Received: 21 July 2022 | Accepted: 17 October 2022

DOI: 10.1111/dme.14980

DIABETIC Medicine

REVIEW

Gaps in our knowledge of managing inpatient dysglycaemia and diabetes in non-critically ill adults: A call for further research

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Abstract

Aims: To describe the gaps in knowledge for the care of people in the hospital who have dysglycaemia or diabetes.

Methods: A review of the current literature and the authors' knowledge of the subject.

Results: Recent data has suggested that the prevalence of hospitalised people with diabetes is approximately three times the prevalence in the general population and is growing annually. A wealth of observational data over the last 4 decades has shown that people with hyperglycaemia, severe hypoglycaemia or diabetes, all experience more harm whilst in the hospital than those who do not have the condition. This often equates to a longer length of stay and thus higher costs. To date, the proportion of federal funding aimed at addressing the harms that people with dysglycaemia experience in hospitals has been very small compared to outpatient studies. National organisations, such as the Joint British Diabetes Societies for Inpatient Care, the American Diabetes Association and the Endocrine Society have produced guidelines or consensus statements on the management of various aspects of inpatient care. However, whilst a lot of these have been based on evidence, much remains based on expert opinion and thus low-quality evidence.

Conclusions: This review highlights that inpatient diabetes is an underfunded and under-researched area.

KEYWORDS

dysglycaemia, harms, hyperglycaemia, hypoglycaemia, inpatient diabetes, perioperative care, technology

1 | INTRODUCTION

Recent data from Europe and the USA suggest that the prevalence of people in hospital with diabetes is approximately three times higher than the prevalence in the general population.[1–3] In the USA, the proportion of adults being hospitalised who have diabetes is rising, on average, by 2.5% annually.[4] For any given reason for admission, people with diabetes often spend longer in the hospital than those without the condition.[5] In addition, there are

now ample observational data to suggest that people who develop hyperglycaemia or hypoglycaemia requiring assistance whilst in hospital experience greater harm, resulting in longer lengths of stay.[6,7] These, and other data would suggest that the cost impact of dysglycaemia and diabetes in hospitalised inpatients is very large. By extension, any interventions that improved glycaemic control are likely to result in a reduction in harms, shorter length of stay and a lowering of costs.[8]

In the UK, the Joint British Diabetes Societies for Inpatient Care (JBDS) have produced a series of documents and guidelines to help in the management of people in hospitals with diabetes and dysglycaemia.[9] These cover a variety of situations that cover much of the 'patient journey'—including, but not limited to, admissions avoidance,[10] managing hyperglycaemia and diabetes in the emergency department,[11] hypoglycaemia,[12] peri-operative diabetes care,[13] and discharge planning.[14] The American Diabetes Association (ADA) and the American Association Clinical Endocrinology (AACE), and the Endocrine Society have also produced guidelines and recommendations but, unlike the JBDS documents, their emphasis is often not on specific aspects of inpatient care.[15–18] They have also produced a systematic review of the evidence behind some of their recommendations.[19] All of these documents have been produced by a multidisciplinary team of interested professionals.[20] However, the authors of these documents freely admit that whilst many of the recommendations are based on the available evidence from randomized controlled trials and observational studies, a lot of the guidance is based on consensus, driven by expert opinion.

There are several similarities amongst the guidelines, in particular aiming to improve glycaemic control to reduce complications and length of hospital stay. The use of insulin as part of this strategy is also a common feature. However, there are also differences between the documents. These include (but are not limited to) glycaemic targets (see Table 1), use of technology and which agents to use in particular circumstances. These differences are almost always driven by a lack of evidence.

Given the increasing prevalence, the associated morbidity, and the costs of (mis)management of people in hospital with diabetes it may have been expected that research funding and prioritisation of inpatient care would be proportionate to the public health impact. In the UK, Diabetes UK has a Diabetes Research Steering Group focused on identifying research priorities in acute care. Whilst the group have raised a number of priorities, there has been difficulty stimulating research in those areas, highlighting a need for further capacity building and investment in inpatient care research. It is also notable that inpatients do not feature in the National Institute of Health Research James Lind Alliance list of research priorities for diabetes, which was developed by people with diabetes, carers and healthcare professionals.[21] This highlights a need to raise awareness of the importance and potential impact of research in this area. Table 2 shows that the number of publications listed on PubMed mentioning 'inpatient diabetes' more than doubled from 1990–1999 to 2010–2019 but remained at just over 1% of all publications mentioning 'diabetes'. For comparison, data are given for the terms 'geriatric medicine' and 'inpatient geriatric medicine', 'heart failure' and 'inpatient heart failure', 'chronic obstructive pulmonary disease' and 'inpatient chronic obstructive pulmonary disease' showing greater proportions over the years referring to inpatients. Thus, there remains a need to invest more time, energy and resources into inpatient diabetes.

The continuing output from the UK National Diabetes Inpatient Safety Audit (NDISA) will be a valuable tool in determining what aspects of care should be targeted to prevent the development of in-hospital severe hypoglycaemia, DKA, hyperosmolar hyperglycaemic syndrome and foot wounds.[22] The Getting It Right First Time (GIRFT) programme for diabetes and the Diabetes UK Research Steering Group focussed on acute care have also identified several aspects of inpatient care that needed to be addressed, including identifying people with diabetes in hospital, increasing the numbers of staff who have trained in insulin safety and improving peri-operative care pathways.[23] Currently, the best way of implementing the lessons learnt from these national datasets remains unanswered and should be actively explored.

Novelty Statement

- The number of hospital inpatients with diabetes is approximately three times the prevalence in the outpatient population.
- People with diabetes experience more complications and poorer outcomes than those without diabetes, when admitted for the same condition.
- There remains a need to do more research on the management of inpatient diabetes along the whole 'patient journey'.
- This review highlights some of the areas of need.

