T *et al*. Joint British Diabetes Societies Inpatient Care Group. The management of diabetic ketoacidosis in adults. Second edition.

Update: September 2013. <http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm>.
2013. [Last accessed 17th August 2017]

- [97] Dhatariya KK, Nunney I, Higgins K, Sampson MJ, Iceton G. A national survey of the management of diabetic ketoacidosis in the UK in 2014. *Diabetic Med* 2016; **33**(2):252-260.
- [98] Dhatariya K, Nunney I, Iceton G. Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. *Diabetic Med* 2016; **33**(2):269-270.
- [99] Dhatariya K. The evolution of DKA management. *Br J Diabetes Vasc Dis* 2015; **15**(1):31-33.
- [100] Dhatariya K, James J. In-hospital treatment and surgery in people with diabetes. Holt RI, Cockram C, Flyvbjerg A, Goldstein BJ eds. *Textbook of Diabetes*. Wiley-Blackwell, 2017.
- [101] Health and Social Care Information Centre. National Diabetes Inpatient Audit (NaDIA) - 2015. <http://www.hscic.gov.uk/catalogue/PUB20206>. 2016. [Last accessed 17th August 2017]
- [102] Lipsky BA, Berendt AR, Cornia PB *et al*. *Clin Infect Dis* 2012; **54**(12):e132-e173.
- [103] Allan B, Walton C, Kelly T, Walden E, Sampson M. Admissions avoidance and diabetes: Guidance for clinical commissioning groups and clinical teams. http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_Admissions_Avoidance_Diabetes.pdf. 2013. [Last accessed 17th August 2017]

- [104] Dhatariya K. Admission avoidance using intramuscular antibiotics for the treatment of borderline foot infections in people with diabetes in a tertiary care foot clinic. *BMJ Quality Improvement Reports* 2013; **2**(1).
- [105] Lipsky BA, Silverman MH, Joseph WS. A proposed new classification of skin and soft tissue infections modeled on the subset of diabetic foot infection. *Open Forum Infectious Diseases* 2017; **4**(1):ofw255.
- [106] International Working Group of the Diabetic Foot. International consensus. <http://www.iwgdf.org>. 2011. [Last accessed 17th August 2017]
- [107] Gooday C, Hallam C, Sieber C *et al*. An antibiotic formulary for a tertiary care foot clinic: admission avoidance using intramuscular antibiotics for borderline foot infections in people with diabetes. *Diabetic Med* 2013; **30**(5):581-589.
- [108] Stone MA, Camosso-Stefinovic J, Wilkinson J *et al*. Incorrect and incomplete coding and classification of diabetes: a systematic review. *Diabetic Med* 2010; **27**(5):491-497.
- [109] Health and Social Care Information Centre. HRG4+ 2015/16 reference costs grouper code to group workbook. http://www.hscic.gov.uk/media/19406/HRG4-201516-Reference-Costs-Grouper-Code-to-Group-Workbook/xls/HRG4__201516_Reference_Costs_Grouper_Code_to_Group_Workbook_v1.0.xlsx. 2016. [Last accessed 17th August 2017]
- [110] Scott A, Claydon A, Brennan G *et al*. The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes. The Joint British Diabetes Societies Inpatient Care Group. <http://www.diabetologists->

abcd.org.uk/JBDS/JBDS_IP_HHS_Adults.pdf. 2012. [Last accessed 17th August 2017]

- [111] Royal College of Physicians. The management of glucocorticoid induced osteoporosis. <https://www.nos.org.uk/NetCommunity/Document.Doc?id=422>. 2002. [Last accessed 17th August 2017]
- [112] Fardet L, Petersen I, Nazareth I. Prevalence of long-term oral glucocorticoid prescriptions in the UK over the past 20 years. *Rheumatology* 2011; **50**(11):1982-1990.
- [113] Roberts A, James J, Dhatariya K. Joint British Diabetes Societies for Inpatient Care: Management of hyperglycaemia and steroid (glucocorticoid) therapy. http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_Steroids.pdf. 2014. [Last accessed 17th August 2017]
- [114] Dhatariya K. Does dexamethasone-induced hyperglycaemia contribute to postoperative morbidity and mortality? *Br J Anaesth* 2013; **110**(5):674-675.
- [115] Vasilopoulos T, Morey TE, Dhatariya K, Rice MJ. Limitations of significance testing in clinical research: A review of multiple comparison corrections and effect size calculations with correlated measures. *Anesth Analg* 2016; **122**(3):825-830.
- [116] Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *Lancet* 2000; **355**(9206):773-778.

