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Evidence Check

Inpatient Insulin Management

An **Evidence Check** rapid review brokered by the Sax Institute for the NSW Agency for Clinical Innovation. October 2016.

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This report was prepared by:

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March 2017

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Suggested Citation:

Wong V, Lai J, Inpatient Insulin Management: an Evidence Check rapid review brokered by the Sax Institute (www.saxinstitute.org.au) for the NSW Agency for Clinical Innovation, 2016.

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Contents

Glossary of terms

ADS	Australia Diabetes Society
BBB	Basal-bolus-booster
BGL	Blood glucose level
CGM	Continuous glucose monitoring
DISN	Diabetes inpatient specialist nurse service
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
ED	Emergency department
GCT	Glycaemic control team
HbA1c	Glycosylated haemoglobin
ISS	Insulin sliding scale
JMO	Junior medical officer
LOS	Length of stay
NSW	New South Wales
POC	Point of care
UK	United Kingdom
USA	United States of America

1 Executive summary

The objective of this Evidence Check is to assess the evidence on approaches to improve the management of diabetes in an acute inpatient hospital setting. The focus is on the role of subcutaneous insulin inpatient management.

The Evidence Check involved a detailed search of peer-reviewed literature, an internet grey literature search, material obtained through authors who have published in this area and guidelines from the Australian Diabetes Society.

Question 1: What are the critical components of best practice insulin management for adult patients admitted to acute hospitals with a primary or secondary diagnosis of diabetes (requiring insulin)?

- The critical components of best practice insulin management for adult patients with inpatient hyperglycaemia requiring insulin therapy are:
    1) The recognition of abnormal blood glucose level (BGL) at the earliest point of a patient's admission
    2) Appropriate triaging and management of their hyperglycaemia and/or hypoglycaemia
    3) Transitioning their management from inpatient care to outpatient/community care
    4) A current system of feedback/auditing of the system for management of inpatient hyperglycaemia.
- Early recognition of hyperglycaemia requires early testing of BGL. The first point of contact with the acute healthcare system is typically through the emergency department. Implementation of BGL as a sixth vital sign (as part of routine inpatient monitoring) would ensure that all patients have a frequent assessment of their blood sugar level. Blood glucose level should be assessed in all patients admitted to hospital. Earlier detection enables earlier implementation of glycaemic control strategies, which translates to fewer complications and, in general, decreased lengths of stay for the health system. If the admission glucose level is elevated, regular BGL monitoring should be continued even if the patient is not known to have diabetes.
- An HbA1c test would be a useful tool to predict inpatient hyperglycaemia and the need for glycaemic management and ongoing post-discharge follow up.
- Education is the cornerstone of best practice insulin management for adult inpatients with hyperglycaemia. The key points are:
    - Most junior medical staff are not confident in initiating insulin therapy in insulin-naïve patients
    - There is a significant need to phase out insulin sliding scale (ISS) as an insulin regimen and encourage the use of basal-bolus-booster (BBB)
    - Electronic insulin dosing decision aids are an effective and safe tool in supporting junior medical officers to prescribe insulin.
- Use of standardised insulin charts is effective in reducing insulin-related prescribing errors.
- Established protocols, including weight-based algorithms are an effective and safe tool if used correctly by medical and nursing staff.
- Inpatient interdisciplinary glucose control teams are a valuable means for staff members to seek assistance and to improve glycaemic control for inpatients. The presence of a glucose control team

establishes a direct referral pathway for non-Endocrinology teams to access advice regarding inpatient hyperglycaemia. GCTs may also be a vehicle to educate and empower nursing and medical staff regarding diabetes management.

- Nursing staff can be empowered to improve postprandial hyperglycaemia through a streamlined approach to meal delivery and timely administration of mealtime insulin.

Question 2: What process and patient health outcomes have been recorded as a result of adopting best practice strategies?

- Adopting best practice strategies has results in improved reduced mean blood glucose levels for patients, reduced hypoglycaemic episodes and reduced rates of complications.
- Patients also have a reduced length of stay, which may translate into cost-saving mechanisms for the hospital.
- Improvement of a patient's glycaemic control during their admission may translate into better BGLs in the community after discharge. This may reduce early readmission into the healthcare system.

Question 3: For all articles reviewed to answer Question 1 and 2, extract recommendations and commentary on the enablers of successful implementation of best practice components of inpatient insulin management.

- Recognising the significance of hyperglycaemia and introducing regular BGL measurements as a sixth vital sign, which is also subjected to "Clinical Reviews".
- Engaging the emergency department in measuring blood glucose levels regularly and implementing early management according to a protocol or referring to the relevant specialties.
- The use of HbA1c is very effect in triaging patients who are at risk of inpatient hyperglycaemia, and who would benefit from detailed glycaemic review prior to transitioning to community-based care. At the very least, HbA1c should be measured in all patients with known diabetes, or patients without known diabetes but had elevated admission glucose levels.
- Development of an educational package for registered nurses and junior medical officers is critical in teaching them about the hospital diabetes protocols, teaching them about the different types of insulin and regimens of insulin delivery.
- State-wide accessibility and purchase of electronic glycaemic management software (as a decision-making aid).
- Ongoing education for nursing and medical staff regarding the NSW health subcutaneous insulin chart – in particular, emphasising BBB regimen rather than ISS, and encouraging the use of supplemental short acting insulin.
- Consideration of establishing an inpatient glucose management team that will case-find patients with unstable glycaemic control and provide support for medical and nursing staff.
- Establish insulin initiation protocols using safe and effective weight-based algorithms.
- Emphasis on optimal glucose testing and timely administration of insulin therapy (in co-ordination with meal delivery).
- Developing a framework to allow safe transition of patients on insulin therapy from hospital to community.
- Developing a system that enables implementation of strategies to be actively reviewed, so valuable feedback and audit data can be used to improve current mechanism.

2 Background

There is an increasing prevalence of people with diabetes mellitus (DM) in our community. Consequently, more people who are admitted to hospital also have DM. With acute infections and stress associated with acute illness, people with diabetes mellitus requiring hospitalisation typically have an elevation of their blood glucose levels, resulting in 'inpatient hyperglycaemia'. On the other hand, patients may also be at risk of hypoglycaemia in hospital as a result of prolonged periods of fasting and reduced oral intake.

Patients who have suboptimal glycaemic control have been demonstrated to have poorer health outcomes and longer lengths of stay (LOS) compared to patients who have adequate glycaemic control. Patients with hyperglycaemia are at higher risk of infection, and have poorer wound healing and a poorer immune response, to name a few. Managing glycaemic control in patients with DM has become a major challenge for clinicians working in hospitals.

In accordance with the recommendations from the Australian Diabetes Society (ADS) on glucose management in hospital, the target blood glucose range for patients during an inpatient admission in non-critical care wards should be between 5-10mmol/L.[1] Previous studies have shown that tighter glycaemic targets, below 5-10mmol/L, increases mortality in the critical care setting.

In 2013, NSW Health introduced a standardised subcutaneous insulin prescribing chart, which has been rolled out to all NSW Health hospitals. The structure of the standardised subcutaneous insulin chart is based on the regimen, known has the 'basal-bolus-booster'. Unfortunately, a review in four Local Health Districts demonstrates a "lack of awareness and understanding about components of current best practice in the management of diabetes patients in a hospital setting outside of specialist endocrinology units". Hence this Evidence Check examines the existing evidence for strategies towards improving inpatient hyperglycaemia.

The specific questions to be answered by the Evidence Check, as identified by the NSW Diabetes Taskforce from the Agency for Clinical Innovation (ACI), are:

- Question 1: What are the critical components of best practice insulin management for adult patients admitted to acute hospitals with a primary or secondary diagnosis of diabetes (requiring insulin)?
- Question 2: What process and patient health outcomes have been recorded as a result of adopting best practice strategies?
- Question 3: For all articles reviewed to answer Question1 and 2, extract recommendations and commentary on the enablers of successful implementation of best practice components of inpatient insulin management.

3 Methods

The background research for the Evidence Check questions were conducted through three search strategies:

1) Systemic review of the peer-reviewed literature
2) Systematic and targeted internet search (via Google)
3) Request for information from professional organisations and individuals from Australian State and Territories who are known to have published in the field of inpatient hyperglycaemia.

The search strategies were supplemented by a review of the reference lists of identified documents for additional reports and studies, not previously identified by the authors.