2 | TYPE 1 VS TYPE 2 DIABETES

Much of the data on harm in people with diabetes makes no differentiation between those with type 1 or type 2

TABLE 1 Glucose targets for those in a general ward

Joint British Diabetes Society for Inpatient Care[9]	Glucose levels in most people of between 6.0–10 mmol/L with an acceptable range of between 6.0–12.0 mmol/L
Endocrine Society (USA)[16]	Pre-meal glucose target <7.8 mmol/L and random blood glucose <10.0 mmol/L. A lower target may be appropriate in those able to achieve it without developing hypoglycaemia. A higher target (<11.0 mmol/L), may be appropriate for others, e.g., end-of-life care
American Diabetes Association/ American Association Clinical Endocrinology[94]	Target 7.8–10.0 mmol/L for most people
American College of Physicians[95]	No specific glucose targets but avoid dropping below 7.8 mmol/L
American Society of Parenteral and Enteral Nutrition (ASPEN)[96]	Target 7.8–10.0 mmol/L for those receiving nutritional support
Society for Ambulatory Anaesthesia[97,98]	Pre-meal glucose target <7.7 mmol/L and random blood glucose <10.0 mmol/L

TABLE 2 The proportion of publications on PubMed mentioning 'inpatient diabetes' as a proportion of all publications mentioning 'diabetes' between 1990 and 2019. By comparison, the same data are given for the terms 'heart failure', 'inpatient heart failure', 'chronic obstructive pulmonary disease' and 'inpatient chronic obstructive pulmonary disease'

Years	Publications mentioning 'Inpatient diabetes'	Publications mentioning 'Diabetes'	Inpatient diabetes vs diabetes publications (%)
1990–1999	399	84,348	0.47
2000–2009	1390	180,060	0.77
2010–2019	3869	368,760	1.05
Total	5658	633,168	0.89
Years	**Publications mentioning 'Inpatient geriatric medicine'**	**Publications mentioning 'geriatric medicine'**	**Inpatient geriatric medicine vs geriatric medicine (%)**
1990–1999	309	9365	3.3
2000–2009	550	18,097	3.0
2010–2019	1817	53,743	3.4
Total	2676	81,205	3.3
Years	**Publications mentioning 'Inpatient heart failure'**	**Publications mentioning 'congestive cardiac failure'**	**Inpatient heart failure vs congestive cardiac failure (%)**
1990–1999	200	31,530	0.63
2000–2009	742	64,383	1.15
2010–2019	2406	116,915	2.06
Total	3348	212,828	1.57
Years	**Publications mentioning 'Inpatient chronic obstructive pulmonary disease'**	**Publications mentioning 'chronic obstructive pulmonary disease'**	**Inpatient chronic obstructive pulmonary disease vs chronic obstructive pulmonary disease (%)**
1990–1999	71	6221	1.14
2000–2009	357	19,569	1.82
2010–2019	887	40,786	2.17
Total	1315	66,576	1.98

diabetes. Part of the reason for this is the difficulty with coding, and how many people are unable to differentiate between those with type 1 or insulin-treated type 2 diabetes. An exception to this is the data from the UK National Inpatient Diabetes Audit.[24,25] This is because these data were collected by members of the diabetes team, often at the bedside of the person with diabetes. There are several trials based around critical illness or peri-operative care that have been funded by the American Diabetes Association or the UK National Institute for Health Research looking at interventions in those with or expected to have, critical illness.[26–29] To our knowledge, however, there are no interventional trials funded for non-critical illness.

Type 1 diabetes often requires a different approach to treatment to type 2 diabetes. In particular, the requirement is to ensure that insulin treatment is always given, regardless of the clinical state of the individual. The risk of hypoglycaemia or the development of diabetic ketoacidosis (DKA) must be regularly assessed. There are very few data to show differences in outcomes between type 1 and type 2 diabetes, but there are no randomised controlled trial data looking exclusively at those with type 1 diabetes—a major deficiency in our opinion. One study from 2012 of over 8725 people with type 1 diabetes compared outcomes with over 57,000 people with type 2 diabetes. They showed that all forms of harm were worse in those with type 1 diabetes, leading to increased length of stay and subsequent costs.[30] To date, there have also been no prospective randomised controlled trials to determine the best treatment protocols, e.g., the use of insulin pumps, or closed loops. Thus, there remain many uncertainties on how best to manage people with type 1 who are in the hospital.[31]

When considering hyperglycaemic emergencies, DKA is one area of inpatient diabetes care that has been extensively studied over the last 100 years.[32,33] However, there remain areas of uncertainty. One example is 'what is the correct resuscitation fluid to administer'? Despite the large numbers of people admitted to DKA, there have been very few trials looking at this and the answer remains unclear.[34–37] Cerebral oedema, another feared complication, was thought to be due to the rate of fluid administration, administration of bicarbonate or the rapid shifts in osmolality.[38] However, the largest randomised controlled trial from 2018 has questioned those theories.[39] Whether the factors that predispose children to develop cerebral oedema are the same in adults remains unknown.

When considering hyperosmolar hyperglycaemic syndrome (HHS), to date there have been no prospective studies assessing the optimal management of this population, despite a 10-fold higher mortality than DKA. The current protocols used have evolved over time and remain largely based on expert consensus.[40,41]

3 | GLUCOSE TARGETS

Because of the lack of good quality randomised controlled trials, there is inconsistent advice from learned societies around the world on what the glucose targets should be for those in general wards and those in an intensive care unit. Table 1 shows the targets for those in a general ward. Again, despite 20% or more of all inpatients having diabetes or hyperglycaemia, there remains debate on what the optimal target glucose concentration should be.