- [117] Eurich DT, Gamble JM, Marrie TJ, Majumdar SR. Dysglycaemia and 90 day and 1 year risks of death or readmission in patients hospitalised for community-acquired pneumonia. *Diabetologia* 2010; **53**(3):497-503.
- [118] Williams LS, Rotich J, Qi R *et al.* Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke. *Neurology* 2002; **59**(1):67-71.
- [119] Foo K, Cooper J, Deaner A *et al.* A single serum glucose measurement predicts adverse outcomes across the whole range of acute coronary syndromes. *Heart* 2003; **89**(5):512-516.
- [120] Herring R, Russell-Jones DL, Pengilley C *et al.* Management of raised glucose, a clinical decision tool to reduce length of stay of patients with hyperglycaemia. *Diabetic Med* 2013; **30**(1):81-87.
- [121] National Patient Safety Agency. Safer administration of insulin. <http://www.nrls.npsa.nhs.uk/resources/type/alerts/?entryid45=74287>. 2010. [Last accessed 17th August 2017]
- [122] NHS England. Never Events List 2015/16. <https://www.england.nhs.uk/wp-content/uploads/2015/03/never-evnts-list-15-16.pdf>. 2016. [Last accessed 17th August 2017]
- [123] Sampson MJ. Adoption and outcomes of JBDS guidelines. Diabetes UK Annual Professional Conference. 2013.
- [124] American Diabetes Association. Economic consequences of diabetes mellitus in the U.S. in 1997. *Diabetes Care* 1998; **21**(2):296-309.

- [125] James J. Safety and insulin: Implementation of national guidance at a local level. *J Diab Nurs* 2013; **17**(5):180-185.
- [126] Cousins D, Rosario C, Scarpello J. Insulin, hospitals and harm: a review of patient safety incidents reported to the National Patient Safety Agency. *Clinical Medicine* 2011; **11**(1):28-30.
- [127] Diabetes UK. Inpatient care for people with diabetes in England.
<http://www.diabetes.org.uk/Documents/Position%20statements/diabetes-uk-position-statement-inpatient-care-0614.pdf>. 2014. [Last accessed 17th August 2017]
- [128] Flanagan D, Moore E, Baker S, Wright D, Lynch P. Diabetes care in hospital - the impact of a dedicated inpatient care team. *Diabetic Med* 2008; **25**(2):147-151.
- [129] Bradley C. The Diabetes Satisfaction Questionnaire (DTSQ). Bradley C ed. *The Handbook of Psychology and Diabetes: a guide to psychological measurement in diabetes research and practice*. Chur, Switzerland: Harwood Academic, 1994: 111-32.
- [130] Bradley C, Todd C, Gorton T *et al*. The development of an individualized questionnaire measure of perceived impact of diabetes on quality of life: the ADDQoL. *Qual Life Res* 1999; **8**(1-2):79-91.
- [131] Woodcock A, Bradley C, Plowright R *et al*. The influence of diabetic retinopathy on quality of life: Interviews to guide the design of a condition-specific, individualised questionnaire: the RetDQoL. *Patient Educ Couns* 2004; **53**(3):365-383.

- [132] Mitchell J, Wolffsohn J, Woodcock A *et al.* The MacDQoL individualized measure of the impact of macular degeneration on quality of life: reliability and responsiveness. *Am J Ophthalmol* 2008; **146**(3):447-454.
- [133] Hommel I, van Gurp PJ, Tack CJ *et al.* Perioperative diabetes care: room for improving the person centredness. *Diabetic Med* 2015; **32**(4):561-568.
- [134] Rajendran R, Rayman G. Glycaemic management in patients with diabetes in hospital. *Medicine* 2014; **42**(12):718-722.
- [135] Lachin JM, Orchard TJ, Nathan DM, for the DCCT/EDIC Research Group. Update on cardiovascular outcomes at 30 years of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study. *Diabetes Care* 2014; **37**(1):39-43.
- [136] Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Eng J Med* 2008; **359**(15):1577-1589.
- [137] Chua HR, Venkatesh B, Stachowski E *et al.* Plasma-Lyte 148 vs 0.9% saline for fluid resuscitation in diabetic ketoacidosis. *J Crit Care* 2012; **27**(2):138-145.
- [138] Van Zyl DG, Rheeder P, Delport E. Fluid management in diabetic-acidosis - Ringer's lactate versus normal saline: a randomized controlled trial. *QJM* 2012; **105**(4):337-343.
- [139] Fletcher S. The critical care/acute medicine interphase. *Future Hosp J* 2016; **3**(1):55-57.