Systematic review of the peer-reviewed literature

Databases searched

The following electronic databases were searched: MEDLINE (1946); Embase (1947); PubMed (1996); Cochrane Library (1993); and CINAHL (1937).

Study eligibility criteria

Published studies were eligible for inclusion if they fulfilled the following criteria:

- Written in English
- Published from January 2006 to January 2017
- Conducted in an inpatient setting in an acute or sub-acute hospital/medical institution. Studies for which the setting was unclear or were predominantly non-hospital based were excluded
- The focus of the Evidence Check is on patients in a ward inpatient setting – patients in critical care, intensive care or high dependency units were excluded
- Described the results of at least one practice change strategy to improve the management of inpatient hyperglycaemia, and not only measured the clinical outcomes of improved glycaemic control in patients admitted into hospital
- Involved studies that included the use of multiple daily doses of subcutaneous insulin; consequently intravenous insulin, insulin infusions and continuous subcutaneous insulin infusions were excluded
- Studies were included regardless of the level or quality of evidence – evidence reviewed included conference papers/abstracts, case reports, observational studies, cohort studies, randomised control trials or policies/guidelines from professional bodies
- Studies focusing on paediatric populations and gestational diabetes or pregnant women with pre-existing diabetes (type 1 or type 2 diabetes) were excluded.

Review of evidence was limited to studies from Australia, UK, US, Canada and New Zealand. However, some exceptions were made for valuable evidence published in English from other European countries (e.g. Austria).

In addition to the above studies related to management of inpatient hyperglycaemia, supplemental evidence was also provided in the Evidence Check in regards to referral pathways, transfers between parts of the hospital and discharge planning.

Study selection/screening

Following the removal of duplicate articles, one author independently screened and reviewed the titles and abstracts of all identified studies for inclusion in the review. The full articles of the identified studies were subsequently reviewed. Both authors independently reviewed the short-listed articles and compiled the final list of studies to be included in the review. The full articles were reviewed and the evidence extracted. Both authors reviewed the titles and abstracts of the articles to be included in the review. The reviewers were not blinded to any information pertaining to the authors or the institutions to which the authors were affiliated. Data for each study was extracted independently by one author and reviewed independently by the second author.

Internet search for grey literature

Google and Google Scholar were used to identify grey literature studies and reports. The search terms used were "inpatient hyperglycaemia and insulin management".

The first 50 articles identified were reviewed and identified, if not previously identified via the peer-reviewed literature search.

Information from Australian and New Zealand health jurisdiction

Professional bodies and authors in this review group who had previously published or consulted in the field of inpatient hyperglycaemia were contacted. The Australian Diabetes Society (ADS) provided a document from 2012 titled *"ADS Guidelines for Routine Glucose Control in Hospital"*.

Review limitations

A comprehensive literature search was carried out for this Evidence Check. It is likely that some reports, studies or data may not have been identified and reviewed in the process. This may be due to:

- Inability to access unpublished data
- Differences in the definitions and terms used by individuals reports, studies or articles
- Reliance on best practice and jurisdictional information accessible via the internet and through library resources (hospital and university resources).

4 Findings

Question 1: What are the critical components of best practice insulin management for adult patients admitted to acute hospitals with a primary to secondary diagnosis of diabetes (requiring insulin)?

The critical components of best practice insulin management for adult patients in the hospital system include:

1) The recognition of abnormal BGLs at the earliest point of their admission
2) Appropriate triaging and management of hypoglycaemia and hyperglycaemia
3) Transitioning their management from inpatient care to outpatient/community care
4) A current system of feedback/auditing of the system for management of inpatient hyperglycaemia.

The recognition of abnormal blood glucose levels at the earliest point of a patient's admission

Recognition of patients who are at risk of unstable blood glucose level (BGL) at the earliest point of their admission is the first step towards optimising their blood glucose levels. This may simply be recognition of a patient who has a known history of type 1 or type 2 diabetes through medical history or analysis of their medication list by the medical officer. Or alternatively, introducing blood glucose monitoring as a routine parameter – specifically, as a sixth vital sign.[2]

In a study carried out in a USA emergency department, it was demonstrated that hyperglycaemia in admitted patients was often overlooked.[3] Their retrospective cohort study demonstrated that in a one-year period, of the 27,688 blood glucose readings measured in the emergency department, 3517 (13%) were 7.8-11mmol/L, and 2304 (8%) values were $\geq$11.1mmol/L. From these charts, 385 patient charts were randomly sampled for further analysis. In a subset of patients, of the 194 patients with BGLs between 7.8-11mmol/L, 107 (55%) were not known to have diabetes, while 31 out of 191 patients with BGL $\geq$11.1mmol/L (16%) did not have, a previous diagnosis of diabetes mellitus. Only 61 (16%) patients received insulin in the emergency department for their hyperglycaemia. Rendell et al, have proposed that BGLs should be considered part of routine vital sign monitoring to highlight its clinical significance.[2] With the increasing burden of diabetes and the detrimental outcomes of hyperglycaemia and hypoglycaemia, this recognition would ensure more BGL measurements. The recognition of hyperglycaemia in a proactive environment would hopefully translate to the management of a patient's blood glucose levels and the use of appropriate resources to do so. Currently there are no recommendations as to how often BGLs need to be monitored in emergency departments or in the non-critical care wards.

Two conference posters examined the association between HbA1c at the time of admission and glycaemic status among inpatients.[4, 5] The studies which recruited 211 and 296 patients respectively demonstrated that an admission HbA1c $\geq$ 7% was predictive of inpatient hyperglycaemia, but no correlation was found with increased length of stay (LOS) or hospital complications. To date, there is no study looking at the cost benefit of performing HbA1c on all patients admitted to hospital. It may be appropriate to perform HbA1c on all patients with known diabetes or those with admission hyperglycaemia (that is, glucose levels exceeding 7.8mmol/L).

Appropriate triaging and management of their hyperglycaemia and hypoglycaemia

Most of the evidence in the management of inpatient hyperglycaemia is related to the education and clinical practices of medical officers and allied health staff. The decision to initiate insulin therapy or adjust insulin regimen in response to unstable BGLs is critical in improving glycaemic control among inpatients.

The recognition of abnormal BGLs and prescription of insulin therapy is typically within the responsibilities of junior medical officers (JMOs) within a public hospital system. However, results of two audits, published as conference abstract papers demonstrated that the knowledge and confidence of British JMOs in prescribing and initiating insulin was inadequate. Gouveia et al, found that within a group of 30 JMOs, ≤ 50% doctors could identify the key biochemical features of diabetic ketoacidosis (DKA); recognised the significance of serum ketones in DKA and could correctly interpret an inpatient blood capillary glucose chart. Fewer than 60% of doctors recognised the difference between short-acting and long-acting insuli.[6] In another study, Zaidi et al, that more than two-thirds of junior doctors were not confident in initiating insulin therapy in an insulin-naïve patient without supervision and all felt the need for further training.[7] The lack of confidence in prescribing insulin was also supported by a study carried out by Cheekati et al.[8]

Furthermore, in a study by Arif et al in the USA, they demonstrated that uptake and utilisation of a new standardised subcutaneous insulin chart only improved with repeated and proactive education for all staff.[9] Prior to the introduction of the chart, an initial eight-week period was used to educate all hospital staff regarding the changes. Physicians were informed via a letter from the chairman of the Department of Medicine and established mandatory training programs for pharmacist and nursing staff members were implemented. The use of the basal, bolus and correction (booster) components of the insulin chart was only at 9%. A second educational pilot was then carried out hospital-wide, which improved full use of the subcutaneous chart to 12%. This illustrates that continued education regarding the adverse outcomes of hyperglycaemia and ongoing upskilling of all staff members is needed to manage elevated blood glucose levels in the hospital setting.

Prescribing errors involving insulin therapy had been a major problem in hospitals. Poor documentation of the insulin dose (for example, confusion over "u" and "0" leading to the administration of 10 times the prescribed dose), constant re-writing of insulin order when the insulin doses were adjusted, and easy omission of insulin doses (not recognised by the team) are some of the common problems encountered. As a result, a standardised subcutaneous insulin ordering set has been developed with the intention of improving insulin prescription and minimising error. This subcutaneous insulin set is similar to the current NSW Health Subcutaneous Insulin Charts, which have been implemented prior to this Evidence Check. Some recommendations have been made to include the preprandial and bedtime blood glucose targets to assist JMOs when prescribing a dose of insulin.