4 | HYPOGLYCAEMIA

This is an area of diabetes management that has had a great deal of attention paid to it and is often a significant study endpoint. In their systematic review and meta-analysis, Lake et al showed that inpatient hypoglycaemia was associated with harm—in particular increased length of stay and higher in-hospital mortality.[7] Thus, avoidance of hypoglycaemia should be seen as a priority for inpatient research. The use of technology, which is discussed in more detail in the section below, is helping to change this aspect of diabetes care within the hospital.[42–44]

5 | DRUG CHOICE AND DRUG SAFETY

In the UK, it has been commonplace to continue oral medication when someone with type 2 diabetes is admitted to the hospital. Unless there are clear contraindications—-e.g. hypoglycaemia (sulfonylureas), acute kidney injury (metformin), heart failure (pioglitazone) and these agents are often continued. This is different to the US, where a series of publications have suggested that it is safer to use insulin, either as a basal-bolus regimen, basal plus regimen or with a DPP4 inhibitor.[45–49] The latter agents were particularly beneficial when there was only mild or modest hyperglycaemia.[50] There remains the need to do studies comparing outcomes for those changing their admission medication—where it is not needed and done because of hospital protocols vs those in whom medications are left unchanged. The safety and efficacy of using many of the non-insulin agents in the hospital have recently been reviewed.[3] Of course, an area of contention is the use of sodium-glucose-like transporter 2 (SGLT2) inhibitors in inpatients with type 2 diabetes. In the outpatient setting, whilst the absolute risk of DKA with these agents is low, the relative risk is significantly higher when compared to placebo or other glucose-lowering agents.[51] As a result, and because of the physiological stress of acute hospital admission, together with variable carbohydrate intake,

possible changes in fluid status and the use of drugs that may induce or worsen insulin resistance, e.g., glucocorticoids, it is recommended that these agents be stopped at the time of hospital admission. However, there are few data on the continuation of these agents in hospitals, or indeed starting them de novo in acute illness. The added complexity is that these agents are also licensed for use in those without diabetes who have chronic kidney disease or heart failure. Thus, there are four lines of evidence to be considered: those who do not have diabetes who are on these drugs and who are admitted unwell; those who have diabetes who are on these drugs as outpatients and who are admitted acutely unwell; those who do not have diabetes and who are started on them whilst in hospital whilst acutely unwell; those who have diabetes who are not on these drugs but are started on them whilst in hospital. The data for those with and without diabetes who start them as outpatients are well recognised and beneficial, in terms of cardiovascular protection, as well as benefits in heart failure and chronic kidney disease.[52–55] There are theoretical reasons why their use may be advantageous in inpatients.[56] However, there are very few data on initiating their use in acutely unwell inpatients with diabetes. To date, the DARE-19 study, using dapagliflozin in people admitted with COVID infection remains one of the very few studies in this area.[57] That study showed that only 2 people, both of whom were known to have diabetes, developed DKA, which swiftly resolved when the drug was stopped. The continuation or initiation of SGLT2 inhibitors in acutely unwell people in hospitals with and without diabetes remains an area for further research.[58,59]

The inpatient use of the GLP-1 receptor class is also relatively unexplored. Their side effect profile of gastrointestinal disturbance makes them seem potentially unattractive.[3] However, studies using twice-daily exenatide, low-dose liraglutide or dulaglutide have resulted in better glycaemic control compared to insulin use alone in non-critically ill individuals.[60–62] However, whether this translates to better outcomes is unknown.

6 | ADDING GLUCOSE TO THE NATIONAL EARLY WARNING SCORE?

The updated National Early Warning Score (NEWS2) was launched in 2017. It measures physiological parameters (oxygen saturation, respiratory rate, temperature, blood pressure, pulse rate) and assigns a score when these deviate outside the norm.[63] The higher the score, the greater the need for urgent assessment and intervention. Recent data (yet to be peer-reviewed) looking at the use of NEWS2 showed that after the initial 24 h after an acute admission, 10% of people have a score warranting intervention (a score of ≥5), with 0.19% needed admission to intensive care or transitioning to palliative care.[64] These authors did an additional analysis and showed that if the score needed to trigger an intervention increased, there would be an increase in false negative referrals and this would come at a significant cost. However, what remains unknown is whether the addition of a bedside capillary glucose measurement (or indeed continuous glucose monitor reading) to the NEWS2 alters prognosis or costs.[65] Most of the data surrounding dysglycaemia and resultant harms are observational, and there are few data looking at the effect of normalising glucose concentrations and subsequent outcomes. This also remains an important unanswered question.

7 | ENTERAL AND PARENTERAL FEEDING

Data from 2005 showed that those on total parenteral nutrition who developed hyperglycaemia experienced a larger number of adverse events than those who maintained glucose concentrations within the reference range.[66] Unpublished data from a recent UK national survey has suggested that there is no consistency in what feeding regimen is used across the UK for those on enteral or parenteral feed. As a result, there is also no consistency in the insulin regimens used. These data are being used to update the next edition of the JBDS guideline on glycaemic management in this group of individuals. However, a small study of 43 non-critically ill people receiving nutritional support in the hospital who were randomised to a fully closed loop insulin delivery system compared to standard of care subcutaneous insulin showed that there was a significant increase in time in range (68.4% vs 36.4%, $p < 0.0001$), with no episodes of severe hypoglycaemia, hyperglycaemia or ketonaemia.[67] However, the use of this technology is still in its infancy and is not yet widely available.