- [140] Carson SS, Stocking C, Podsadecki T. Effects of organizational change in the medical intensive care unit of a teaching hospital: A comparison of 'open' and 'closed' formats. *JAMA* 1996; **276**(4):322-328.
- [141] Basu A, Close CF, Jenkins D *et al.* Persisting mortality in diabetic ketoacidosis. *Diabetic Med* 1993; **10**(3):282-284.
- [142] Faich GA, Fishbein HA, Ellis SE. The epidemiology of diabetic acidosis: a population-based study. *Am J Epidemiol* 1983; **117**(5):551-558.
- [143] Ellemann K, Soerensen JN, Pedersen L, Edsberg B, Andersen OO. Epidemiology and treatment of diabetic ketoacidosis in a community population. *Diabetes Care* 1984; **7**(6):528-532.
- [144] Bui TP, Werther GA, Cameron FJ. Trends in diabetic ketoacidosis in childhood and adolescence: a 15-yr experience. *Pediatr Diabetes* 2002; **3**(2):82-88.
- [145] Dunger DB, Sperling MA, Acerini CL *et al.* European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society Consensus Statement on diabetic ketoacidosis in children and adolescents. *Pediatrics* 2004; **113**(2):e133-e140.
- [146] Rewers A, Dong F, Slover RH, Klingensmith G, Rewers M. Incidence of diabetic ketoacidosis at diagnosis of type 1 diabetes in Colorado youth, 1998-2012. *JAMA* 2015; **313**(15):1570-1572.
- [147] Usher-Smith JA, Thompson M, Ercole A, Walter FM. Variation between countries in the frequency of diabetic ketoacidosis at first presentation of type 1 diabetes in children: a systematic review. *Diabetologia* 2012; **55**(11):2878-2894.

- [148] Wong B, Cheng A, Yu C, Goguen J. Examining the "Killer K" of diabetic ketoacidosis at a tertiary care hospital: A descriptive study. *Can J Diabetes* 2016; **40**(3):204-209.
- [149] Carlotti AP, St George-Hyslop C, Bohn D, Halperin ML. Hypokalemia during treatment of diabetic ketoacidosis: Clinical evidence for an aldosterone-like action of insulin. *J Pediatr* 2013; **163**(1):204-212.
- [150] Varadarajan M, Patel M, Kakkar N *et al.* Are the results from the 2014 UK national survey on the management of diabetic ketoacidosis applicable to individual centres? *Diabetes Res Clin Pract* 2017; **127**:140-146.
- [151] Joint British Diabetes Societies Inpatient Care Group. Self management of diabetes in hospital. http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_SelfManagement.pdf. 2012. [Last accessed 17th August 2017]
- [152] Wolfsdorf J, Glaser N, Sperling MA. Diabetic ketoacidosis in infants, children, and adolescents: A consensus statement from the American Diabetes Association. *Diabetes Care* 2006; **29**(5):1150-1159.
- [153] Schade DS, Eaton RP. Dose response to insulin in man: Differential effects on glucose and ketone body regulation. *J Clin Endocrinol Metab* 1977; **44**(6):1038-1053.
- [154] Wolfsdorf JI, Allgrove J, Craig ME *et al.* Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes* 2014; **15**(S20):154-179.

- [155] British Society of Paediatric Endocrinology and Diabetes. BSPED recommended guideline for the management of children and young people under the age of 18 years with diabetic ketoacidosis 2015.
<http://www.bsped.org.uk/clinical/docs/DKAGuideline.pdf>. 2015. [Last accessed 17th August 2017]
- [156] Sato H, Carvalho G, Sato T *et al*. The association of preoperative glycemic control, intraoperative insulin sensitivity, and outcomes after cardiac surgery. *J Clin Endocrinol Metab* 2010; **95**(9):4338-4344.
- [157] O'Sullivan CJ, Hynes N, Mahendran B *et al*. Haemoglobin A1c (HbA1C) in non-diabetic and diabetic vascular patients. Is HbA1C an independent risk factor and predictor of adverse outcome? *Eur J Vasc Endovasc Surg* 2006; **32**(2):188-197.
- [158] Vriesendorp TM, Morelis QJ, DeVries JH, Legemate DA, Hoekstra JB. Early post-operative glucose levels are an independent risk factor for infection after peripheral vascular surgery. A retrospective study. *Eur J Vasc Endovasc Surg* 2004; **28**(5):520-525.
- [159] Bilotta F, Spinelli A, Giovannini F *et al*. The effect of intensive insulin therapy on infection rate, vasospasm, neurologic outcome, and mortality in neurointensive care unit after intracranial aneurysm clipping in patients with acute subarachnoid hemorrhage: A randomized prospective pilot trial. *J Neurosurg Anesthesiol* 2007; **19**(3):156-160.
- [160] Marchant MH, Viens NA, Cook C, Vail TP, Bolognesi MP. The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. *J Bone Joint Surg Am* 2009; **91**(7):1621-1629.