Computerised or online software (such as GlucoTab) may be considered to assist medical staff as a decision-making tool when prescribing insulin for patients with type 2 diabetes mellitus.[10] The use of decision-aiding tools, should also help phase out the use of 'Insulin Sliding Scale' (ISS) and encourage the use of 'Basal-Bolus-Booster' (BBB) regimens. Studies have shown that patients who are prescribed ISS have higher complications in hospital, a higher number of hypoglycaemic events and higher glycaemic variability when compared to the traditional basal-bolus regimen, or the new BBB regimen.[11, 12] The use of basal-bolus insulin, rather than ISS was also associated with significantly lower complications, ICU admissions and lower resource use and hospital costs.[13]

Glycaemic control teams (GCTs) are inpatient interdisciplinary teams consisting of endocrinologist/hospitalist, clinical nurse specialists/nurse practitioners, pharmacists and dieticians. In the study by Rodriguez et al, they reviewed the role of GCTs in 20 hospitals in the USA and looked at the best practice strategies for these teams to improve blood glucose levels in a hospital system.[14] In addition to the involvement of interdisciplinary members mentioned above, some other key members included quality improvement staff members, informatics specialists, graduate trainees (i.e. residents, interns or endocrine fellows), surgeons and anaesthesiologists may also contribute to the improvement in glycaemic control among inpatients. The best practice findings found that these GCTs operated throughout the hospital in

non-critical care and critical care units. They provided direct evaluation and medical management recommendations. The referral pathways to access the GCTs were:

1) Direct requests for consultation from the primary inpatient team
2) From nursing staff
3) Due to pre-specified high- or low-glucose triggers that prompted calls to the primary team to provide suggestions
4) Patient requests and referrals from ancillary personnel.

These GCTs also provided diabetes self-management education. The referral pathway for patients to access diabetes education was in response to pre-specified glycaemic triggers, or directly from nursing staff, providers or patients.

There are also special populations within the hospital, who are particularly susceptible to hyperglycaemia; specifically, these include patients receiving enteral or parenteral feeding and those on glucocorticoid therapy, patients with renal disease and the geriatric population. Hyperglycaemia in patients on enteral or parenteral feeding can be managed by either adjustment of the carbohydrate content of the feeds in discussion with a dietician or use of pharmacological therapy to lower blood glucose levels. In patients on glucocorticoid therapy, the impact of blood glucose levels may be influenced by the type of glucocorticoid, the dose, the timing of glucocorticoid administration and the presence or absence of pre-existing diabetes mellitus/impaired glucose tolerance.[15]

Studies have also been taken to adjust the timing of hospital meal-deliveries so that patients received their short-acting insulin within 30 minutes of their meal. Engle et al implemented a process of streamlining blood glucose monitoring, with meal delivery and insulin administration.[16] The nursing staff was given the opportunity to assess the expected carbohydrate intake and administer correction insulin doses if required.

With the increasing availability of technology in managing of diabetes mellitus, Gomez and Umpierrez examined the role of continuous glucose monitoring (CGM) versus point of care (POC) blood sugar testing in a non-critical care testing.[17] CGM sensors create a pattern of blood sugar patterns by measuring blood glucose levels in subcutaneous interstitial fluid every 5–10 minutes over 24 hours, while POC testing requires a manual finger prick, traditionally four times a day to obtain BGL readings. The use of CGM in patients admitted to hospital is currently limited due to lack of large-scale studies, but also financial limitations due to the high costs of the sensors. Some also have concerns regarding the absolute accuracy of the sensor monitors, as there is an acceptable 20% variability in the accuracy of the BGL readings. However, the opinion is that by having CGM, the information from 24-hour blood glucose patterns detects more hypoglycaemic events and allows tightening of glycaemic control.

Transitioning their glycaemic control from inpatient care to outpatient/community care

According to the best practice review by Rodriguez et al for hospital medical teams, 80% of respondents did not feel that there was reliable access to outpatient diabetes education and clinics for ongoing management of inpatients with hyperglycaemia.[14] Even though the majority of hospitals had post-discharge referrals in place available for patients and medical staff, only a quarter had a written protocol to standardise access to these resources. There was particular difficulty accessing these resources on the weekend since there were no specialist services to support the transition of patients' glycaemic control from an inpatient to outpatient service. Consequently, ensuring a clear and accessible system in transitioning a patient on insulin therapy from inpatient care to community-based care encourages a smooth flow of patient through the healthcare system. There are only few studies in the literature that examined the best process for the safe transition of these patients from hospital to community.

A current system of feedback/auditing of the system for management of inpatient hyperglycaemia

The introduction of any clinical management system requires ongoing auditing, feedback and strong leadership to oversee the running of a program. Furthermore, the foundation for any quality improvement project also depends on the availability of valid and up-to-date policies, consistent with best practice. Within the leadership, there also needs to be mechanisms to provide ongoing education for all JMOs, nursing and allied health staff. Recognition of improvements and implementation of quality assurance projects in particular wards or sections of the hospital would foster a positive atmosphere.

Question 2: What process and patient health outcomes have been recorded as a result of adopting best practice strategies?

The recognition of hyperglycaemia at the earliest point of a patient's admission

Early recognition and management of abnormal glucose level is the first step towards blood glucose control. In a study carried out by Munoz et al, a subcutaneous insulin protocol was introduced in their emergency department (ED) at Rush University Medical Center.[18] Patients with a BGL $\geq$ 11.1mmol/L were treated with subcutaneous insulin aspart (Novorapid®) every two hours until BGLs was < 11.1mmol/L. Patients in hyperglycaemic emergencies, such as diabetes ketoacidosis or hyperglycaemic hyperosmolar state were excluded. When the outcomes of 54 control (non-protocol) patients were compared to 54 interventional (protocol-following) patients, proactive management of hyperglycaemia reduced in a significant improvement of BGLs and reduced mean hospital length of stay. In the control group, the mean BGL on admission to ED was 17.8$\pm$6.9mmol/L and on discharge was 13.4$\pm$4.3mmol/L ($p<0.001$), while in the intervention group there was larger BGL decline from 18.4$\pm$5.7mmol/L to 8.7$\pm$3.7mmol/L. More patients who initially presented to the ED from the intervention group (69%) were admitted than the control group (67%). However, the mean length of stay in hospital was significantly less in the intervention group, 3.8$\pm$3.3 days, when compared to the control group 5.3$\pm$4.1 days ($p<0.05$). Consequently, as suggested by Rendell et al, the future of inpatient diabetes management lies in the recognition of its clinical significance. Hence, they have suggested that BGLs should be considered a sixth vital sign.

A novel concept introduced by Roberts et al, is relative hyperglycaemia or 'stress hyperglycaemia ratio' in critically ill patients who are admitted into hospital. Stress hyperglycaemia ratio was defined as *"admission glucose divided by estimated average glucose derived from glycosylated haemoglobin"*.[19] This ratio was used to determine if a patient's elevated BGLs in hospital was due to chronic poor diabetes control or a transient stress response. The higher the stress hyperglycaemia ratio, the higher the physiological stress and acute illness of a patient. Subsequently, rather than simply identifying patients with absolute hyperglycaemia, stress hyperglycaemic ratio may recognise those who had a higher risk for critical illness. This is an interesting concept, which may assist in triaging critically unwell patients with hyperglycaemia. Further studies will need to be carried out to validate the utility of this entity.