8 | INSTITUTIONAL CARE SETTINGS

Inpatients do not exist only in hospitals. Long-term care facilities, for those who are elderly or frail, those requiring inpatient psychiatric care, prisons and other correction facilities all have a disproportionate percentage of people with diabetes. The few randomised controlled trials on the management of people in long-term care facilities have shown a high rate of hypoglycaemia in sulfonylurea and insulin-treated individuals,

resulting in a longer length of stay, higher transfer to the hospital and mortality.[68,69] The relationship between diabetes and mental health has been well recognised.[70] Commonly used drugs in treating those with mental health problems may also exacerbate obesity, and precipitate hyperglycaemic emergencies.[71] Whilst there is JBDS guidance to help those working in mental health, these are almost exclusively consensus-based, with very little work being published in the management of diabetes (or pre-diabetes) in this area.[72] It remains largely unknown if people with diabetes or hyperglycaemia in these settings experience the same adverse outcomes as those in an acute hospital. Thus, there remains a need for further work to be done.

9 | TECHNOLOGY

This may be the area of inpatient diabetes care that is changing quickly. There is increasing use of wearable technology for use by people with diabetes. These include continuous glucose monitoring (real-time or intermittently scanned—rtCGM or isCGM), but also insulin pumps, and for a very few, closed-loop systems. In the near future, wearable technology is likely to play an important role in managing inpatient dysglycaemia. Currently, available trial data suggest that for outpatients with type 1 diabetes the ability to measure interstitial glucose in real-time, coupled with continuous insulin delivery systems—i.e., closed loops—results in improved time in range with a lower likelihood of dysglycaemia.[73,74] However, to date no randomised controlled studies have reported on the type of insulin administration (multiple daily injections, pumps, or closed loop) or as mentioned, management of hyperglycaemia in inpatients with type 1 diabetes. Limited data is available on the use of intermittent or continuous real-time interstitial glucose monitoring for those with type 2.[42,44,75,76] This may be particularly useful for those with cognitive impairment or who are unable to communicate appropriately if their blood glucose is low or high. Promising early work—albeit from a single institution, has shown that CGM use enables the recognition of symptomatic and asymptomatic dysglycaemia, frequently missed by bedside capillary testing.[44,76] Preventing dysglycaemia is beneficial, particularly when it has been recognised that having episodes of severe hypoglycaemia significantly increases the length of stay, and high glucose concentrations are also associated with increased harm.[7]

In DKA, the current standard of care is regular measurement of bedside capillary β hydroxybutyrate concentrations.[77] Along with wearable technology, the ability to link data from bedside glucose and ketone point-of-care testing machines should allow members of the inpatient diabetes team to target those people who would most benefit from their intervention. It has previously been shown how an inpatient diabetes team, or diabetes inpatient specialist nurse intervention reduces the length of stay.[78,79] However, as the prevalence of diabetes amongst inpatients rises, it becomes more important that the team focuses their efforts on those who would most benefit. The ability to remotely view results would allow a targeted approach. This hypothesis has yet to be tested. How the use of recently developed continuous ketone monitoring may help guide management also remains unknown.[80]

Similarly, using an electronic prescribing system would allow those on intravenous insulin to be identified—in particular, if they were prescribed a fixed rate intravenous insulin infusion, for which the only indication would be either DKA or hyperosmolar hyperglycaemic state. An ideal situation would be the linking of the point-of-care results, with the electronic prescribing system, to help further inform the inpatient diabetes team. Once again, work to show this would improve outcomes remains to be done.

Most of these technologies are used by those with type 1 diabetes, but recent guidance will increase their availability for those with insulin-treated type 2 diabetes.[81] There remain concerns about the use of these devices if an individual is too unwell to use their own device. In this circumstance, it is likely that the device will be removed and only re-applied when the person is able and willing to manage their diabetes themselves. Many acute care staff will be unfamiliar with such devices and risk ignoring them. In people who are well enough and willing to use them, the governance aspects of their use in hospitals remain unclear—the readings that they generate, how will they be transferred to the electronic (or paper) hospital records? Calibration and quality assurance may be unreliable, although a recent study of rtCGM in the perioperative period suggested their performance was consistent and accurate during elective abdominal surgery.[82] This is important given the wealth of observational data showing poor outcomes in people with and without diabetes undergoing surgery.[83–85] Thus, there remain several questions as to how to best use the technology to its best advantage and translate that to optimising inpatient care. Staff education and acceptance of these technologies will also be a barrier to overcome.

The amount of data generated by these devices could overwhelm non-specialists. It remains to be seen whether nursing time or the confidence of staff looking after people using this technology will change. Certainly, the use of networked glucose meters and other technologies has been shown to help specialist inpatient diabetes teams, with the implementation of a virtual glucose management system being associated with less dysglycaemia.[86,87] With the advent of the COVID pandemic

accelerating remote working, including for inpatients, there is a gradual acceptance that this may make consultations more effective and efficient.[88] However, all these data are preliminary and beyond easy identification of people in hospitals with diabetes, and have yet to show direct patient benefits, such as reduced length of stay, reduced in-hospital medication error rates, or adverse outcomes. In addition, in the USA, the use of remote technology in the management of people with diabetes is challenging because of the complexities surrounding billing for virtual consultations.[89] One small study of the benefits of such remote working showed that people with diabetes liked bedside remote consultations.[90] In 2020, Diabetes UK launched a call looking to assess the use of technology in the inpatient setting.[91]

10 | QUALITATIVE DATA

It is incumbent on those looking after people with diabetes in the hospital to regularly survey their experiences and to help determine future priorities. How people with diabetes feel about the care they have received whilst in hospital has been previously formally evaluated and was also a part of the regular National Diabetes Inpatient Audit (NaDIA) carried out annually by NHS Digital.[1,92] However, with NaDIA no longer being carried out across the UK and being replaced by NDISA, data about how people with diabetes feel about their care is no longer formally collected. In the UK, the Royal College of Physicians, together with JBDS and others will shortly be starting a pilot to accredit adult inpatient diabetes teams.[93] Part of this will also be to explore the experiences of those people with diabetes who are in the hospital. It is likely that with the increasing use of technology and individual feedback from the person with diabetes, the ability to deliver more personalised care will increase.