- [161] Walid MS, Newman BF, Yelverton JC *et al.* Prevalence of previously unknown elevation of glycosylated hemoglobin in spine surgery patients and impact on length of stay and total cost. *J Hosp Med* 2010; **5**(1):E10-E14.
- [162] Gustafsson UO, Thorell A, Soop M, Ljungqvist O, Nygren J. Haemoglobin A1c as a predictor of postoperative hyperglycaemia and complications after major colorectal surgery. *Br J Surg* 2009; **96**(11):1358-1364.
- [163] Kreutziger J, Schlaepfer J, Wenzel V, Constantinescu MA. The role of admission blood glucose in outcome prediction of surviving patients with multiple injuries. *J Trauma* 2009; **67**(4):704-708.
- [164] Vilar-Compte D, Alvarez de Iturbe I, Martin-Onraet A *et al.* Hyperglycemia as a risk factor for surgical site infections in patients undergoing mastectomy. *Am J Infect Control* 2008; **36**(3):192-198.
- [165] Park C, Hsu C, Neelakanta G *et al.* Severe intraoperative hyperglycemia is independently associated with surgical site infection after liver transplantation. *Transplantation* 2009; **87**(7):1031-1036.
- [166] Ambiru S, Kato A, Kimura F *et al.* Poor postoperative blood glucose control increases surgical site infections after surgery for hepato-biliary-pancreatic cancer: a prospective study in a high-volume institute in Japan. *J Hosp Infect* 2008; **68**(3):230-233.
- [167] Chuang SC, Lee KT, Chang WT *et al.* Risk factors for wound infection after cholecystectomy. *J Formos Med Assoc* 2004; **103**(8):607-612.

- [168] Shibuya N, Humphers JM, Fluhman BL, Jupiter DC. Factors associated with nonunion, delayed union, and malunion in foot and ankle surgery in diabetic patients. *J Foot Ankle Surg* 2013; **52**(2):207-211.
- [169] Royal College of Surgeons, Department of Health. The Higher Risk General Surgical Patient: towards improved care for a forgotten group. https://www.rcseng.ac.uk/-/media/files/rcs/library-and-publications/non-journal-publications/higher_risk_surgical_patient_2011_web.pdf. 2011. [Last accessed 17th August 2017]
- [170] Barker P, Creasey PE, Dhataria K *et al*. Peri-operative management of the surgical patient with diabetes 2015. *Anaesthesia* 2015; **70**(12):1427-1440.
- [171] National Institute for Health and Care Excellence. Routine preoperative tests for elective surgery (NG45). <https://www.nice.org.uk/guidance/ng45>. 2016. [Last accessed 17th August 2017]
- [172] Dhataria KK, Wiles MD. Pre-operative testing guidelines: a NICE try but not enough. *Anaesthesia* 2016; **71**(12):1403-1407.
- [173] Underwood P, Askari R, Hurwitz S, Chamarthi B, Garg R. Preoperative A1C and clinical outcomes in patients with diabetes undergoing major noncardiac surgical procedures. *Diabetes Care* 2014; **37**(3):611-616.
- [174] PRISMA. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). <http://www.prisma-statement.org/>. 2009. [Last accessed 17th August 2017]

- [175] Stanisstreet D, Walden E, Jones C *et al.* The hospital management of hypoglycaemia in adults with diabetes mellitus. http://www.diabetologists-abcd.org.uk/subsite/JBDS_IP_Hypo_Adults_Revised.pdf. 2013. London, Joint British Diabetes Societies Inpatient Care Group for NHS Diabetes. [Last accessed 17th August 2017]
- [176] George S, Stanisstreet D. The use of variable rate intravenous insulin infusion (VRII) in medical inpatients. <http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm>. 2014. [Last accessed 17th August 2017]
- [177] Diabetes on the net. The six steps to insulin safety. http://www.cpd.diabetesonthenet.com/index.php?area=modules&page=module_questions. 2017. [Last accessed 17th August 2017]
- [178] Rajendran R, Kerry C, Round R-M *et al.* Impact of the Diabetes Inpatient Care and Education (DICE) project and the DICE Care Pathway on patient outcomes and trainee doctor's knowledge and confidence. *Diabetic Med* 2015; **32**(7):920-924.
- [179] Hommel I, van Gorp PJ, Tack CJ *et al.* Major gaps between recommended perioperative diabetes care and current practice. *Eur J Intern Med* 2016; **34**:e11-e13.
- [180] Hommel I, Wollersheim H, Tack CJ *et al.* Impact of a multifaceted strategy to improve perioperative diabetes care. *Diabetic Med* 2017; **34**(2):278-285.
- [181] Woolf SH, Grol R, Hutchinson A, Eccles M, Grimshaw J. Potential benefits, limitations, and harms of clinical guidelines. *BMJ* 1999; **318**(7182):527-530.