Appropriate triaging and management of their hyperglycaemia and hypoglycaemia

a) Basal-bolus-booster versus insulin sliding scale

Management of inpatient hyperglycaemia has been overwhelmed with evidence demonstrating that that the newer concept of basal-bolus-booster (BBB) regimen is superior to the historical insulin sliding scale (ISS) in terms of glycaemic control and lower complication rates.[11] The Rabbit-2 Surgery study showed that target glycaemic control was achieved in 66% of patients on BBB, as opposed to 38% in the ISS. In calculating the BBB regimen, patients were commenced on 0.4 units/kg for blood glucose concentration between 7.7 – 11.0mmol/L or 0.5 units/kg for those between 11.1 – 22.2mmol/L. One half of the total daily insulin was given as long-acting, while the remaining half was divided into three equal doses to cover

mealtime blood glucose rise. Additional correctional insulin was given four times a day with meals or at bedtime if BGLs ≥ 10mmol/L. The admission blood glucose level for the BBB group was 12.7±3.9mmol/L, while for the ISS group it was 12.4±3.3mmol/L. However, after commencing the two insulin regimens, the mean BGL during hospital admission was markedly lower in the BBB group at 9.2±1.7mmol/L as compared with the ISS group at 10.7±2.9mmol/L. In addition to the clinical benefits of BBB, a post-hoc analysis of the Rabbit-2 Surgery study also demonstrates financial benefits. The financial impact of ISS was higher at USD$26.8±15.9K, while the BBB regimen had a lower cost burden at USD$23.0±12.0K.[13]

Following the results of this study, a Sydney-based hospital has developed a BBB regimen, based on the protocol used in the Rabbit-2 Surgery Study.[20] This BBB was implemented in insulin-naïve hospital patients who had elevated glucose levels. The BBB regimen was a weight-based algorithm that prescribed insulin glargine (Lantus®) at 0.2 units/kg/day for type 1 diabetes patients and cardiac patients or 0.25 units/kg/per day for other patients with diabetes mellitus in the evening. The bolus insulin (insulin aspart or insulin lispro) was given in three equally divided doses at 0.2 – 0.25 units/kg/day. The short-acting insulin was withheld if the patient was nil by mouth. Booster insulin (insulin aspart or lispro) was added in addition to the pre-meal short-acting insulin dose if the patient was hyperglycaemic prior to eating. Patients were continued on their oral hypoglycaemic agents if appropriate. The protocol was taught and implemented by nursing and JMOs. When comparing the outcomes of the BBB and the ISS group (a historical control group), the mean BGL was lower at 11.2 ± 2.6mmol/L vs 13.6 ± 2.4 mmol/L respectively *(p<0.0001)*. The number of BGL ≥ 15mmol/L events were also less in the BBB group. In another Australian Study by Roberts et al, they compared the outcomes of basal-bolus insulin against ISS.[21] The mean BGLs in the basal-bolus group remained significantly lower than the ISS group by 1.6 – 2.4mmol/L through the study *(p<0.001)*.

b) Use of a standardised insulin prescribing chart

Despite these benefits of BBB, ISS is still prevalent in NSW hospital setting in managing hyperglycaemia.[22] However, with the introduction of the standardised insulin charts, the use of ISS has reduced. Similar to other international structured ordering sets, the NSW subcutaneous insulin chart has been introduced to ensure that patients receive the insulin that they are prescribed, to reduce the number of missed insulin doses, to reduce prescribing errors and to improve glycaemic control. In an Australian audit carried out by Wong et al, the glycaemic control and insulin charts in the first week of July 2014 (pre-standardised NSW Health insulin chart) was compared with that the first week of July 2015 (post-introductions of NSW Health insulin charts). The improvements in glycaemic control after the introduction of the NSW subcutaneous insulin chart are demonstrated below:

	July 2014 (PRE-chart)	**July 2015 (POST-chart)**	***P-Value***
Mean BGL for each subject (mmol/L ± SD)	10.4 ± 2.6	9.4 ±2.0	0.021
Pooled data, % of BGL readings > 10mmol/L	44.7%	34.9%	<0.001
Pooled data, % of BGL readings > 15mmol/L	15.0%	9.7%	<0.001
Pooled data, % of BGL readings > 20mmol/L	3.6%	1.3%	<0.001

Pooled data, % of BGL readings < 4mmol/L	2.4%	1.9%	0.292
Pooled data, % of BGL readings 5-10mmol/L	48.1%	55.2%	<0.001
Pooled data, BGL readings missed	11.6%	9.1%	0.032

The improvements in proactive prescribing habits after introduction of the NSW subcutaneous insulin chart are demonstrated below:

	July 2014 (PRE-chart)	**July 2015 (POST-chart)**	***P-Value***
Sliding scale insulin as sole therapy	16.7%	3.2%	0.014
Patients whose insulin dose was adjusted during audit week	42.6%	71.0%	0.002
Patients with 10% of BGL above 15mmol/L and had insulin dose adjusted	53.3%	80.8%	0.047
Patients with mean BGL >10mmol/L during audit week and had dose adjusted	50.0%	78.3%	0.036
Mean number of insulin dose adjustments per patient during the audit week	1.2 $\pm$ 1.7	3.2 $\pm$3.0	<0.001
Patients with supplemental (booster) insulin charted	24.1%	54.8%	<0.001
Patients with insulin doses missed without documented reason	40.7%	43.6%	0.763

In another hospital in Sydney, some improvements in glycaemic control with the implementation of a local subcutaneous insulin chart were also seen. In an audit carried out by Cheung et al, they implemented a locally designed insulin chart, prior to the roll out of the NSW Health subcutaneous chart.[23] In terms of the whole population, the number of BGLs < 4mmol/L was significantly lower after introduction of the chart (5.2% in the pre-chart group, compared with 3.4% in the post-chart group). Furthermore, the proportion of BGLs within the normal range (BGLs 4 – 9.9mmol/L) were also significantly higher (51.8% pre-chart vs 54.1% post-chart, *p=0.01*).

In Queensland, McIver et al, introduced two standardised insulin charts – a subcutaneous chart and an intravenous chart.[24] The introduction of these charts aimed to improve insulin management without adversely worsening glycaemic control. The design of the chart also aimed to encourage safe prescribing and insulin administration. Like the NSW Health subcutaneous chart, the QLD Health subcutaneous chart also follows a similar structure to basal-bolus-booster concept. Prior to the introduction of the charts, routine subcutaneous insulin was prescribed 75.6%, as compared to 85.7% post-implementation of charts *(p value = not significant)*. There was a trend towards a decrease in the use of subcutaneous insulin sliding scale reduced after introduction of the charts from 22.2% to 16.3%, while the use of supplemental insulin significantly increased from 4.4% to 28.6% *(p=0.002)*. The authors also identified that the use of state-wide insulin charts reduced training costs in a highly mobile workforce and reduced prescribing errors.

c) Upskilling medical and nursing staff in managing insulin therapy in wards

In three surveys carried out in separate US hospitals, the most commonly perceived barriers to prescribing insulin by JMOs included: knowing what insulin type or regimen works best; knowing how to adjust insulin; risk of causing patient hypoglycaemia; unpredictable changes of inpatient diet and meal times; and unpredictable timing of patient procedures.[8, 25, 26] In a conference abstract reported by Jeffrie Seley et al [27], a week-long educational program reduced inpatient hyperglycaemia from 39.1% to 35.55% (*p<0.001*). The educational program involved a one-on-one educational session with a diabetes educator, where they used problem-based learning (PBL) methods to learn about a standardised insulin chart and titration of insulin according to blood glucose patterns. This was subsequently followed by four days' practical placement with the inpatient diabetes team to apply their knowledge.

In addition to educational programs, electronic decision support systems to provide insulin dosing advice (e.g. GlucoTab and Glucommander), has been demonstrated to improve glycaemic control in hospitals. In the study by Neubauer et al, The GlucoTab software calculated an initial insulin dose at 0.5 units/Kg of body weight.[10, 28, 29] In patients who were >70 years old or had renal impairment with a creatinine $\geq$175µmol/L, the initial total daily insulin dose was reduced at 0.3 units/kg. Half of the insulin was administered as long-acting insulin, while the other half was administered as bolus insulin three times a day. Correctional bolus doses of insulin were also calculated by the GlucoTab program. In the study by Neubauer et al, patients continued their metformin and/or incretin-based therapies, but stopped all other oral hypoglycaemic agents during their inpatient admission. On discharge, these oral hypoglycaemic agents were recommenced and their insulin doses adjusted accordingly.[28]

In 97.5% of the time, medical professionals adhered to the advised doses recommended by the GlucoTab software. When compared to historical controls, the group that used GlucoTab had a higher percentage in the target of 3.9 – 10.0mmol/L – 73% vs 53%. When the GlucoTab program was used, 86% participants in the survey reported that there was a reduction in endocrinologist/physician consults. The survey also reviewed whether the workload increased with the use of the system: 13 participants felt there was an increase in workload, while 33 reported a reduction in workload and 12 indicated no change. There were seven participants who did not answer the question.

d) Specialised glucose control teams in hospital

Glycaemic control teams (GCTs) are multidisciplinary teams that provide an inpatient diabetes service in hospitals. The introduction of these teams has demonstrated a reduction in patient length of stay (LOS) and subsequent financial savings for the hospital.[30] Flanagan et al, introduced a team consisting of five diabetes specialist nurses (two part-time nurses and three part-time specialist nurses, filling the equivalent of three full-time positions), a diabetes registrar and an endocrinologist to encourage early identification and treatment of patients admitted with diabetes mellitus.[31] In a 1200-bed large teaching hospital, throughout a

period from 2001 to 2006, they demonstrated a reduction in the LOS from a mean of 8.3 ± 0.18 days in 2002 to 7.7 ± 0.10 days in 2006 *(p=0.002)*. Significant falls in LOS were seen predominantly from admission through the emergency department (9.7 ± 0.23 vs 9.2 ± 0.20, *p<0.001*) but not elective admission.