11 | SUMMARY

The number of people with diabetes in the hospital continues to rise. They experience more harm and ultimately cost healthcare systems more. The focus for funding on diabetes research has, for several decades essentially ignored the needs of this vulnerable population. The Endocrine Society in the USA has recently updated its guidance on the management of hyperglycaemia in hospitalised individuals and has an accompanying systematic review which gives the reasons for their recommendations, and the strength of the evidence.[17,19] However, they only cover 10 questions. Resources are needed to enable such systematic reviews of the available evidence to identify the many other gaps in our knowledge for the whole of the patient journey and in all circumstances and facilities for which a person with diabetes may be admitted. Such work would be crucial in the ultimate goal of ensuring that people with diabetes do not suffer excess harm as a result of their condition.

AUTHOR CONTRIBUTIONS

KD is the chair of the Joint British Diabetes Society for Inpatient Care. GEU is the current President, Medicine & Science, of the American Diabetes Association. KD wrote the initial draft of the manuscript. GEU and KD edited subsequent drafts. Both authors saw and approved the final version of the manuscript.

ACKNOWLEDGMENTS

None.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST

KKD Has received speaker fees, travel or taken part in advisory boards for AstraZeneca, Sanofi Diabetes, Boehringer Ingelheim, Lilly and Novo Nordisk. GEU has received unrestricted research support for research studies (to Emory University) from Dexcom Inc., Bayer and Abbott.

Dexcom Inc., and Sanofi.

DATA AVAILABILITY STATEMENT

I confirm that my Data Availability Statement (pasted below) complies with the Expects Data Policy.

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REFERENCES

1. NHS Digital. National Diabetes Inpatient Audit (NaDIA) – 2019. 2020. Available from https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-inpatient-audit/2019. [Last accessed 11th October 2022].
2. Ena J, Gómez-Huelgas R, Romero-Sánchez M, et al. Hyperglycemia management in patients admitted to internal medicine in Spain: a point-prevalence survey examining adequacy of glycemic control and guideline adherence. *Eur J Intern Med*. 2015;26:392-398.
3. Galindo RJ, Dhatariya K, Gomez-Peralta F, Umpierrez GE. Safety and efficacy of inpatient diabetes management with non-insulin agents: an overview of international practices. *Curr Diab Rep*. 2022;22:237-246.

4. Zhang Y, McKeever Bullard K, Imperatore G, Holliday CS, Benoit SR. Proportions and trends of adult hospitalizations with diabetes, United States, 2000–2018. *Diabetes Res Clin Pract*. 2022;187:109862.
5. 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 Research & Clinical Practice*. 2007;77:92-98.
6. Evans NR, Dhatariya KK. Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. *Clin Med*. 2012;12:137-139.
7. Lake A, Arthur A, Byrne C, Davenport K, Yamamoto JM, Murphy HR. The effect of hypoglycaemia during hospital admission on health-related outcomes for people with diabetes: a systematic review and meta-analysis. *Diabet Med*. 2019;36:1349-1359.
8. NHS Diabetes. Inpatient care for people with diabetes: the economic case for change. 2013. Available from http://webarchive.nationalarchives.gov.uk/20130513172211/http://www.diabetes.nhs.uk/document.php?o=3034. [Last accessed 11th October 2022]
9. Joint British Diabetes Societies for Inpatient Care. Guidelines for the management of inpatient diabetes. 2022. Available from https://abcd.care/joint-british-diabetes-societies-jbds-inpatient-care-group. [Last accessed 11th October 2022]
10. Joint British Diabetes Societies for Inpatient Care. Admissions avoidance and diabetes: Guidance for clinical commissioning groups and clinical teams. 2013. Available from http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_Admissions_Avoidance_Diabetes.pdf. [Last accessed 11th October 2022].
11. James J, Kong M-F, Berrington R, Dhatariya K. Diabetes and the front door. 2020. Available from https://abcd.care/resource/jbds-16-diabetes-front-door. [Last accesed 4th November 2022].
12. Joint British Diabetes Societies for Inpatient Care. The hospital management of hypoglycaemia in adults with diabetes mellitus. 2021. Available from https://abcd.care/sites/abcd.care/files/site_uploads/JBDS_01_Hypo_Guideline_FINAL_23042021_0.pdf. [Last accessed 11th October 2022].
13. Centre for Perioperative Care. Guideline for perioperative care for people with diabetes mellitus undergoing elective and emergency surgery. 2021. Available from https://cpoc.org.uk/guidelines-resources-guidelines-resources/guideline-diabetes.
14. Joint British Diabetes Societies for Inpatient Care. Discharge planning for adults with diabetes. 2022. Available from https://abcd.care/sites/abcd.care/files/site_uploads/JBDS_Guidelines_Current/JBDS_10_Discharge_Planning_Guideline_240122.pdf. [Last accessed 11th October 2022].
15. American Diabetes Association. Diabetes care in the hospital: standards of medical Care in Diabetes—2022. *Diabetes Care*. 2022;45:S244-S253.
16. Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2012;97:16-38.
17. Korytkowski MT, Muniyappa R, Antinori-Lent K, et al. Management of hyperglycemia in hospitalized adult patients in non-critical care settings: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2022;107:2101-2128.
18. Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: developing a diabetes mellitus comprehensive care plan - 2022 update. *Endocr Pract*. 2022;28:923-1049. doi:10.1016/j.eprac.2022.08.002
19. Seisa MO, Saadi S, Nayfeh T, et al. A systematic review supporting the Endocrine Society clinical practice guideline for the management of hyperglycemia in adults hospitalized for noncritical illness or undergoing elective surgical procedures. *J Clin Endocrinol Metab*. 2022;107:2139-2147.
20. Joint British Diabetes Societies for Inpatient Care. A good inpatient diabetes service. 2019. Available from https://abcd.care/resource/jbds-14-good-inpatient-diabetes-service. [Last accessed 11th October 2022].
21. James Lind Alliance. Top 10s of priorities for research. 2022. Available from https://www.jla.nihr.ac.uk/top-10-priorities/. [Last accessed 11th October 2022].
22. NHS Digital. National Diabetes Inpatient Safety Audit. 2022. Available from https://digital.nhs.uk/data-and-information/clinical-audits-and-registries/national-diabetes-inpatient-safety-audit. [Last accessed 11th October 2022].
23. Getting it Right First Time. *Diabetes. GIRFT Programme National Specialty Report*. NHS England; 2020. Available from https://www.gettingitrightfirsttime.co.uk/wp-content/uploads/2020/11/GIRFT-diabetes-report.pdf. [Last accessed 11th October 2022]
24. NHS Digital. *National Diabetes Inpatient Audit - Harms 2020 England*. NHS Digital; 2020. Available from https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-inpatient-audit---harms/national-diabetes-inpatient-audit---harms-2020. [Last accessed 11th October 2022].
25. NHS Digital. NaDIA - Insulin use, oral hypoglycaemic agent use and insulin infusion use. Data from the National Diabetes Inpatient Audit (NaDIA), England, 2019, 2022. Available from https://digital.nhs.uk/supplementary-information/2021/nadia-insulin-use-oral-hypoglycaemic-agent-use-insulin-infusion-use. [Last accessed 11th October 2022].
26. Umpierrez G, Cardona S, Pasquel F, et al. Randomized controlled trial of intensive versus conservative glucose control in patients undergoing coronary artery bypass graft surgery: GLUCO-CABG trial. *Diabetes Care*. 2015;38:1665-1672.
27. Wallia A, Schmidt K, Oakes DJ, et al. Glycemic control reduces infections in post-liver transplant patients: results of a prospective, randomized study. *J Clin Endocrinol Metab*. 2017;102:451-459.
28. Hermayer KL, Egidi MF, Finch NJ, et al. A randomized controlled trial to evaluate the effect of glycemic control on renal transplantation outcomes. *J Clin Endocrinol Metab*. 2012;97:4399-4406.
29. Holt RI, Dritsakis G, Barnard-Kelly K, et al. The Optimising cardiac surgery ouTcOmes in people with diabeteS (OCTOPuS) randomised controlled trial to evaluate an outpatient pre-cardiac surgery diabetes management intervention: a study protocol. *BMJ Open*. 2021;11:e050919.
30. Viens NA, Hug KT, Marchant MH, Cook C, Vail TP, Bolognesi MP. Role of diabetes type in perioperative outcomes after hip and knee arthroplasty in the United States. *J Surg Orthop Adv*. 2012;21:253-260.
31. Mendez CE, Umpierrez GE. Management of type 1 diabetes in the hospital setting. *Curr Diab Rep*. 2017;17:98.

32. Dhatariya K. The evolution of DKA management. *Br J Diabetes Vasc Dis*. 2015;15:31-33.
33. Umpierrez GE, Abbas E, Kitabchi PD. MD: an exemplary Mentor and clinical researcher. *Diabetes Care*. 2016;39:333-336.
34. Dhatariya KK. Diabetic ketoacidosis. *Br Med J*. 2007;334:1284-1285.
35. Ramanan M, Attokaran A, Murray L, et al. Sodium chloride or Plasmalyte-148 evaluation in severe diabetic ketoacidosis (SCOPE-DKA): a cluster, crossover, randomized, controlled trial. *Intensive Care Med*. 2021;47:1248-1257.
36. Self WH, Evans CS, Jenkins CA, et al. Clinical effects of balanced crystalloids vs saline in adults with diabetic ketoacidosis: a subgroup analysis of cluster randomized clinical trials. *JAMA Netw Open*. 2020;3:e2024596.
37. Van Zyl DG, Rheeder P, Delport E. Fluid management in diabetic-acidosis - Ringer's lactate versus normal saline: a randomized controlled trial. *QJM*. 2012;105:337-343.
38. Dunger DB, Edge JA. Predicting cerebral edema during diabetic ketoacidosis. *N Eng J Med*. 2001;344:302-303.
39. Kuppermann N, Ghetti S, Schunk JE, et al. Clinical trial of fluid infusion rates for pediatric diabetic ketoacidosis. *N Eng J Med*. 2018;378:2275-2287.
40. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335-1343.
41. Joint British Diabetes Societies for Inpatient Care. The management of hyperosmolar hyperglycaemic state (HHS) in adults. 2022. Available from https://abcd.care/resource/management-hyperosmolar-hyperglycaemic-state-hhs. [Last accessed 11th October 2022].
42. Spanakis EK, Urrutia A, Galindo RJ, et al. Continuous glucose monitoring–guided insulin administration in hospitalized patients with diabetes: a randomized clinical trial. *Diabetes Care*. 2022;45:2369-2375.
43. Singh LG, Levitt DL, Satyarengga M, et al. Continuous glucose monitoring in general wards for prevention of hypoglycemia: results from the glucose telemetry system pilot study. *J Diabetes Sci Technol*. 2020;14:783-790.
44. Singh LG, Satyarengga M, Marcano I, et al. Reducing inpatient hypoglycemia in the general wards using real-time continuous glucose monitoring: the glucose telemetry system, a randomized clinical trial. *Diabetes Care*. 2020;43:2736-2743.
45. Umpierrez GE, Gianchandani R, Smiley D, et al. Safety and efficacy of sitagliptin therapy for the inpatient management of general medicine and surgery patients with type 2 diabetes: a pilot, randomized, controlled study. *Diabetes Care*. 2013;36:3430-3435.
46. Umpierrez GE, Smiley D, Jacobs S, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). *Diabetes Care*. 2011;34:256-261.
47. Umpierrez GE, Smiley D, Hermayer K, et al. Randomized study comparing a basal-bolus with a basal plus correction insulin regimen for the hospital management of medical and surgical patients with type 2 diabetes: basal plus trial. *Diabetes Care*. 2013;36:2169-2174.
48. Pasquel FJ, Gianchandani R, Rubin DJ, et al. Efficacy of sitagliptin for the hospital management of general medicine and surgery patients with type 2 diabetes (Sita-Hospital): a multicentre, prospective, open-label, non-inferiority randomised trial. *Lancet Diabetes Endocrinol*. 2017;5:125-133.
49. Vellanki P, Rasouli N, Baldwin D, et al. Glycaemic efficacy and safety of linagliptin compared to a basal-bolus insulin regimen in patients with type 2 diabetes undergoing non-cardiac surgery: a multicentre randomized clinical trial. *Diabetes Obes Metab*. 2019;21:837-843.
50. Pasquel FJ, Lansang MC, Dhatariya K, Umpierrez GE. Management of diabetes and hyperglycaemia in the hospital. *Lancet Diabetes Endocrinol*. 2021;9:174-188.
51. Colacci M, Fralick J, Odutayo A, Fralick M. SGLT2 inhibitors and the risk of diabetic ketoacidosis: a systematic review and meta-analysis. *Can J Diabetes*. 2022;26:10-15.
52. Heerspink HJ, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. *N Eng J Med*. 2020;383:1436-1446.
53. McMurray JJ, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Eng J Med*. 2019;381:1995-2008.
54. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Eng J Med*. 2015;373:2117-2128.
55. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Eng J Med*. 2017;377:644-657.
56. Koufakis T, Mustafa OG, Ajjan RA, et al. The use of sodium-glucose co-transporter 2 inhibitors in the inpatient setting: is the risk worth taking? *J Clin Pharm Ther*. 2020;45:883-891.
57. Kosiborod MN, Esterline R, Furtado RH, et al. Dapagliflozin in patients with cardiometabolic risk factors hospitalised with COVID-19 (DARE-19): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Diabetes Endocrinol*. 2021;9:586-594.
58. Khunti K, Aroda VR, Bhatt DL, et al. Re-examining the widespread policy of stopping SGLT2 inhibitors during acute illness: a perspective based on the updated evidence. *Diabetes Obes Metab*. 2022;24:2071-2080.
59. Dhatariya K. Initiation and continuation of sodium-glucose cotransporter 2 inhibitors in hospital inpatients – ready for prime time? *Diabetes Care*. 2023. https://doi.org/10.2337/dci22-0039.
60. Fayfman M, Galindo RJ, Rubin DJ, et al. A randomized controlled trial on the safety and efficacy of exenatide therapy for the inpatient management of general medicine and surgery patients with type 2 diabetes. *Diabetes Care*. 2019;42:450-456.
61. Polderman JA, van Steen SC, Thiel B, et al. Peri-operative management of patients with type-2 diabetes mellitus undergoing non-cardiac surgery using liraglutide, glucose-insulin-potassium infusion or intravenous insulin bolus regimens: a randomised controlled trial. *Anaesthesia*. 2018;73:332-339.
62. Fushimi N, Shibuya T, Yoshida Y, Ito S, Hachiya H, Mori A. Dulaglutide-combined basal plus correction insulin therapy contributes to ideal glycemic control in non-critical hospitalized patients. *J Diabetes Invest*. 2020;11:125-131.
63. Royal College of Physicians of London. National Early Warning Score (NEWS) 2. 2017. Available from https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2. [Last accessed 11th October 2022].
64. Pankhurst T, Sapey E, Gyves H, et al. Are current NEWS2 clinical response thresholds optimised for a general in-patient population? *medRxiv*. 2020. 2020.2009.2012.20136804.
65. Fortmann AL, Spierling Bagsic SR, Talavera L, et al. Glucose as the fifth vital sign: a randomized controlled trial of continuous

glucose monitoring in a non-ICU hospital setting. *Diabetes Care*. 2020;43:2873-2877.
66. Cheung NW, Napier B, Zaccaria C, Fletcher JP. Hyperglycemia is associated with adverse outcomes in patients receiving total parenteral nutrition. *Diabetes Care*. 2005;28:2367-2371.
67. Boughton CK, Bally L, Martignoni F, et al. Fully closed-loop insulin delivery in inpatients receiving nutritional support: a two-Centre, open-label, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2019;7:368-377.
68. Umpierrez GE, Cardona S, Chachkhiani D, et al. A randomized controlled study comparing a DPP4 inhibitor (linagliptin) and basal insulin (glargine) in patients with type 2 diabetes in long-term care and skilled nursing facilities: linagliptin-LTC trial. *J Am Med Dir Assoc*. 2018;19:399-404.e393.
69. Pasquel FJ, Powell W, Peng L, et al. A randomized controlled trial comparing treatment with oral agents and basal insulin in elderly patients with type 2 diabetes in long-term care facilities. *BMJ Open Diabetes Res Care*. 2015;3:e000104.
70. Holt RI. Diagnosis, epidemiology and pathogenesis of diabetes mellitus: an update for psychiatrists. *Br J Psychiatry*. 2004;184:s55-s63.
71. Polcwiartek C, Vang T, Bruhn CH, Hashemi N, Rosenzweig M, Nielsen J. Diabetic ketoacidosis in patients exposed to antipsychotics: a systematic literature review and analysis of Danish adverse drug event reports. *Psychopharmacology (Berl)*. 2016;233:3663-3672.
72. Joint British Diabetes Societies for Inpatient Care. The management of diabetes in adults and children with psychiatric disorders in inpatient settings. 2017. Available from https://abcd.care/resource/jbds-13-management-diabetes-adults-and-children-psychiatric-disorders-inpatient-settings. [Last accessed 11th October 2022].
73. Hovorka R, Kumareswaran K, Harris J, et al. Overnight closed loop insulin delivery (artificial pancreas) in adults with type 1 diabetes: crossover randomised controlled studies. *BMJ*. 2011;342:d1855.
74. Tauschmann M, Thabit H, Bally L, et al. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. *Lancet*. 2018;392:1321-1329.
75. Davis GM, Spanakis EK, Migdal AL, et al. Accuracy of Dexcom G6 continuous glucose monitoring in non–critically ill hospitalized patients with diabetes. *Diabetes Care*. 2021;44:1641-1646.
76. Galindo RJ, Migdal AL, Davis GM, et al. Comparison of the FreeStyle libre pro flash continuous glucose monitoring (CGM) system and point-of-care capillary glucose testing (POC) in hospitalized patients with type 2 diabetes (T2D) treated with basal-bolus insulin regimen. *Diabetes Care*. 2020;43:2730-2735.
77. Dhatariya KK. On behalf of the joint British diabetes societies for inpatient care. The management of diabetic ketoacidosis in adults—an updated guideline from the joint British diabetes Society for Inpatient Care. *Diabet Med*. 2022;39:e14788.
78. 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. *Diabet Med*. 2006;23:1008-1015.
79. Flanagan D, Moore E, Baker S, Wright D, Lynch P. Diabetes care in hospital - the impact of a dedicated inpatient care team. *Diabet Med*. 2008;25:147-151.
80. Nguyen KT, Xu NY, Zhang JY, et al. Continuous ketone monitoring consensus report 2021. *J Diabetes Sci Technol*. 2022;16:689-715.
81. National Institute for Haelth and Care Excellence. Type 2 diabetes in adults: management. NICE guideline [NG28]. 2022. Available from https://www.nice.org.uk/guidance/ng28. [Last accessed 11th October 2022].
82. Tripyla A, Herzig D, Joachim D, et al. Performance of a factory-calibrated, real-time continuous glucose monitoring system during elective abdominal surgery. *Diabetes Obes Metab*. 2020;22:1678-1682.
83. Frisch A, Chandra P, Smiley D, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care*. 2010;33:1783-1788.
84. Kotagal M, Symons RG, Hirsch IB, et al. Perioperative hyperglycemia and risk of adverse events among patients with and without diabetes. *Ann Surg*. 2016;261:97-103.
85. Kwon S, Thompson R, Dellinger P, Yanez D, Farrohki E, Flum D. Importance of perioperative glycemic control in general surgery: a report from the surgical care and outcomes assessment program. *Ann Surg*. 2013;257:8-14.
86. Rushakoff RJ, Sullivan MM, MacMaster H, et al. Association between a virtual glucose management service and glycemic control in hospitalized adult patients: an observational study. *Ann Intern Med*. 2017;166:621-627.
87. Sheen YJ, Huang CC, Huang SC, et al. Implimentation of an electronic dashboard with a remote management system to improve glycemic management among hospitalized adults. *Endocr Pract*. 2020;26:179-191.
88. Cheung NW, Hor A, Hng T-M. The virtual inpatient diabetes management service: COVID-19 brings the future to inpatient diabetes management. *Med J Australia*. 2022;216:321-322.
89. Judson TJ, Mourad M, Wachter RM. Building a targeted automatic e-consult (TACo) program. *Jt Comm J Qual Patient Saf*. 2022;48:114-119.
90. Vilendrer S, Sackeyfio S, Akinbami E, et al. Patient perspectives of inpatient telemedicine during the COVID-19 pandemic: qualitative assessment. *JMIR Form Res*. 2022;6:e32933.
91. Diabetes UK. New glucose monitoring technologies in inpatient care highlight notice (2020). 2020. Available from https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/public/2021-01/Highlight%20Notice%20-%20new%20glucose%20monitoring%20tech%20in%20inpatient%20care.pdf. [Last accessed 11th October 2022].
92. Rutter CL, Jones C, Dhatariya KK, et al. Determining in-patient diabetes treatment satisfaction in the UK—the DIPSat study. *Diabet Med*. 2013;30:731-738.
93. Royal College of Physicians of London. Diabetes Care Accreditation Programme (DCAP). 2022. Available from https://www.dcap.org.uk/. [Last accessed 11th October 2022].
94. 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;32:1119-1131.
95. Qaseem A, Humphrey LL, Chou R, Snow V, Shekelle P, Clinical Guidelines Committee of the American College of Physicians. Use of intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2011;154:260-267.
96. McMahon MM, Nystrom E, Braunschweig C, Miles J, Compher C, et al. A.S.P.E.N. clinical guidelines: nutrition support of

adult patients with hyperglycemia. *J Parenter Enteral Nutr*. 2013;37:23-36.

97. Wang B, Wukich DK, Sambandam S. Complications from ankle arthrodesis in diabetes-related Charcot foot syndrome. *J Diabetes Complications*. 2021;35:108071.
98. Joshi GP, Chung F, Vann MA, et al. Society for Ambulatory Anesthesia consensus statement on perioperative blood glucose management in diabetic patients undergoing ambulatory surgery. *Anesth Analg*. 2010;111:1378-1387.

How to cite this article: Dhatariya KK, Umpierrez G. Gaps in our knowledge of managing inpatient dysglycaemia and diabetes in non-critically ill adults: A call for further research. *Diabet Med*. 2022;00:e14980. doi: 10.1111/dme.14980