Another study carried out by Sampson et al, in a different hospital, also demonstrated that with the introduction of a diabetes inpatient specialist nurse service (DISN), there was a reduction in LOS.[32] in a 989-bed acute teaching hospital. The DISN consists of specialist diabetes nurses who targeted specific areas of the hospital: orthopaedics, general surgery, urology, general medicine, medicine for the elderly and other medical specialty wards. Patients were referred if they were treated with insulin with variable blood glucose control, had recurrent hypoglycaemia, had been managed with sliding scale insulin, had newly diagnosed type 2 diabetes mellitus, had type 2 diabetes requiring inpatient or outpatient insulin conversion, was admitted with diabetic ketoacidosis or acute hypoglycaemia. The mean excess bed days per diabetes inpatient under 60 years of age was estimated to be 1.9 days before introduction of DISN, and this was reduced to 1.2 bed days (*p=0.03*).

Bozzo et al, presented retrospective data of the positive impact of an inpatient glucose team in a 944-bed tertiary care hospital in the US.[33] Their inpatient diabetes team consisted of a nurse practitioner, a certified diabetes educator, an endocrine fellow and a consultant. Over an eight-year period, the number of blood glucose readings within the optimal range when compared to baseline improved by 113.9% with involvement of the inpatient diabetes team.

In many ways, the specialised glucose control team is the 'enabler' for better glucose and insulin management in the hospital setting. They provide clinical advice in the ward and play an important role in education of medical and nursing staff. In Australia, there are few hospitals that have a dedicated inpatient glucose control team that perform blanket review of patients with diabetes or on insulin therapy. Perhaps a specialised glucose control team would be most beneficial in regional or district hospitals where there is no on-call diabetologist or a proper diabetes service in place.

Most of the studies involving specialised glucose control teams were performed in the UK, where the health system and funding structure is different from that in Australia. A proper cost-benefit analysis needs to be performed in Australia to assess potential cost savings of having a specialised in-hospital glucose control team.

In the UK, the National Health Service (NHS) introduced a quality and productivity project on inpatient diabetes management, called "ThinkGlucose". The initiative involved a holistic implementation of strategies, including the formation of a dedicated consultant-led diabetes outreach team, a teaching program for nursing and medical staff, a six-day ThinkGlucose service and education on the most updated protocols and guidelines. The complete implementation of the project was achieved within 1-3 years with significant organisational changes across teams and departments. Barriers in the implementation of the ThinkGlucose project across the Dudley Group of Hospitals was the absence of inpatient diabetes specialist teams in 1 in 3 hospitals, to drive the change required. The success of the ThinkGlucose project also required the support of executive administrative teams. In summary, the savings delivered by the Dudley Hospitals were approximately £411,000, or £103,000 per 100,000 population. The cost savings were achieved through a shorter length of stay in hospital (reduced by 0.61 days), due to service improvements (70% staff were educated through ThinkGlucose) and better clinical pathways to manage inpatient hyperglycaemia. In addition to this, clinical parameters also improved in the form of greater HbA1c reduction, reduced insulin prescription errors (from 24.6% to 6.4%), appropriate hypoglycaemic management (improved from 26.1% to 65%) and reduction in inappropriate referral to the specialist team (dropped from 23.3% to 13.8%). The ThinkGlucose program has subsequently been introduced to other hospitals such as Worcestershire Acute

Hospital Trust, University Hospitals Leicester, Sheffield Teaching Hospitals Foundation Trust, Portsmouth Hospitals and Cambridge University Hospital NHS Foundation Trust where its implementation has demonstrated quality and productivity improvements. This program included multiple facets of diabetes management, and goes beyond the specific area of safe insulin prescription in the hospital setting.

e) Special populations in the hospital

There are special populations within the hospital where glycaemic control deviates from the norm or is more challenging when compared to the general type 2 diabetes population. These groups include patients on enteral or parenteral feeding, patients receiving glucocorticoids, patients with renal disease and the geriatric population. In patients who are on feeding regimens, their glycaemic control can either be managed in two ways: Firstly, dieticians can change the carbohydrate content in patients' enteral or parenteral feeds.[15] Alternatively, diabetes-specific enteral formula may be used.[34] Secondly, elevated glucose levels can be managed by pharmacological means such as subcutaneous insulin. In a randomised control trial by Korytkowski et al, the efficacy of a ISS regimen was compared with a basal insulin glargine (Lantus®) plus ISS regimen. In the ISS group, if patients had persistent hyperglycaemia, a rescue dose of isophane insulin (NPH) was administered.[35] The ISS involved administration of regular insulin every 4–6 hours depending on the measured BGL. The target BGL was 5.6 – 10mmol/L. This study demonstrated that both interventional groups had similar efficacy. However, within the ISS group, 48% of patients required rescue NPH to lower a persistent hyperglycaemia. On the other hand, in an Australian study, management of patients with hyperglycaemia on enteral feed by a specialised diabetes team using four-hourly regular insulin subcutaneously had resulted in better glycaemic control compared to patients managed by their treating team during the period of enteral feeding. The glycaemic control was also better in the 24 hours after cessation of enteral feeding, and these patients had shorter LOS in hospital.[36]

In patients on corticosteroids for medical therapy, it is not uncommon for their treatment to exacerbate any underlying diabetes mellitus. In an Australian study by Burt and et al [37], a clinical basal bolus insulin protocol was introduced to assess the efficacy in controlling steroid induced hyperglycaemia. Patients in this study took prednisolone $\geq$ 10mg per day to treat an acute inflammatory condition. Patients where prescribed a basal bolus insulin regimen according to their body weight. Their total daily insulin dose was calculated as 0.3 units/kg for diet controlled diabetes; 0.4 units/kg for patients on oral hypoglycaemic agents; and current daily insulin dose for insulin-treated patients. The total daily insulin dose was given as 50% long-acting basal insulin glargine and 50% short-acting bolus insulin aspart. Insulin aspart was divided evenly between three meals. The protocol recommended insulin dose adjustment of 10–25% if BGL was outside 4–10mmol/L. The results found that mean daily BGL was higher in the prednisolone group than the control group, 12.2 $\pm$ 0.3mmol/L vs 10.0 $\pm$ 0.1mmol/L respectively. The mean BGL was higher at 1700 hours and 2100 hours in the prednisolone group. The mean daily insulin dose was significantly higher in the prednisolone group than the control group, 0.67 – 0.7 units/kg vs 0.6 – 0.65 units/kg, respectively. Unfortunately, optimal glycaemic control (<10mmol/L) was not achieved with the basal bolus insulin regimen in patients treated with corticosteroids.

In patients with renal impairment, due to reduced renal clearance of systemic insulin, they are particularly susceptible to hypoglycaemic episodes. Consequently, management of inpatient hyperglycaemia is a challenge. In a multicentre, prospective randomised trial carried out by Baldwin et al, they compared the efficacy of two dosing regimens of basal bolus insulin (0.5 units/kg per day vs 0.25 units/kg per day) in patients admitted into hospital with type 2 diabetes mellitus and eGFR<45mL/min (not on dialysis).[38, 39] The total daily insulin dose was divided into 50% long-acting insulin and 50% short-acting insulin (evenly distributed between three meals per day). Patients stopped all other forms of glucose-lowering medications. The target BGL was 5.5 – 10mmol/L. There was no significant different between the percentage of patients

within the target BGL. However, the group receiving 0.5units/kg per day had much higher rates of hypoglycaemia, 30% vs 15.8% *(p=0.08)*.

The last special population discussed in this Evidence Check are patients within the geriatric population, defined as ≥ 70 years of age. There is limited evidence within this population as this group of patients are usually excluded from most studies. In a conference abstract by Neubauer et al [40], they demonstrated the efficacy and safety of using a weight-based algorithm within the admitted geriatric population. This algorithm was supported using GlucoTab (insulin dosing decision aid). Geriatric inpatients with elevated BGLs were commenced on a total daily insulin dose of 0.3 units/kg, with 50% as long-acting basal insulin and 50% as short-acting insulin divided between three meals. The overall mean BGL was 8.7 ± 1.7mmol/L. Using this algorithm, the number of BGLs within 3.8 – 9.9mmol/L was 71.8% in the geriatric population; while there were 25.5% within 9.9 – 16.6mmol/L. There were 1.7% BGLs ≥16.6mmol/L and no BGLs <2.2mmol/L.

In a survey carried out among 127 nurses regarding inpatient management of diabetes, the most commonly perceived barriers against optimal glycaemic control included: unpredictable timing of patient procedures (55.1%), unpredictable changes in patient diet and mealtimes (53.5%) and patients not following the diet plan (49.6%).[41] A quality improvement project designed by Engle et al, proposed a strategy to empower nursing staff a streamlined process of timing a patient's meal delivery with their glycaemic management.[16] The process involved the meal delivery staff contacting ward nurses when 'diabetic diets' for patients on insulin were ready for delivery. This then prompted the ward nurses to carry out point of care (POC) blood glucose level (BGL) monitoring. Once the meals arrived on the wards, the nurses would deliver the meals to the patients on insulin therapy. With the patient, the nurse would assess the anticipated carbohydrate intake and administer the mealtime insulin. Implementation of this process, resulted in an increased of BGL within the range of 3.8 – 9.9mmol/L from 45% to 53% while the proportion of BGL > 16.6mmol/L was reduced from 8.3% to 5%. Furthermore, the percentage of patients who received their insulin within 30 minutes of POC BGL increased from 35% to 73%. Feedback from nursing staff after implementation of this change was positive as it enabled a smoother workflow. It allowed nurses to know exactly when the administer mealtime insulin and allowed them to be in control of the entire process from POC BGL, insulin administration and meal delivery.

There are limited studies that have investigated the role of continuous glucose monitoring (CGM) in a hospital setting. In a cohort of 40 patients, Gomez and Umpierrez compared the glycaemic control between POC blood glucose monitoring and the use of CGM in insulin naïve patients who commenced a basal bolus regimen.[17, 42] A total daily insulin dose of 0.4 units/kg were used if BGLs were between 7.7 – 11.1mmol/L and 0.5 units/kg if BGLs were 11.1 – 22.2mmol/L. There was no difference in blood glucose after the first day, however the CGM detected more episodes of hypoglycaemia. However, another study carried out by Donsa et al, they found that as the number of BGL readings within target range improved as CGM was used for longer and that there were fewer BGL fluctuations.[43]

f) Other special populations with insufficient evidence

We recognise that metabolic disease is highly prevalent in the Aboriginal and Torres Strait Islander population and patients on the psychiatric ward. However, the literature review did not identify any data that investigated the optimal management of these populations as inpatients. Furthermore, there was no study looking at the hospital management of insulin therapy in patients from a non-Caucasian background.

Transitioning their management from inpatient care to outpatient/community care

An efficient way of transferring a patient's diabetes management from inpatient care to outpatient care is also an essential part of diabetes management in the context of the health system. Unfortunately, there were only few studies that looked into the safe transitioning of patients in this context, and it would be difficult to decide what would be the best practice. In a retrospective cohort study by Wei et al, they demonstrated that over a two-year period, 17% of patients who newly commenced on insulin or commenced on a new oral hypoglycaemic agent were re-admitted within 30 days.[44] The characteristics of these patients who had an early readmission include: male gender (58% vs 52%, $p=0.03$), a higher Charlson comorbidity score, longer length of stay (5 vs. 3.9 days, $p<0.01$) and were more often discharged home with nursing services (38% vs 32%, $p=0.03$). Within this study cohort, patients who were admitted under the medical teams who had an elevated baseline HbA1c $\geq$ 8%, had a reduced early readmission risk if they had intensification of the glycaemic control (adjusted odds radio 0.33, 95% CI 0.12-0.88, $p=0.03$). This evidence shows that intensification and management of inpatient hyperglycaemia, reap benefits during the patient's admission, but also in the long term for the healthcare system.

Wei et al carried out a subsequent study to investigate whether patients who were discharged after a hospital admission with insulin therapy would benefit from remote glucose monitoring by an endocrinologist.[45] After discharge, patients uploaded their BGLs from their glucometer, which was electronically emailed to an endocrinologist who reviewed their results. Their insulin doses were subsequently titrated remotely. Patients were subsequently reviewed in clinic at 14 days and 30 days post-discharge. This randomised control trial, involving 28 patients showed that there was no difference in glycaemic control between patients who had remote glycaemic monitoring and those who did not. The small number of participants in the study may have resulted in inadequate power for the trial. However, one of the benefits that the remote glucose monitoring was higher rates of hypoglycaemic events in the short term post-discharge period, which allowed timely titration of insulin doses. Maintaining good glycaemic control in the longer term among patients on insulin therapy in the community is beyond the scope of this review.

A current system of feedback/auditing of the system for management of inpatient hyperglycaemia

Unfortunately, there is limited statistical evidence regarding the direct benefits of having feedback or auditing assessments on the management of inpatient hyperglycaemia. However, it is recognised that for any system to function efficiently, mechanisms that provide active feedback and surveillance is essential for improvement.

Question 3: For all articles reviewed to answer Question 1 and 2, extract recommendations and commentary on the enablers of successful implementation of best practice components of inpatient insulin management.

Reference	Recommendations
Rendell, et al.[2]	• Recognising the significance of hyperglycaemia and introducing regular BGL measurements as a sixth vital sign, which is also subjected to 'Clinical Reviews'
Ginde, et al.[3]	• Engaging the emergency department in measuring blood glucose levels regularly and implementing early management according to a protocol or referring to the relevant specialties
Farrokhi, et al.[4] Pasquel, et al.[5]	• The use of HbA1c is very effect in triaging patients who are at risk of inpatient hyperglycaemia, and who would benefit from detailed glycaemic review prior to transitioning to community-based care

Zaidi, et al.[7]
Cheekati, et al.[8]
Arif, et al.[9]
	• Development of an educational package for registered nurses and junior medical officers is critical in teaching them about the hospital diabetes protocols, teaching them about the different types of insulin and regimens of insulin delivery
	  ○ Consider developing an educational package similar to the 'Between the Flags' modules, which is presented to Interns during Orientation Week
	  ○ Each hospital can also present information on referral pathways
	• Ongoing JMO education with practical problem-based learning case studies to learn simple technique for insulin titration – consider education in small groups rather than individual sessions for cost-effectiveness
	• Providing distributable educational resources (e.g. diabetes management pocket cards) for JMOs

Neubauer, et al.[29]	• State-wide accessibility and purchase of electronic glycaemic management software (as a decision-making aid)
Umpierrez, et al.[11] Becker, et al. [12]	• Ongoing education for nursing and medical staff regarding the NSW health subcutaneous insulin chart – in particular, emphasising BBB regimen rather than ISS, and encouraging the use of supplemental short-acting insulin
Rodriguez, et al.[14]	• Consideration of establishing an inpatient glucose management team that will case-find patients with unstable glycaemic control and provide support for medical and nursing staff
Baldwin and Apel.[39].	• When starting subcutaneous insulin treatment, it is important to consider the patient's renal function (especially <45mL/min) when calculating weight-based dosing algorithms • If eGFR <45mL/min, consider a total daily insulin of 0.25 units/kg/day. Within 50% basal insulin and 17% short-acting insulin with each meal • If using NPH insulin, a once daily dose in the morning will be enough. A night-time dose may cause overnight hypoglycaemia

	• Consider reducing basal insulin in patients with end-stage renal disease by 25% on days when they receive haemodialysis
Neubauer, et al.[10]	• In geriatric patients ≥ 70 years of age, for an initial insulin dose algorithm based on body weight, consider using 0.3 units/kg per day, with 50% as long-acting basal insulin and 50% as short-acting bolus insulin divided between three meals
Engle, et al.[16].	• Emphasis on optimal glucose testing and timely administration of insulin therapy (in co-ordination with meal delivery)
Rodriguez, et al.[14]	• Developing a framework to allow safe transition of patients on insulin therapy from hospital to community
Rodriguez, et al.[14]	• Developing a system that enables implementation of strategies to be actively reviewed, so valuable feedback and audit data can be used to improve current mechanism

5 Conclusions

Conclusions and recommendations applicable to NSW health hospitals

In conclusion, the two main key components to improve glycaemic control in adult patients is firstly, early recognition of abnormal BGLs and secondly, maintenance of good glycaemic control possibly through appropriate use of subcutaneous insulin therapy. Long-term benefits of improving inpatient glycaemic control can also be achieved by ensuring the safe transition of patients on insulin therapy from an inpatient environment to an outpatient setting and establishing a system of ongoing feedback, education and administrative leadership.

Currently in NSW Health hospitals, a standardised subcutaneous insulin chart has been introduced to all health districts. However, the ongoing education and uptake of this chart (for example, correct use of correctional/booster insulin) has been limited and variable between local health districts. The availability of a dedicated inpatient glucose control team also varies between tertiary hospitals. Access to an inpatient glucose control team could potentially be the vehicle driving change in the current practice culture, a proactive resource in managing inpatient hyperglycaemia and an educational resource for all hospital staff members.

NSW Health, as a healthcare system has the opportunity to focus resources on educating medical officers, nursing staff and other relevant allied health staff. Historical strategies of glycaemic control such as the insulin sliding scale (ISS) needs to be phased out of the current workforce and new junior medical officers (interns and resident medical offers) need to be educated on the basal-bolus-booster concept. Up-to-date protocols, such as weight-based algorithms and access to electronic insulin dose decision aids may support junior medical officers in initiating insulin earlier. Perhaps education should begin at the level of medical and nursing students.

The implementation of best practice strategies for the management of inpatient hyperglycaemia has long-term benefits for the healthcare system. In the initial period, there will no doubt be challenges as changes are being made to current practices. However, it is essential to remind those involved that an optimal patient-focused care and an improvement to the healthcare system are the long-term goals of these changes.

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7 Appendices

Appendix 1: Databases searched

Database	Initial search hit numbers	Duplicates identified using "find duplicates"	Hits identified as outside 2006-2016	Hits identified as published in non-English language	Articles removed after screening of abstract/full article	Final number of studies for inclusion
Medline	1200	103	281	88	421	338
Embase	3288	108	537	0	2221	422
PubMed	410	0	94	17	169	130
CINAHL	151	0	17	0	75	59
Cochrane	0	n/a	n/a	n/a	n/a	n/a

- Total after combining all database searches: 949
- Total after removing duplicates from combined database searches: 733

Appendix 2: Search Strategies

Medline – Searched on 12 December 2016

#	Search strings	Results
1	exp Inpatients/	14,795
2	hospitali*.mp.	172,986
3	admitted.mp	116,146
4	admission.mp	115,400
5	exp Patient Admission/	16,417
6	ward.mp	19,987
7	exp Hyperglycemia/	25,901
8	Diabetes Mellitus/	60,225
9	Diabetes Mellitus, Type 2/	101,008
10	Diabetes Mellitus, Type 1/	48,138
11	exp Blood Glucose/	91,385
12	BGL.mp	580
13	blood sugar.mp	3946
14	BSL.mp	551

15	Insulin/	100,013
16	Injections, Subcutaneous/	17,192
17	basal bolus.mp.	540
18	1 or 2 or 3 or 4 or 5 or 6	354,866
19	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	263,204
20	15 or 16 or 17	115,855
21	18 and 19 and 20	1695
22	exp Child/	988,968
23	Infant/	384,064
24	paediatric.mp	34,642
25	Pediatrics/	32,981
26	pediatric.mp	168,401
27	Pregnancy/	410,591
28	pregnant.mp	98,481
29	Diabetes, Gestational/	7693
30	22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	153,0650
31	21 not 30	1450
32	Administration, Intravenous/	3257
33	intravenous.mp	202,287
34	32 or 33	202,287
35	31 not 34	1200

EMBASE – Searched on 17 December 2016

#	Search strings	Results
1	hospital patient/	266,313
2	inpatient*.mp	107,850
3	in-patient*.mp	1,657,799
4	ward.mp	164,187
5	hospital/	602,985
6	hospital admission/	146,215
7	hospital patient/	266,313
8	hospital care/	19,608
9	or/1-8	2,412,746
10	hyperglycemia/	72,919
11	diabetes mellitus/	473,997
12	insulin dependent diabetes mellitus/	76,499
13	non insulin dependent diabetes mellitus/	185,962
14	glucose blood level/	173,226
15	bgl.mp	857
16	blood sugar.mp	9581
17	bsl.mp	835
18	or/10-17	715,444
19	insulin/sc [Subcutaneous Drug Administration]	5202
20	insulin/	226,551
21	subcutaneous.mp. or subcutaneous drug administration/	136,996
22	20 and 21	9985
23	basal bolus.mp.	1472
24	or/19,22-23	14,860
25	and/9,18,24	3288

PubMed – Searched on 27 December 2016

Results: 410

Translations:

inpatient	"inaptients" [MeSH Terms] OR "inpatients" [All Fields] OR "inpatient" [All Fields}
patient admission	"patient admission" [MeSH Terms] OR ("patient" [All Fields] AND "admission" [All Fields]) OR "patient admission" [All Fields]
diabetes mellitus	"diabetes mellitus" [MeSH Terms] OR ("diabetes" [All Fields] AND "mellitus" [All Fields]) OR "diabetes mellitus" [All Fields]
hyperglycaemia	"hyperglycaemia: [All Fields] OR "hyperglycemia" [MeSH Terms] OR "hyperglycemia" [All Fields]
type 1 diabetes	"diabetes mellitus. Type 1" [MeSH Terms] OR "type 1 diabetes mellitus" [All Fields] OR "type 1 diabetes" [All Fields]
type 2 diabetes	"diabetes mellitus, type 2" [MeSH Terms] OR "type 2 diabetes mellitus" [All Fields] OR "blood glucose" [All Fields]
blood glucose	"blood glucose" [MeSH Terms] OR ("blood" [All Fields] AND "glucose" [All Fields]) OR "blood glucose" [All Fields]
insulin	"insulin" [MeSH Terms] OR "insulin" [All Field]
child	"child" [MeSH Terms] OR "child" [All Fields]
infant	"infant" [MeSH Terms] OR "infant" [All Fields]
paediatric	"pediatrics" [MeSH Terms] OR "pediatrics" [All Fields] OR "paediatrics" [All Fields]
adult	"adult" [MeSH Terms] OR "adult" [All Fields]
pregnancy	"pregnancy" [MeSH Terms] OR "pregnancy" [All Fields]
gestational diabetes	"diabetes, gestational" [MeSH Terms] OR ("diabetes" [All Fields] AND "gestational" [All Fields] OR "gestational diabetes" [All Fields] OR ("gestational" [All Fields] AND "diabetes" [All Fields])

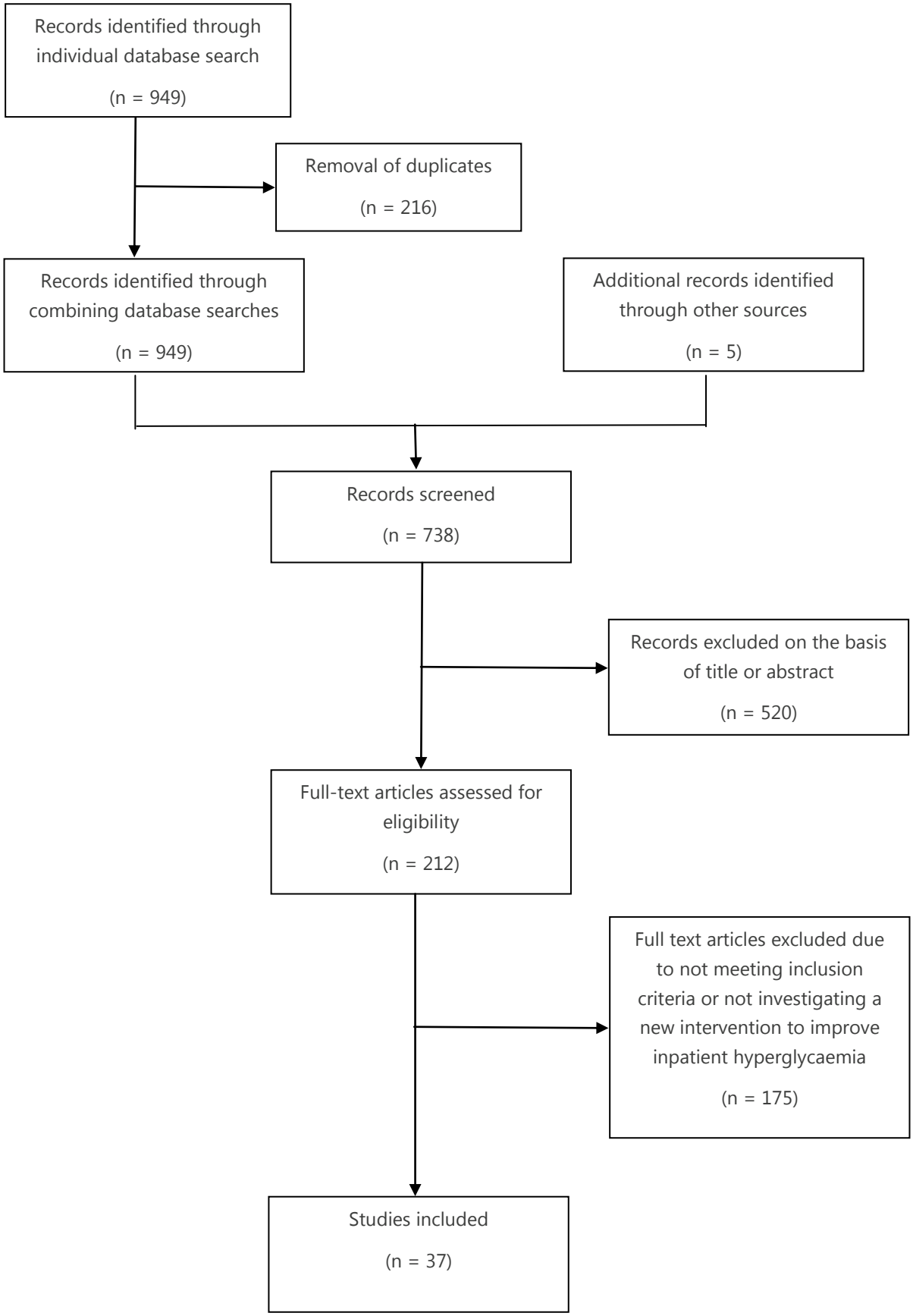
CINAHL – Searched on 27 December 2016

#	Query	Results
S25	S17 not S24	151
S24	S18 OR S19 OR S20 OR S21 OR S22 OR S23	728,118
S23	gestational diabetes	3844
S22	pregnant	24,588
S21	pregnancy	154,946
S20	infant	208,028
S19	paediatric	114,895
S18	child	494,756
S17	S5 and S11 and S16	177
S16	(S12 and S13) or S14 or S15	2566
S15	basal bolus	256
S14	subcutaneous insulin	804
S13	subcutaneous	11,921
S12	insulin	46,598
S11	S6 OR S7 OR S8 OR S9 OR S10	126,122
S10	"blood sugar"	1247
S9	"bgl"	51
S8	(MH "Blood Glucose")	24703
S7	(MH "Diabetes Mellitus+") OR (MH "Diabetes Mellitus, Type 2") OR (MH "Diabetes Mellitus, Type 1+")	112,674
S6	(MH "Hyperglycemia")	6426
S5	S1 OR S2 OR S3 OR S4	387,356
S4	"ward"	10,762
S3	(MH "Health Facilities+") OR (MH "Hospitals+") OR (MH "Hospital Units+")	331,015
S2	(MH "Patient Admission")	11,761
S1	(MH "Inpatients") OR (MH "Surgical Patients")	70,531

Cochrane Library – Searched on 27 December 2016

#	Query	Results
1	MeSH descriptor: [Hyperglycemia] explode all trees	1758
2	MeSH descriptor: [Insulin] explode all trees	9678
3	subcutaneous	15,656
4	MeSH descriptor: [Injections, Subcutaneous] explode all trees	3920
5	MeSH descriptor: [Inpatients] explode all trees	875
6	MeSH descriptor: [Diabetes Mellitus] explode all trees	19,557
7	ward	8475
8	MeSH descriptor: [Hospitalization] explode all trees	14,124
9	MeSH descriptor: [Adult] explode all trees	1645
10	1 and 2 and (3 or 4) and (5 or 7 or 8) and 6 and 9	0
11	1 and 2 and (3 or 4) and (5 or 7 or 8) and 6	0

Appendix 3: PRISMA flow chart



Appendix 4: NHMRC Levels of Evidence for Recommendations

Recommendations	Study	NHMRC Level of Evidence	NHMRC Grade of Recommendations
BSL as the sixth vital sign for routine monitoring	Rendell et al.[2]	Review article with expert opinion	B
Early monitoring and management of BGL in Emergency Department	Ginde, et al.[3]	III-2 Retrospective cohort study	C
	Munoz, et al.[18]	III-3 Cohort study with historical controls	C
	Harper, et al.[46]	III-1 Pseudorandomised controlled trial	C
HbA1c is effective in triaging those who are at risk of inpatient hyperglycaemia	Farrokhi, et al.[4]	II Randomised controlled trial	B
	Pasquel, et al.[5]	III-3 Retrospective cohort study	C
Increased educational resources for junior medical officers	Zaidi, et al.[7]	III-2 Prospective cohort study	C
	Cook, et al.[25]	III-2 Prospective cohort study	C
	Cheekati, et al.[8]	III-2 Prospective cohort study	C
	Gouveia, et al.[6]	Survey of junior doctor's knowledge	C
	Latta, et al.[26]	Survey of junior doctor's knowledge	C

Implementation of standardised subcutaneous insulin order form – actively introducing basal bolus regimen and phasing out insulin sliding scale	Arif, et al.[9]	III-3 Cohort study with historical controls	C
	Wong, et al.[36]	III-3	C
	Perera, et al.[20]	III-3	C
	Roberts, et al.[21]	III-3	C
	Doyle, et al.[47]	III-3	C
	McIver, et al.[24]	II Prospective cohort study	B
	Becker, et al.[12]	III-2	C
	Adeel, et al.[13]	II Randomised control trial post-hoc analysis	A
	Maynard, et al.[48]	Review article with expert opinion	B
Increased educational resources of nursing staff	Leey, et al.[41]	II Prospective cohort study	B
State wide access to electronic glycaemic management software (decision-making aids)	Neubauer, et al.[29]	III-2 Non-controlled intervention study	C
	Neubauer, et al.[28]	III-2 Non-controlled intervention study	C
Inpatient glucose team	Rodriguez, et al.[14]	III-2	C
	Flanagan, et al.[31]	III-3	C
	Newton and Young.[30]	III-3	C
	Sampson, et al.[32]	III-3	C
	Bozzo, et al.[33]	III-3	C

Weight based insulin dosing regimen	Umpierrez, et al.[11]	II Randomised control trial	A
	Baldwin, et al.[38]	II Randomised control trial	A
Weight based dosing regimens for corticosteroids induced hyperglycaemia	Baldwin and Apel.[39]	Review article with expert opinion	B
	Burt, et al.[37]	III-3	C
Weight based regimens for enteral feeding	Cheng.[15]	Review article with expert opinion	B
	Korytkowski, et al.[35]	II	B
Continuous glucose monitoring of BSLs	Donsa, et al.[43]	IV	D
	Gomez and Umpierrez.[17]	I	A
Improved glycaemic control by redesigning meal delivery and insulin administration	Engle, et al.[16]	III-3	C

NHMRC Evidence Hierarchy: Designations of "levels of evidence" according to type of research question (including explanatory notes)

Level	Intervention	Diagnostic accuracy	Prognosis	Aetiology	Screening Intervention
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with an independent, blinded comparison with a valid reference standard, among consecutive persons with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive persons with a defined clinical presentation	All or none	All or none	A pseudorandomised controlled trial (i.e. Alternate allocation or some other method)
III-2	A comparative study with concurrent controls: • Non-randomised experimental trial • Cohort study • Case-control study • Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: • Non-randomised, experimental trial • Cohort study • Case-control study
III-3	A comparative study without concurrent controls: • Historical control study • Two or more single arm study • Interrupted time series without a parallel	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: • Historical control study • Two or more single arm study

	control group				
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study or persons at different stages of disease	A cross-sectional study or case series	Case series

Definitions of NHMRC grades of recommendations

Grade of Recommendation	**Description**
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution