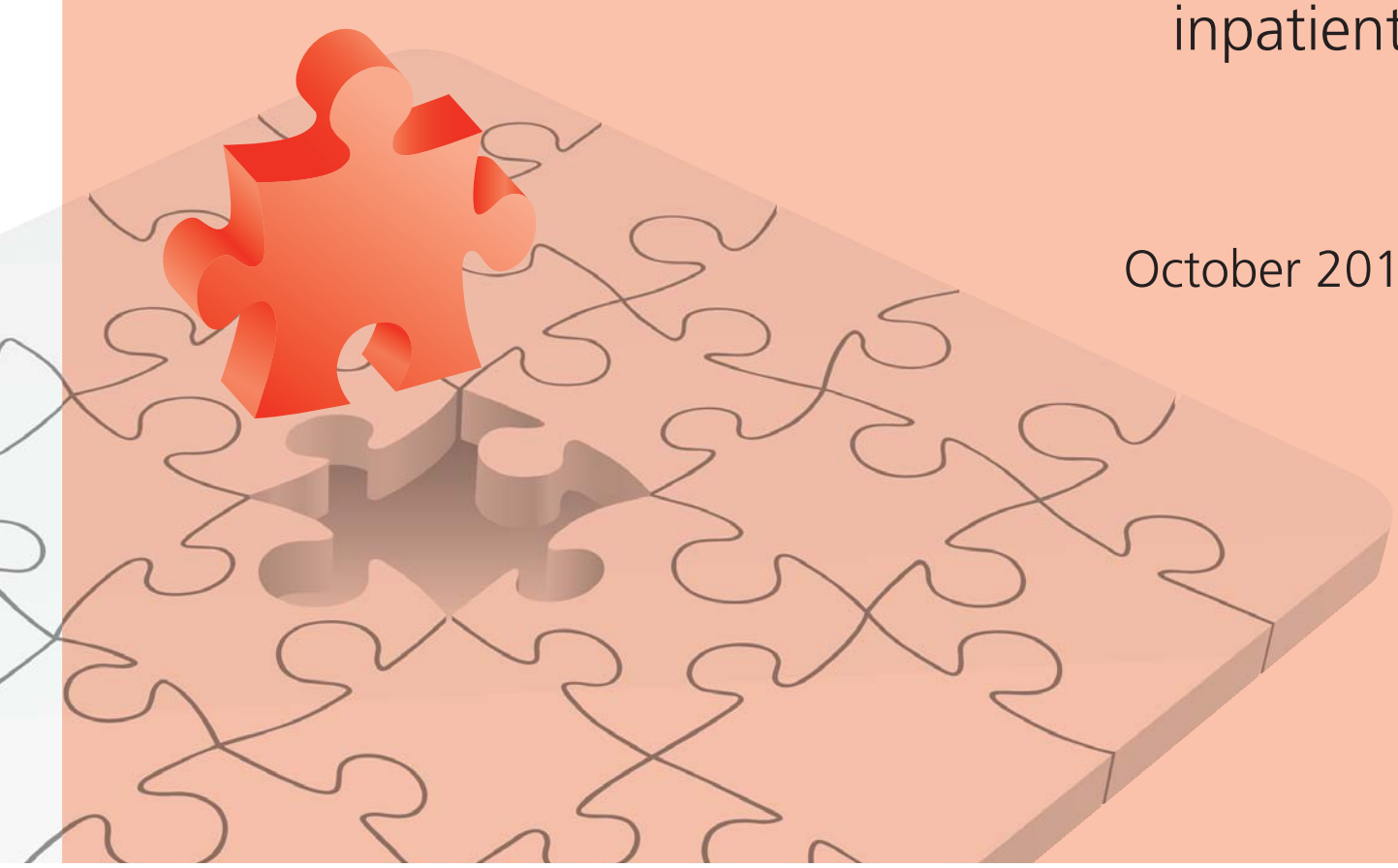
JBDS-IP Joint British Diabetes Societies for inpatient care

The use of variable rate intravenous insulin infusion (VRIII) in medical inpatients



October 2014

DIABETES UK CARE. CONNECT. CAMPAIGN.

ABCD Association of British Clinical Diabetologists

DISN UK GROUP

WEDS welsh endocrine and diabetes society

trend UK TRAINING RESEARCH AND EDUCATION FOR NURSES IN DIABETES

diabetesFRAIL The emergence of a concept

This document is coded JBDS 09 in the series of JBDS documents:

Other JBDS documents:

Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy October 2014 JBDS 08

Admissions avoidance and diabetes: guidance for clinical commissioning groups and clinical teams December 2013 JBDS 07

The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes August 2012 JBDS 06

Glycaemic management during the inpatient enteral feeding of stroke patients with diabetes June 2012 JBDS 05

Self-Management of Diabetes in Hospital March 2012 JBDS 04

Management of adults with diabetes undergoing surgery and elective procedures: improving standards April 2011 JBDS 03

The Management of Diabetic Ketoacidosis in Adults Revised September 2013 JBDS 02

The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus Revised September 2013 JBDS 01

These documents are available to download from the ABCD website at http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm and the Diabetes UK website at www.diabetes.org.uk

We are eager to find out about your experiences using this guideline- particularly any data from audits of its use in situ. This will be used in the next update of the guideline. Please contact Dr Stella George at: stellageorge@nhs.net

Scope of the guideline

This guideline is for the use of a variable rate intravenous insulin infusion (VRIII) in adult inpatients with medical conditions and diabetes/hyperglycaemia, who require intravenous administration of insulin to keep their blood glucose within the recommended target range during an acute illness or a period of starvation.

This document is designed to guide non specialist teams in the appropriate and safe use of a VRIII.
Seek help from your local diabetes team at the earliest opportunity.

This guideline is not suitable for use in certain situations. We make the following recommendations for those circumstances.

Diabetic Ketoacidosis (DKA)	The management of DKA in Adults [JBDS 02; March 2012, revised June 2013] www.diabetologists-abcd.org.uk or www.diabetes.org.uk
Hyperosmolar hyperglycaemic State (HHS)	The management of the hyperosmolar hyperglycaemic state [JBDS 06; August 2012] www.diabetologists-abcd.org.uk or www.diabetes.org.uk
Patients who are perioperative or are undergoing procedures requiring a period of starvation	Management of adults with diabetes undergoing surgery and elective procedures: improving standards [JBDS 03; April 2011] currently being updated www.diabetologists-abcd.org.uk or www.diabetes.org.uk
Patients who require enteral feeding who have suffered a stroke	Glycaemic management during the inpatient enteral feeding of stroke patients with diabetes [JBDS 05; June 2012] www.diabetologists-abcd.org.uk or www.diabetes.org.uk
Acute Coronary Syndrome	Use local guideline
Patients requiring Total Parenteral Nutrition	Use local guideline
Antenatal patients	Use local guideline
Patients who are hyperglycaemic due to steroid therapy	Use local guideline- JBDS guideline in development

Abbreviations used in this guideline

Term	Abbreviation
Variable rate intravenous insulin infusion	VRIII
Capillary blood glucose	CBG
Diabetic Ketoacidosis	DKA
Hyperosmolar Hyperglycaemic State	HHS
Total Parenteral Nutrition	TPN
Continuous Subcutaneous Insulin Infusion	CSII
Total Daily Dose	TDD
Sodium Chloride	NaCl
Potassium Chloride	KCl
National Institute of Clinical Excellence	NICE

Lead authorship

Dr Stella George, Consultant Diabetes and Endocrinology, East and North Hertfordshire NHS Trust

Debbie Stanisstreet, Diabetes Inpatient Specialist Nurse, East and North Hertfordshire NHS Trust

Supporting organisations

Diabetes UK: Tracy Kelly, Head of Care

Joint British Diabetes Societies (JBDS) for Inpatient Care, Chair: Professor Mike Sampson (Norwich)

Diabetes Inpatient Specialist Nurse (DISN) UK Group, Chair: Esther Walden (Norwich)

Association of British Clinical Diabetologists (ABCD), Chair: Dr Rob Gregory (Leicester)

Endorsed by

Diabetes Frail

The Diabetes Management and Education Group (DMEG) of the British Dietetic Association

Royal College of Physicians (RCP)

The Renal Association

The Society for Acute Medicine (SAM)

UK Clinical Pharmacy Association (UKCPA) Diabetes and Endocrinology Committee

Writing group

Dr Ali Abbara, Imperial Healthcare College NHS Trust

Linda Balian, Yeovil District Hospital NHS Foundation Trust

Dr Mithun Bhartia, Sandwell and West Birmingham Hospitals NHS Trust

Alison Cox, Kings College Hospital NHS Foundation Trust

Dr Frances Coyle, Frimley Park Hospital NHS Foundation Trust

Anne Currie, East and North Hertfordshire NHS Trust

Dr Jane Dale, The Dudley Group NHS Foundation Trust

Dr Ketan Dhatariya, Norfolk and Norwich University Hospitals NHS Foundation Trust

Dr Philip Dyer, Heart of England NHS Foundation Trust

Dr Haleema Hayat, Burton Hospitals NHS Foundation Trust

Dr Anne Kilvert, Northampton General Hospital NHS Trust

Dr Abbi Lulsegged, Kings College Hospital NHS Foundation Trust

Dr Samson Oyibo, Peterborough and Stamford Hospitals NHS Trust

Tobi Parkin, Northern Devon Healthcare NHS Trust

JBDS IP Group

Dr Belinda Allan, Hull and East Yorkshire Hospital NHS Trust

Dr Hamish Courtney, Belfast Health and Social Care Trust, Northern Ireland

Dr Ketan Dhatariya, Norfolk and Norwich University Hospitals NHS Foundation Trust

Dr Daniel Flanagan, Plymouth Hospitals NHS Trust

Dr Stella George, East and North Hertfordshire NHS Trust

Dr Rob Gregory, University Hospitals of Leicester NHS Trust

June James, University Hospitals of Leicester NHS Trust

Tracy Kelly, Diabetes UK

Dr Rif Malik, King's College Hospital NHS Foundation Trust

Dr Colin Perry, NHS Greater Glasgow and Clyde

Dr Gerry Rayman, The Ipswich Hospitals NHS Trust

Dr Stuart Ritchie, NHS Lothian

Dr Aled Roberts, Cardiff and Vale University Health Board

Professor Mike Sampson (Norwich), Chair, Joint British Diabetes Societies (JBDS) for Inpatient Care

Dr Maggie Sinclair-Hammersley, Oxford University Hospitals NHS Trust

Debbie Stanisstreet, East and North Hertfordshire NHS Trust

Professor Jonathan Valabhji, National Clinical Director for Obesity and Diabetes

Esther Walden, Norfolk and Norwich University Hospital NHS Foundation Trust

Dr Peter Winocour, East and North Hertfordshire NHS Trust

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Foreword

It is recognised that the use of a variable rate intravenous insulin infusion (VRIII) is a tool commonly used to achieve normoglycaemia in hospital inpatients.

Most acute trusts have guidelines for its use, but there is a wide variation across the country in, for example, the indications for its use, in rates of infusion, or duration of use. This heterogeneity increases the risk of errors which can potentially lead to significant morbidity and mortality. It also makes it inherently difficult to study its efficacy, optimisation and safety profile. In addition, despite guidelines, both local and national audits have shown that VRIII is often used when not indicated, its duration is unnecessarily prolonged and the step down to other glucose lowering medication is often not practiced safely.

It is also acknowledged that achieving optimal glycaemia in this group of often complex patients, is not easy to achieve and individual targets are often needed.

In response to these issues, the Joint British Diabetes Societies (JBDS) for Inpatient Care has produced this guideline. It has been designed to be a practical guide to be used by any healthcare professional who manages medical in-patients with hyperglycaemia. Its main aim is to allow the VRIII to be used safely, effectively and efficiently for this specific group of inpatients. It is divided into several sections, including the evidence base for its recommendations, the practicalities of when to use a VRIII, how it is to be set up, when it should be discontinued and how a safe transition to other medication can be achieved. Safety of the use of the VRIII is emphasised throughout.

The appendices have been designed to be used as standalone summary documents, i.e. 'how to guides' which can be easily adapted and used on the wards.

It is hoped that its adoption nationally will help harmonise the the use of the VRIII and therefore enable multicentre studies to be carried out, and thus allow continual refinement in its use.

Introduction

Variable Rate Intravenous Insulin Infusion (VRIII), formerly known as sliding scale insulin, has been used for decades to achieve normoglycaemia in hospitals. It is a very useful tool when used in the right context and has been shown to improve outcomes. However, when used incorrectly, it can result in morbidity from hypoglycaemia, excess length of stay, rebound hyperglycaemia and even DKA[1].

Guidelines already exist for patients with DKA, HHS, stroke, myocardial infarction and those in the perioperative period. The writing group have also worked in conjunction with the authors of the JBDS perioperative guidelines and have agreed a scale that will be concordant across both guidelines. This will be reflected in the revised surgical guideline, currently in development.

This guideline is designed for acutely unwell patients, including those with a pre-existing diagnosis of diabetes and those who present with hyperglycaemia for the first time.

The guideline is intended for use by any healthcare professional who manages patients with diabetes on hospital wards. It aims to be a practical guide for when and how to use an intravenous insulin infusion and how to transition patients to other glucose lowering medication after stabilisation.

Most studies of the use of intravenous insulin infusions in hospital have been in the critical care setting or in patients who have undergone surgery. To date there is only one randomised trial focused on the management of medical inpatients[2]. This compared the use of different types of subcutaneous insulin regimens in the management of acutely unwell patients with Type 2 diabetes and did not assess the effectiveness of an intravenous insulin infusion.

The recommendations in this guideline are therefore based on a combination of:

- extrapolated evidence from other relevant patient groups
- guidelines from other JBDS groups where relevant
- NHS Diabetes e-learning module 'Safe use of Intravenous insulin infusion'
- consensus of experts who contributed to the development of this guideline

Until advances in technology produce a system that can automatically adjust the insulin infusion rate in response to changes in the blood glucose, the safe and effective use of a VRIII will depend on close monitoring and decision making by health care professionals. The emphasis throughout this guideline is on the safe use of a VRIII when clinically indicated, aiming for target blood glucose levels that are appropriate for this group of patients. It should be used for as short a duration as possible, with plans for a safe and effective step-down to other agents as soon as the clinical situation allows.

Referral to local diabetes teams as soon as possible after admission is ideal since individual patients' needs must be assessed and appropriate action taken to ensure the VRIII is used safely. However, this may not be possible in some trusts depending on availability so local policies should be followed.

We recommend that healthcare professionals also complete the e-learning module available via the healthcare e-academy: 'Intravenous Insulin Infusion (III) e-learning module' currently available on: http://nhsdiabetes.healthcareea.co.uk/Default.aspx

Chapter 1: Background and definitions

1.1 Background

Approximately 15% of hospital inpatients have diabetes[1] of whom 70% are admitted as medical emergencies, the majority with diabetes as a secondary diagnosis. There is evidence from both medical and surgical settings to indicate that if the blood glucose is not controlled the outcomes, measured by mortality, morbidity or length of stay, are worse[3].

While the evidence that lowering the blood glucose to a specified target range improves outcomes is more limited, it has been shown to be beneficial in some settings[4]. This is discussed in more detail in Chapter 2.

In the acute setting the options for controlling blood glucose are limited. On some occasions it may be possible to achieve glycaemic control using subcutaneous insulin but this requires a degree of expertise. If the diabetes team is not available to advise, the method of choice in an unwell or fasting patient is a VRIII – previously known as a sliding scale. This guideline specifies the clinical circumstances in which a VRIII should be used and how it should be initiated, managed and discontinued safely.

1.2 Definition of a variable rate intravenous insulin infusion

The infusion of intravenous insulin at a variable rate according to regular capillary blood glucose measurements with the aim of controlling serum glucose levels within a specified range. The VRIII is usually accompanied by an infusion of fluid containing glucose to prevent insulin-induced hypoglycaemia.

1.3 Classification of hyperglycaemia in acutely unwell patients

Known Diabetes

Diabetes diagnosed and treated before admission.

Newly diagnosed diabetes

Fasting glucose greater than 7.0 mmol/L or random glucose greater than 11.1 mmol/L during hospital stay and confirmed after discharge.

Hospital–related hyperglycaemia (also known as stress hyperglycaemia)[5].

Fasting glucose greater than 7.0 mmol/L or random glucose greater than 11.1 mmol/L during hospital stay but glucose tolerance reverts back to the normal range after discharge.

1.4 Use of a VRIII in UK hospitals

1.4.1 The National Diabetes Inpatient Audit

The annual National Diabetes Inpatient Audit[1], a snapshot audit of diabetes inpatient care in England and Wales, has yielded some important findings relating to the real world use of VRIII.

Inappropriate use:

6.5% of patients were thought to have been treated with a VRIII unnecessarily.

Inappropriate duration of use: In 2012, 10.6% of inpatients with diabetes received an insulin infusion during the previous 7 days, of whom 7.8% were treated with an insulin infusion for 7 days or longer. 7.7% of insulin infusions were deemed unnecessarily long by the diabetes team.

Inadequate monitoring:

1.7% of patients on an insulin infusion had between 1 and 3 glucose measurements in the previous 24 hours (equivalent to less than one every eight hours), with 0.8% having no glucose monitoring in the previous 24 hours.

1.4.2 Dynamic Sliding Scale Intravenous Insulin Regimes

Some centres in the UK and the US use both the current blood glucose level as well as the previous blood glucose level to determine the rate of insulin to be infused - a 'dynamic sliding scale'[6]. This way of delivering a VRIII is quite different to that used by the majority of UK centres. To date there have been no studies comparing these two methods of insulin delivery and until a comparative study is available, we recommend the traditional UK method as described in this document because of the wider clinical experience and greater simplicity of use.

1.4.3 Combined Glucose, Potassium, Insulin Infusions (GKI, GIK regimes)

Some centres in the UK use infusions where all three solutes are in one infusion bag for indications similar to the use of a VRIII as well as in surgical patients. This is outside the scope of this document which deals solely with the use of a VRIII regime in medical inpatients.

Chapter 2: Evidence base for recommendations

The physiological release of catabolic hormones during illness may lead to loss of blood glucose control in people with diabetes and can cause stress-related hyperglycaemia in those not previously known to have diabetes[5]. There is good evidence from a variety of clinical areas to demonstrate that hyperglycaemia during inter-current illness is related to adverse outcomes, but studies designed to demonstrate the benefits of restoring good glycaemic control and to identify treatment targets have produced conflicting results.

The discussion below concentrates in the main on the available evidence for medical inpatients, the target population for this guideline. The evidence for surgical inpatients is discussed comprehensively in the JBDS Perioperative Guideline which can be accessed at www.diabetologists-abcd.org.uk or www.diabetes.org.uk. This guideline is currently under review.

2.1 Evidence for adverse effect of hyperglycaemia on outcomes during illness

Hyperglycaemia in hospitalised patients, whether the diabetes is previously known or undiagnosed and irrespective of its cause, is unequivocally associated with adverse outcomes, e.g. critically ill patients[7-14], patients suffering an acute myocardial event[15-18], after surgical procedures[19-22], and in sepsis[23].

Hyperglycaemia in hospital is associated with a significantly increased risk of mortality[3]. In a study by Umpierrez, this risk was shown to be even higher in patients not previously known to have diabetes (16% compared to 3% known diabetes and 1.7% normoglycaemia)[24]. Hyperglycaemia was also associated with increased length of stay, increased risk of requiring admission to intensive care and greater likelihood of discharge to residential or nursing home. It is not clear if these poor outcomes are due to the elevated glucose levels per se, or whether the elevated glucose levels merely serve as an indication of the severity of the underlying disease.

2.2 Evidence for specific blood glucose targets

Intervention directed at reducing blood glucose (BG) concentrations has resulted in improved outcomes in some studies, but not all [7-12, 14-21, 23-26]. Several recent clinical trials in critically ill patients have reported no reduction in mortality from intensive insulin treatment (IIT) (target near normoglycaemia) compared with conventional management (target BG <10.0 mmol/L). Some of these studies report harm associated with intensive insulin regimes, with increased rates of severe hypoglycaemia and, in one study, increased mortality [10-14, 23].

2.2.1 Glycaemic Control in Intensive Care units (ICU)

Most of the studies investigating the optimal blood glucose targets for patients treated with intravenous insulin infusions have been in the critical care setting. Several studies have compared intensive insulin therapy (IIT), in which the aim was to achieve a blood glucose target of 4.0-6.0 mmol/L, with conventional insulin treatment (CIT) usually aiming for 6.0-10.0 mmol/L (Table 1).

In the Leuven I study[7], IIT was associated with a reduction in ICU mortality from 8% to 4.6% and in-hospital mortality from 10.9% to 7.2% amongst surgical ICU patients (mainly cardiac surgery), but a second study from the second unit (Leuven II)[12] showed no mortality benefit in medical ICU patients. However, when patients who required fewer than 3 days in ICU were excluded, IIT conveyed a significant benefit over CIT (43% vs. 52.5%; p=0.009).

Two further studies, NICE SUGAR[11] and COIITSS[27] found an increased risk of severe hypoglycaemia in

patients randomised to receive IIT and in NICE SUGAR this was also associated with an increased 90 day mortality.

It appears though, that it is not simply a matter of relaxing thresholds and treatment targets. In a retrospective study, Lanspa et al[28] compared moderate vs. tight glycaemic control in ICU patients with or without previously diagnosed diabetes, and concluded that a moderate glucose target was independently associated with increased risk of mortality in patients without diabetes (OR, 1.36; 95% CI, 1.01-1.84; P= 0.05) but decreased risk of mortality in patients with diabetes (OR, 0.65; 95% CI, 0.45-0.93; P <0.01).

Thus the picture seems to be more complicated and different patient groups appear to need different targets. Indeed, Van den Berghe commented that "the controversy on how to optimally treat hyperglycaemia in the ICU is continuing"[29].

Table 1. Summary of findings of randomised controlled trials of IIT in adults

Study	Target BG on IIT (mmol/L)	Target BG conventional group (mmol/L)	Mortality	Significance
Leuven Surgical[7]	4.4-6.1	10.0 – 11.1	4.6% IIT vs. 8% control	
Leuven Medical[12]	4.4-6.1	10.0 – 11.1	37.3% IIT vs. 40% control	p <0.33
NICE-SUGAR[11]	4.5-6.0	< 10.0	27.5% IIT vs.24.9% control	p <0.02
COIITSS[27]	4.4-6.1	< 8.3	No difference	
GICI-HPTU[13]	4.4-6.1	10.0-11.1	No difference	
Glucontrol[30]	4.4-6.1	7.8-10.0	Stopped early because of protocol violations. No difference	
GCAO-REA[31]	4.4-6.1	<10.0	No difference	

2.2.2 Glycaemic Control in Hospitalised Medical Patients in Non-ICU Settings

Several observational studies point to a strong association between hyperglycaemia and poor clinical outcomes, including prolonged hospital stay, infection, disability after discharge from the hospital, and death[24, 32-42]. Several studies have found glucose variability to be an independent predictor of mortality in critically ill patients[43-45]. Whether intervention to control glycaemic variability, per se, improves outcomes is not known.

There remains conflicting evidence about the choice of insulin therapy to obtain glycaemic control. One study, Rabbit 2,[46] found a variable regime based on basal-bolus subcutaneous insulin, controlled acute hyperglycaemia in insulin-naïve patients with type 2 diabetes more effectively than a subcutaneous 'sliding scale' regime where 4 injections were given per day with no basal insulin. However, the findings cannot necessarily be extrapolated to other groups of patients and comparison with VRIII was not made. In addition, these patients were reviewed daily by an endocrinologist and this level of input is not readily available in most UK trusts at present.

2.2.3 Glycaemic Control in Acute Myocardial infarction (AMI)

The DIGAMI 1 study[15] was the first randomised control trial to show the benefit of lowering blood glucose in patients with AMI. In this study the starting glucose was 15.7 vs 15.4 mmol/L (control

vs intervention groups). Patients in the intervention group were treated with an insulin infusion for the first 24 hours, followed by 3 months of intensive (basal bolus) insulin therapy. During the first 24 hours blood glucose decreased significantly in both groups, with a greater decrease in the infusion group (5.8 ± 4.9 vs. 4.0 ± 3.9 mmol/L, $p < 0.0001$). This resulted in a reduction in mortality at 1 year (8.6% vs. 26.1% ($p < 0.0273$) and 3.4 years (33% vs. 44% $p < 0.011$) respectively. However, the relative contributions of the initial infusion compared with the following three months of intensive insulin treatment in improving outcomes were not established.

Although this initial glycaemic study showed potential benefit of intravenous insulin, further studies were not positive, possibly due to problems with design[47-51].

Analysis of the UK MINAP (Myocardial Ischaemia National Audit Project) data showed that admission glucose was strongly associated with mortality in all presentations of acute myocardial infarction irrespective of established diabetes diagnosis[52].

Based on current evidence, NICE recommends the use of a dose adjusted intravenous insulin to prevent uncontrolled hyperglycaemia (BG >11.0 mmol/L) in patients with acute coronary syndrome (ACS). Regular BG monitoring is advised, aiming for moderate glycaemic control target BG <11 mmol/L with avoidance of intensive glycaemic control and hypoglycaemia[53].

2.2.4 Hyperglycaemia in Acute Stroke

There is ample evidence to demonstrate that hyperglycaemia on admission is associated with worsened clinical outcome in patients with an acute stroke[35, 54, 55]. Good glycaemic control may also be indicated in patients without diabetes, in whom stress hyperglycaemia has been associated with a 3-fold risk of fatal 30-day outcome and 1.4-fold risk of poor functional outcome, when compared with normoglycaemic patients[35].

2.2.5 Guidelines from national and international societies

Several national and international societies have produced guidelines advising on glycaemic targets with regards to different patient populations – the majority are aimed at patients in the ITU setting. These are summarised in Table 2.

Table 2. Blood glucose targets during hospital admission: summary of recommendations from national and international societies

Organisation	Year	Patient population	Treatment threshold (mmol/L)	Target Glucose (mmol/L)
Surviving Sepsis Campaign[56]	2008	ICU patients	10.0	<5.3
American Heart Association[57]	2009	Patients with ACS	10.0	<7.8
European Society of Cardiology[58]	2009	ICU patients	10.0	7.8-10.0
American Association of Clinical Endocrinologists and American Diabetes Association[59]	2009	ICU patients/ hospitalised patients	10.0	7.8-10.0
American Diabetes Association[60]	2013	ICU patients	10.0	7.8-10.0
American College of Physicians[61]	2011	ICU patients/ hospitalised patients	10.0	7.8-11.1
NHS Diabetes Perioperative Guidelines[62]	2011	Surgical patients	10.0	6-10 (4-12 is acceptable)
An Endocrine Society Clinical Practice Guideline[63]	2012	Hospitalised patients	10.0	7.8-10.0
Society of Critical Care Medicine (SCCM)[64]	2012	ICU patients	10.0	6.1-8.3
American Society of Parenteral and Enteral Nutrition (ASPEN)[65]	2012	Hospitalised patients	10.0	7.8-10.0

2.3 Summary of evidence

(1) Hyperglycaemia in hospital is associated with worse outcomes, whether people are known to have diabetes or not.

(2) There is limited evidence for a threshold for starting intravenous insulin therapy in a medically unwell patient but the consensus view recommends initiation of intravenous insulin if the CBG is greater than 10.0 mmol/L.

(3) Target blood glucose levels have not been established in trials but there is consensus for a range between 6-10 mmol/L. This range should avoid the risks associated with both hyperglycaemia and hypoglycaemia.

Chapter 3: Recommendations for use of VRIII

Key Messages

1. Contact the diabetes team for advice if there is doubt about the best way to manage hyperglycaemia or if the blood glucose is not responding to treatment
2. Continue patients' usual basal* subcutaneous insulin whilst on VRIII and stop rapid acting or mixed insulins
3. Review VRIII frequently to ensure:
    a. Correct rates of infusion are achieving target glucose levels
    b. The ongoing need for the VRIII
    c. Safety measures are continually in place
    d. Hypoglycaemia is treated promptly and adequately and VRIII re-started within 20 minutes in order to prevent rebound hyperglycaemia and possible ketosis

[Basal Insulins: *Detemir (Levemir®), *Glargine (Lantus®),* Degludec (Tresiba®), *Insulatard®* Insuman Basal® or* Humulin I®]

3.1 Indications for VRIII in medical patients

The majority of acutely unwell medical patients can be managed without a VRIII. Avoid intravenous insulin if the patient is eating and drinking normally. Consult the diabetes team who may be able to adjust the patient's own insulin regime. Follow local policy or see Appendix 4 for management of hyperglycaemia if the criteria for use of a VRIII (Box 1) are not met.

Box 1. Indications for use of a VRIII

Indications

Hyperglycaemia in:

Patients with known diabetes or with hospital related hyperglycaemia unable to take oral fluid/food and for whom adjustment of their own insulin regime is not possible.

- Vomiting (exclude DKA)
- Nil by mouth and will miss more than one meal
- Severe illness with need to achieve good glycaemic control e.g. sepsis

Special circumstances*

- Acute coronary syndrome (follow local guidelines)
- TPN/enteral feeding
- Steroid use
- Pregnancy

*Take specialist advice from relevant teams (including diabetes team.)

3.2 Advantages of VRIII

1. Target driven glucose control for the specified indications, with potential to improve clinical outcomes
2. Avoidance of metabolic decompensation

3.3 Disadvantages of a VRIII

1. Frequent CBG monitoring and intravenous infusion is intrusive for patients
2. Difficult to manage if patient is eating (use with caution in this circumstance)
3. If target blood glucose not achieved; requires review of prescription for rate of insulin infusion
4. May prolong length of stay if used inappropriately

3.4 Potential Risks of a VRIII

1. Hyper- and hypoglycaemia due to inappropriate insulin infusion rates or inadequate monitoring
2. Rebound hyperglycaemia and possible ketoacidosis if intravenous access is lost or VRIII is stopped inappropriately
2. Fluid overload
3. Hypokalaemia and/or hyponatraemia
4. Infection related to intravenous line

3.5 Practical aspects of setting up a VRIII

3.5.1 How to set up a VRIII

(For ease of use by clinical staff this section is also supplied as a standalone appendix- Appendix 1)

Two registered nurses must check and prepare the VRIII and every time the rate of infusion is changed.

- INSULIN MUST BE DRAWN UP USING AN INSULIN SYRINGE. NO OTHER SYRINGE TO BE USED
- Draw up 50 units of prescribed Human Actrapid insulin* and add to 49.5 ml of 0.9% sodium chloride in a 50 ml luer lock syringe. Mix thoroughly
- This will provide a concentration of 1 unit/ 1 ml
- Complete the drug additive label in full; signed by 2 registered nurses and placed on the syringe barrel; not obscuring the numerical scale
- Prime through an appropriate giving set with a non-return valve
- Set up an intravenous insulin syringe-driver pump
- Discard any unused insulin solution after 24 hours

- Intravenous fluid must be administered using a volumetric infusion pump
- Delivery of the substrate solution and the VRIII must be via a single cannula or two lumens of a central line with appropriate one-way and anti-siphon valves
- Set the concurrent fluid replacement rate to deliver the hourly fluid requirements of the individual patient as prescribed which must take into account their individual circumstances. (See section 3.7 of main guideline). The rate must not be altered thereafter without senior advice
- Insulin should not be administered without substrate unless done in a critical care setting and upon senior advice
- Insulin must be infused at a variable rate aiming for a glucose of 6-10 mmol/L (acceptable range 4-12 mmol/L)
- Continue the substrate solution and VRIII until the patient is eating and drinking and back on their usual glucose lowering medications

*Although human Actrapid® is the most commonly used insulin in VRIII, Insulin Aspart®, Humulin S® and Insulin Lispro® can also be used as an alternative and have a licence for intravenous use. However these are more expensive alternatives.

In an attempt to increase safety, some hospital trusts in the UK use prefilled / pre-prepared insulin syringes for use in a VRIII. These are prepared in trust pharmacies with rigorous quality controls or have been procured from commercial sources. There is no current published data to evidence that this leads to increased safety when compared to syringes prepared at the time of need.

3.5.2 Suggested insulin infusion rates

Patients have different degrees of insulin sensitivity and insulin resistance related to weight, concurrent illness, medication (particularly steroids) etc. and may require a change in the rate of insulin infusion, depending on the blood glucose response to the initial rate.

Three insulin rates are recommended in Table 3

- Reduced rate for patients thought to be insulin sensitive
- Standard rate for most patients
- Increased rate for patients likely to be insulin resistant

Table 3. Suggested Scales for insulin infusion rate

Glucose mmol/L	Insulin Rates (ml/hour) Start on standard rate unless otherwise indicated				
	Reduced rate (for use in insulin sensitive patients e.g. ≤24 units per day	**Standard rate (first choice in most patients)**	**Increased rate (for insulin resistant patients e.g. ≥100 units per day)**	**Customised scale**	**Customised scale**
N.B. if a patient is on basal subcutaneous insulin – continue this alongside the VRIII					
< 4.0	0*	0*	0*		
4.1-8.0	0.5	1	2		
8.1-12.0	1	2	4		
12.1-16.0	2	4	6		
16.1-20.0	3	5	7		
20.1-24.0	4	6	8		
>24.1	6	8	10		

* Treat Hypoglycaemia and **once CBG >4.0 mmol/L restart IV insulin within 20 minutes**. The half life of intravenous insulin is very short (7-8 minutes) and restarting the VRIII promptly minimises the risk of ketosis.

These rates are starting points only and the prescribing doctor must be prepared to adapt the insulin infusion rate for the individual patient depending on the blood glucose response. Advice should be sought from the diabetes team if the target range is not achieved and maintained. The blood glucose response to the VRIII should be reviewed frequently and a doctor contacted to change the prescription if the target range is not achieved within the specified time frame.

If capillary blood glucose readings remain out of target:

1. Ensure that the cannula is patent
2. Ensure the infusion equipment is working appropriately
3. Ensure that the substrate infusion is running at the correct rate

If all the above criteria are correct, the insulin infusion rate should be altered as follows:

CBG above target (greater than12 mmol/L and not falling* on two or more consecutive occasions):

- Increase the insulin infusion rate to the next scale
- If the patient is already on the increased rate, prescribe a customised insulin infusion rate and seek advice from the diabetes team as soon as possible

*Take into account the initial CBG; for example, if this is 27 mmol/L it will take more than 3 hours for it to fall to target ranges and provided there is

a steady fall in the CBG the insulin rate should not be adjusted.

CBG consistently 'too tight' (CBG levels between 4 and 6 mmol/L on two or more consecutive occasions).

(Although these levels are within target this may be too low for many patients - particularly those with CVA or ACS.)

- Consider reducing to a lower insulin infusion rate
- If the reduced rate is already in use increase the substrate to 10% glucose
- Prescribe a customised insulin infusion rate and seek advice from the diabetes team as soon as possible. A VRIII may not be needed at all

3.5.3 Treatment of hypoglycaemia * during a VRIII

*Defined as CBG less than 4 mmol/L

a. Follow JBDS treatment of hypoglycaemia guideline available at: http://www.diabetologists-abcd.org.uk/subsite/JBDS_IP_Hypo_Adults_Revised.pdf

Box 2. Summary of Treatment of Hypoglycaemia in a patient who is Nil by Mouth

Give 75-100 ml of **20% glucose** over 15 minutes, (i.e. 300-400 ml/hr). A 100 ml preparation of 20% glucose is now available that will deliver the required amount after being run through a standard giving set. If an infusion pump is available use this, but if not readily available the infusion should not be delayed. Repeat capillary blood glucose measurement 15 minutes later. If it is still less than 4.0 mmol/L, repeat.

OR

Give 150-200 ml of **10% glucose** (over 15 minutes, i.e. 600-800 ml/hr). If an infusion pump is available use this, but if not readily available the infusion should not be delayed. Care should be taken if larger volume bags are used to ensure that the whole infusion is not inadvertently administered. Repeat capillary blood glucose measurement 15 minutes later. If it is still less than 4.0 mmol/L, repeat.

b. Stop the VRIII
Note the insulin infusion should generally not be stopped for more than 20 minutes. The half life of intravenous insulin is very short (7-8 minutes) and restarting promptly minimises the risk of ketosis. Aim restart once the CBG is above 4 mmol/L and the patient has recovered.

c. Step down to the next scale when the VRIII is restarted i.e. if using Standard Scale then step down to Reduced Rate Scale.

d. If recurrent hypoglycaemia occurs on the reduced rate scale either downgrade the scale further in the customised section, or use 10% glucose as the infusion fluid (downgrading the scale is the preferred option).

3.6 Maintaining safety during the use of a VRIII

Box 3. Essential measures for the safe maintenance of a VRIII

- Hourly monitoring of CBG
- Regular review of insulin infusion rate to achieve target range of glucose
- At least daily review of the need for the VRIII
- At least daily clinical review of patient including fluid status
- Daily urea and electrolytes

3.6.1 Frequency of capillary blood glucose monitoring

a. CBG levels should be checked hourly. This minimises the risk of uncontrolled hyperglycaemia, prompts a review of the infusion equipment and prescribed insulin rate if the trend is unsatisfactory and ensures prompt treatment of hypoglycaemia (patients may be unaware or too ill to alert staff).

b. Aim to achieve CBG within the range 6-10 mmol/L; 4-12 mmol/L is acceptable in certain situations*.

c. Consider insulin scale adjustment if CBG is not to target within 6 hours of commencing a VRIII or of subsequent scale change, unless there is clear evidence of steady improvement.

d. If levels are persistently >10 mmol/L or <6 mmol/L review the insulin rate, change the insulin prescription to achieve better BG control (Appendix 2) and seek help from the diabetes team.

***Caution in patients with ACS or stroke, who have worse outcomes if hypoglycaemic. Do not allow CBG to drop below 6 mmol/L.**

3.6.2 Measurement of capillary blood ketones Indications

1. Patients with **type 1** diabetes who are unwell or who develop persistent hyperglycaemia whilst in hospital (2 readings >12 mmol/L at least one hour apart) should have a baseline capillary blood ketone measurement with appropriate action taken (Table 4).

2. Patients with **type 2** diabetes may also be prone to ketone production if unwell. We recommend ketone testing in this group of patients when presenting with acute illness. We do not recommend the routine use of capillary blood ketone testing in hyperglycaemic patients with Type 2 diabetes who are not acutely unwell.

Table 4. Blood ketone results and actions to be taken

Blood ketones mmol/L	Action
<0.6	Normal
0.6-1.4	Check ketones in 2 hr
1.5-2.9	Risk of DKA; review patient management, consider reasons for high ketones, e.g. missed insulin dose, inadequate insulin dose and address these. Call diabetes team if in any doubt Check ketones in 1 hr and take action depending on the result
>3.0	Check venous bicarbonate or venous pH, change to DKA guidelines if required. Inform diabetes team

Some hospitals use urine ketones as an initial screen with blood ketones measured if urinary ketone levels are 2+ or more. Local guidelines should be followed.

If blood ketone testing is not available, urinary ketones may be used. If urine ketones are 2+ or more a venous blood gas must be taken to check bicarbonate and venous pH.

If the venous bicarbonate ($HCO3^-$) is below 15 mmol/L and/or venous pH less than 7.3, the patient has DKA. Follow the guideline 'The Management of Diabetic Ketoacidosis in Adults' (www.diabetologists-abcd.org.uk or www.diabetes.org.uk). Further management of this group of patients is beyond the scope of this guideline.

3.6.3 Frequency of patient review and the continuing need for the VRIII

This cohort of patients is likely to be elderly and have multiple co-morbidities which may be adversely affected by prolonged treatment with a VRIII.

Patients treated with a VRIII should be reviewed at least daily to:

- ensure progress and recovery in their presenting illness
- monitor fluid balance
- reassess the need for the VRIII

3.7 Choice of Concurrent Fluids

Aim of the fluid infusion:

- Avoid hypoglycaemia by providing substrate at a steady rate for the insulin infusion
- Maintain the fluid balance and electrolytes in the normal range
- Take the underlying medical condition into account when determining the choice of fluid, the infusion rate and the need for supplements

Once the rate of glucose infusion has been decided, the rate should NOT be altered unless there are concerns about fluid overload. Changing the type of substrate fluid frequently according to the CBG values is discouraged since it leads to highly variable capillary blood glucose readings. If the blood glucose is outside the target range, this should be corrected by altering the rate of insulin infusion, not the glucose containing substrate infusion.

3.7.1 Factors affecting the choice of fluid and rate of infusion

- Fluid status
    - Patients who are vomiting, pyrexial or dehydrated will need additional fluid, usually in the form of 0.9% NaCl. This can be run alongside the glucose infusion.
- Risk of fluid overload
    - Patients with heart failure or severe renal or hepatic impairment may be unable to tolerate standard volumes of fluid and it may be necessary to use 10% glucose to meet the substrate requirements.
    - Fluids containing 0.9% NaCl should be avoided in these patients unless specifically indicated.
    - Frail elderly patients are at particular risk of fluid overload. We recommend 25-30 ml/kg /24 hours (around 2 litres) [66, 67].
- Electrolyte replacement
    - Daily monitoring of electrolytes is required to enable fluid selection to take into account potassium and sodium requirements
    - Patients on a VRIII for more than 24 hours are likely to need fluid containing sodium chloride to avoid hyponatraemia
    - Fluids containing KCl should be selected to maintain serum potassium in the 3.5-5.0 range. The combination of glucose and insulin can lead to life threatening hypokalaemia

3.7.2 Recommended fluid

In line with the guideline: 'Management of adults with diabetes undergoing surgery and elective procedures' April 2011 (currently under review), the VRIII guideline writing group recommends balanced electrolyte solutions (depending on the potassium requirement):

0.45% NaCl with 5% glucose and 0.15% KCl (20 mmol/L)

Or

0.45% NaCl with 5% glucose with 0.3% KCl (40 mmol/L)

However, these fluids are not yet widely available and acceptable alternatives are:

5% glucose with 20 mmol/L or 40 mmol/L KCl

Or

0.18% NaCl with 4% glucose with 0.15% KCl (20 mmol/L) OR 0.18% NaCl with 4% glucose with 0.3% KCl (40 mmol/L).

It is acknowledged that the majority of the readily available fluids are not ideal. A detailed summary of the pros and cons of different fluid options is contained in Appendix 6 of 'Management of adults with diabetes undergoing surgery and elective procedures' guideline, April 2011 (currently under review).

Table 5. Summary of Fluid Recommendations

Patient group	Fluid recommendation	
No concern of fluid overload	**First choice:** 0.45% NaCl and 5% glucose with 0.3% KCl (40 mmol/L) at 125 ml/hr if serum K is 3.5-5.5 mmol/L	**Second choice:** 5% glucose with 40 mmol/L KCl at 125 ml/hr if serum K is 3.5-5.5 mmol/L
	Aim to keep K 4.0 - 5.0 mmol/L If serum K >5.5 no additional K but reassess serum K regularly If serum K <3.5 senior review as extra potassium needs to be given	
Risk of fluid overload	Consider whether VRIII is essential or whether a subcutaneous insulin regime can be used Use fluid rate of 83 ml/hr or less for frail elderly or Consider 10% glucose as substrate at 42 ml/hr to reduce volume further if required If hypoglycaemia occurs on VRIII, reduce VRIII scale to 'insulin sensitive' regime Do not infuse insulin without substrate unless in HDU/ITU setting	
Hyponatraemia or serum sodium falls by >3 mmol/L in 24 hr	Consider whether VRIII is essential or whether a subcutaneous insulin regime can be used If available use a mixed solution with higher sodium content such as 0.9% NaCl with 5% glucose and 0.3% KCl depending on potassium requirement OR Add 0.9% NaCl 42 ml/hr to run alongside glucose infusion, provided fluid overload is not a concern	
Renal or hepatic failure	Use 'insulin sensitive' VRIII scale as these patients may have an increased risk of hypoglycaemia Seek specialist advice from nephrology/hepatology team regarding fluid management	

3.8 Duration of the VRIII

- The aim should be to convert back to standard (oral or subcutaneous) medication as soon as patients are able to eat and drink, provided the VRIII can be discontinued safely
- Avoid recommencing a VRIII if the patient becomes hyperglycaemic when the VRIII is withdrawn. Consult the diabetes team or see Appendix 4
- Consult the diabetes team if the patient had suboptimal diabetes control prior to the VRIII or has newly diagnosed diabetes

3.9 Management of other diabetes medications during a VRIII

- **Withhold usual diabetes treatment during VRIII**

  Most patients will have their usual diabetes medication completely withheld whilst they are on a VRIII including oral and injectable hypoglycaemic drugs as well as most forms of insulin. The exception is long acting analogue or isophane basal insulin, which should be continued (see below).

- **Continue basal long-acting analogues* or isophane insulin** in patients usually taking multiple daily injections of insulin (MDI or basal-bolus insulin therapy).**
- This may help control blood glucose during the VRIII and will avoid rebound hyperglycaemia once the patient's usual diabetes treatment is restarted[68]. This can help reduce the overall length of stay.

[*Detemir (Levemir®), *Glargine (Lantus®),* Degludec (Tresiba®), ** Insulatard®*** Insuman Basal® or** Humulin I®]

3.10 Transferring from a VRIII to subcutaneous insulin and/or oral treatment

Appendix 2 provides detailed guidance on transfer to usual diabetes treatment

Most patients will restart their usual diabetes treatment following a VRIII. Consult the diabetes team in the following circumstances for additional advice on ongoing management:

- diabetes control was sub-optimal prior to admission (recent pre-admission HbA1c >58 mmol/mol [7.5%])
- the patient can no longer manage their previous regime
- the patient cannot recall their previous insulin regime
- contraindications to previous therapy or new medical conditions have arisen
- insulin commenced on this admission

It is important that patients receive education and support in self-management of diabetes, that they are confident to self-inject prior to discharge, and that follow-up support is available from appropriately trained professionals.

Box 4. The principles of a safe step down

- Patient must have recovered from the precipitating illness/condition and be eating and drinking reliably
- Blood glucose targets must be achieved on the VRIII

For insulin treated patients

- Background insulin should have been continued. If it has not been continued or patient insulin naïve, a background insulin either within a mixed insulin or as part of a basal bolus regime MUST be given prior to stopping the VRIII
- VRIII should only be discontinued 30 minutes after subcutaneous insulin has been given. This should ideally be at a meal time, after short-acting insulin or mixed insulin has been given. Avoid stopping VRIII at bedtime where there is less observation by staff
- For insulin naïve patients the insulin dose can be calculated on a weight basis or by calculating the insulin requirement over the last few hours on the VRIII. See Appendix 2 for details
- If the blood glucose rises after VRIII is discontinued, do not restart the infusion. Contact the diabetes team for advice

For non-insulin treated patients

- Give normal treatment prior to discontinuing VRIII
- Consult the diabetes team for detailed guidance if control prior to admission was suboptimal

3.11 Safe Use of Insulin

Errors in insulin prescribing are very common and insulin is one of the five highest-risk medications in the inpatient environment. The wide range of insulin preparations and administration devices increases the potential for error, and it is essential that staff are trained in the safe use of insulin. Dose errors can occur, such as where insulin is incorrectly prescribed, and management errors can cause harm through over - or under-dosing with insulin causing abnormal blood sugars.

The National Patient Safety Agency (NPSA) has made recommendations to promote the safe use of insulin and the Department of Health has added death or severe harm as a result of insulin maladministration to the list of 'Never Events' that are monitored by the NHS.

It is important that health care professionals follow this guidance and refer to local protocols to ensure safe prescribing is maintained.

We recommend that all healthcare professionals caring for patients with diabetes undertake all the relevant modules within the diabetes suite of e-learning available via the healthcare e-academy[69-72].

Chapter 4: Special Circumstances

4.1 Total Parenteral Nutrition (TPN)

Although detailed advice regarding total parenteral nutrition is beyond the scope of this guideline it is widely recognised that although TPN improves the nutritional status of critically ill patients[73], it is associated with the short term complication of hyperglycaemia[74].

4.1.1 Monitoring

- All patients receiving TPN should have their blood glucose levels checked at least twice in 24 hours but the frequency of monitoring should be increased if hyperglycaemia develops or if the patient has pre-existing diabetes. Achieving optimum glycaemic control can reduce morbidity and mortality in patients receiving TPN[73].
- TPN provides essential glucose and electrolytes required in a 24 hour period. However, if the patient is fluid deplete, it may be necessary for additional fluids to be infused.
- If the blood glucose is elevated a VRIII will be required, in which case CBG should be monitored hourly. As for all patients receiving a VRIII, these patients will require daily venous blood glucose and urea and electrolytes. In addition other biochemical tests, e.g. micronutrients etc. may be needed. Consult your local nutrition and diabetes teams.

4.1.2 Delivery

- Intravenous Insulin must always be infused with a substrate; therefore if TPN is delivered via a multi lumen central line, the insulin must also be infused via its own dedicated central line lumen.
- If the TPN is to be delivered via a PICC line, it may be necessary to consider a double lumen PICC line.

4.1.3 Cautions

1. If the TPN is stopped for any reason this will put the patient at risk of hypoglycaemia. In this situation the VRIII should be discontinued and blood glucose monitored hourly until the TPN can be reinstated or other steps taken to avoid hypoglycaemia. If hypoglycaemia develops – treat according to JBDS guideline 'The hospital management of hypoglycaemia in adults with diabetes mellitus'. (www.diabetologists-abcd.org.uk or www.diabetes.org.uk) or see Appendix 2 for summary of action to be taken.
2. Patients on long acting insulin e.g. Detemir (Levemir®), Glargine (Lantus®). Degludec (Tresiba®), or intermediate acting insulins such as Insulatard®, Insuman Basal® or Humulin I® should continue these in addition to the VRIII.

4.1.4 Stepping down from a VRIII in patients on Total Parenteral Nutrition

Once glycaemic control is obtained patients should be stepped down to subcutaneous insulin as soon as possible. The regime chosen should reflect the fact the caloric intake will be a continuous infusion over 24 hours rather than, for instance, as 3 meals a day. The usual regimens of basal bolus or twice daily premixed insulin will not be suitable. In this special circumstance twice daily isophane insulin is recommended.

Once glycaemic control has been obtained on an intravenous infusion:

- Calculate the total daily dose of insulin used over 24 hours on TPN and prescribe as isophane insulin e.g. Humulin I or Insulatard
- Give 50% of the total daily dose at the start of the feed and 50% 12 hours later
- Contact your local diabetes team for further advice

4.2 Patients on Continuous Subcutaneous Insulin Infusions (CSII) also known as Insulin Pumps

CSII is not recommended in situations where self-management is unsafe as in the following:

- Acute illness preventing self-management
- Diabetic Ketoacidosis (DKA)

- Major surgery involving a general anaesthetic
- Patients with reduced conscious level or confusion

If a VRIII is required, this should be commenced prior to removing the CSII infusion set from subcutaneous site. Once removed, the subcutaneous pump should be stored in a safe and secure place.

- ALWAYS commence VRIII before disconnecting CSII pump, since if the CSII pump is discontinued without an alternative provision of insulin, diabetic ketoacidosis is likely to develop within a short space of time because there is no reservoir of long-acting insulin.
- Once patient is well enough to self-manage recommence CSII and stop VRIII (as per step-down guidance)
- Prior to resuming CSII, fill a new reservoir and re-site cannula
- Recommence CSII prior to a meal to allow a bolus to be given with the meal
- Discontinue the VRIII 30 minutes later

Check the BG 2 hours after the initial meal time bolus. If the BG is >14, pump manufacturer's hyperglycaemia guidelines should be followed. A correction should be given via the pump and glucose checked again 1 hour later. If glucose has risen or no improvement is seen, the cannula should be re-sited and the patient should be checked for ketones. This is to establish that the cannula is patent as the cannula may bend/kink on insertion, preventing insulin infusion.

- Patients who are no longer able to self-mange e.g. patients who have had a stroke, should be converted to an appropriate insulin regimen by the diabetes team.

Appendix 1: How to set up a VRIII

Two registered nurses must check and prepare the VRIII and every time the rate of infusion is changed.

- INSULIN MUST BE DRAWN UP USING AN INSULIN SYRINGE. NO OTHER SYRINGE TO BE USED
- Draw up 50 units of prescribed Human Actrapid insulin* and add to 49.5 ml of 0.9% sodium chloride in a 50 ml luer lock syringe. Mix thoroughly
- This will provide a concentration of 1 unit/1ml
- Complete the drug additive label in full; signed by 2 registered nurses and placed on the syringe barrel; not obscuring the numerical scale
- Prime through an appropriate giving set with a non-return valve
- Set up an intravenous insulin syringe-driver pump
- Discard any unused insulin solution after 24 hours

- Intravenous fluid must be administered using a volumetric infusion pump
- Delivery of the substrate solution and the VRIII must be via a single cannula or two lumens of a central line with appropriate one-way and anti-siphon valves
- Set the concurrent fluid replacement rate to deliver the hourly fluid requirements of the individual patient as prescribed which must take into account their individual circumstances. (See section 3.7 of main guideline). The rate must not be altered thereafter without senior advice
- Insulin should not be administered without substrate unless done in a critical care setting and upon senior advice
- Insulin must be infused at a variable rate aiming for a glucose of 6-10 mmol/L (acceptable range 4-12 mmol/L)
- Continue the substrate solution and VRIII until the patient is eating and drinking and back on their usual glucose lowering medications

*Although human Actrapid® is the most commonly used insulin in VRIII, Insulin Aspart®, Humulin S® and Insulin Lispro® can also be used as an alternative and have a licence for intravenous use. However these are more expensive alternatives.

In an attempt to increase safety, some hospital trusts in the UK use prefilled / pre-prepared insulin syringes for use in a VRIII. These are prepared in trust pharmacies with rigorous quality controls or have been procured from commercial sources. There is no current published data to evidence that this leads to increased safety when compared to syringes prepared at the time of need.

Appendix 2: Safe discontinuation of VRIII

General Principles

Review diabetes treatments in all patients admitted with unstable blood sugars, and refer to diabetes in-patient team

Do not discontinue the VRIII until 30 minutes after usual diabetes treatment has been restarted, and the patient is able to eat and drink

Check the CBG one hour after discontinuing VRIII and at least four times for first 24 hours after VRIII has been discontinued, to ensure that there is no rebound hyperglycaemia i.e. pre-meal and pre-bed

Restarting Oral and Injectable Hypoglycemic Agents

Recommence oral and injectable hypoglycaemic agents once the patient is able to eat and drink.

Ensure that no contra-indications to the previous hypoglycaemic therapy have arisen. Review diabetes treatment in all patients admitted with unstable blood sugars, and refer to the in-patient diabetes team.

Table 6. Restarting Therapy in Patients with Type 2 Diabetes

	Diet alone	**Oral hypoglycaemic therapy**	**GLP-1 mimetics (injectable)**
Good Control (HbA1c<59 mmol/mol or 7.5%)	Discontinue VRIII when the patient is stable	Restart usual diabetes treatment when a meal is due Do not stop VRIII until at least 30 minutes after treatment has been given and the patient has eaten Some patients may also be on basal insulin (see Table 6 for additional advice)	Most patients will be taking additional OHG treatments, which should be restarted when a meal is due GLP-1 mimetics should be recommenced at the usual dose and time Do not stop VRIII until at least 30 minutes after treatment has been given and the patient has eaten
Suboptimal control (HbA1c>59 mmol/mol or 7.5%)	In addition to above, discuss with local diabetes in-patient team Patient may need additional hypoglycaemic therapy depending on individualised goals		
Monitor blood glucose	CBG should be checked one hour after discontinuing VRIII and at least four times for the next 24 hours, to ensure that there is no rebound hyper- or hypoglycaemia i.e. pre-meal and pre-bed		
Considerations	Dose of insulin secretagogues e.g. sulphonylureas or glinides may need to be reduced if food intake is likely to be limited Metformin should only be recommenced when eGFR is >30 ml/min/1.73 m^3 Review GLP1 and DDP4 inhibitors if patient was admitted with suspected pancreatitis Review glitazone therapy if patient was admitted with heart failure, has macular oedema or has been admitted with a lower limb fracture following a fall Review dapagliflozin therapy if patient was admitted with urogenital infection		

Restarting insulin for patients previously on subcutaneous insulin

Convert to subcutaneous insulin when the patient is able to eat and drink and has managed at least one meal. Ideally the transfer should take place at a mealtime, usually breakfast or lunch. Ensure that background insulin (either long acting analogue or isophane) has been given before the VRIII is withdrawn[75].

The VRIII should be continued until at least 30 minutes after the administration of a subcutaneous dose of insulin. This is to avoid rebound hyperglycaemia.

Most patients will restart their normal regime (see Table 6 for detailed advice). The pre-admission dose of insulin may need to be reduced if food intake is likely to be limited or the patient was admitted with low blood sugars.

Review diabetes treatment in all patients admitted with unstable blood glucose or HbA1c > 59 mmol/mol (7.5%), and refer to the diabetes in-patient team.

Table 7. Guidance for restarting insulin in patients according to previous regimes

	Good Control (HbA1c <59 mmol/ mol or 7.5%)	Suboptimal Control	Monitoring blood glucose
Basal Insulin	Restart usual dose of insulin when it is due (usually with either breakfast or evening meal). Do not stop VRIII until at least 30-60 minutes after insulin has been given and patient has eaten If it is necessary to stop VRIII but the basal insulin is not due for several hours, give half the usual dose of basal insulin. This will provide background insulin until the usual dose can be recommenced	In addition, discuss with local diabetes in-patient team. Insulin regime may need adjusting	CBG should be checked one hour after discontinuing VRIII and at least four-hourly for the next 24 hours, to ensure that there is no rebound hyper- or hypo- glycaemia
Once or Twice Daily Mixed Insulin	Restart usual dose of insulin together with a meal (either breakfast or evening meal). Do not stop VRIII until at least 30-60 minutes after insulin has been given and the patient has eaten If it is necessary to stop VRIII at lunchtime, give half the usual breakfast dose of mixed insulin. This will provide essential background insulin until the usual dose can be recommenced		
Multiple daily insulin injections **(MDI or basal bolus)**	Restart usual diabetes treatment together with a meal Basal insulin will usually have been continued. Restart bolus dose of insulin together with the next meal. Do not stop VRIII until at least 30-60 minutes after bolus insulin has been given and the patient has eaten If basal insulin has been stopped, background insulin must be restarted prior to stopping VRIII Ideally, continue the VRIII until basal insulin is given and a meal is due, and stop at least 30-60 minutes after basal and bolus insulin is restarted If it is necessary to stop the VRIII, but the basal insulin is not due for several hours, give half the usual daily dose of basal insulin, along with a meal and bolus insulin. This will provide essential background insulin until the usual dose can be recommenced		
Insulin Pump (CSII)	Restart usual basal rate via CSII Do not stop VRIII until at least 30 minutes after insulin has been recommenced via CSII Give bolus insulin according to patient's usual regime. It is not usually necessary to wait until a mealtime to switch back to CSII therapy Avoid restarting CSII at bedtime		

Calculating subcutaneous insulin dose in insulin-naïve patients, or where insulin regime needs altering because of sub-optimal control

It is important that patients starting insulin receive education and support in self-management of diabetes, that they are confident to self-inject prior to discharge, and that follow-up support is available from appropriately trained professionals

If the insulin dose is uncertain because the patient is new to insulin or has previously had poor control there are two possible ways of calculating the starting dose. There is no evidence on which to base a recommendation. The following guidelines are suggestions only, and detailed advice should be sought from local protocols and the diabetes team.

The options are:

Method A - weight based calculation

Method B - based on insulin requirements during the stable phase of the VRIII

- **Step 1- Calculate the total daily dose requirement (TDD) using either method A or B**
- **Step 2- Use the TDD to convert the patient to either a premixed twice daily insulin regime or a multiple dose regime - basal bolus**
    - o For a basal-bolus regime, 50% of the total insulin requirement is usually given as basal insulin, and the remainder as rapid-acting insulin, divided equally between breakfast, lunch and evening meal
    - o For a twice-daily, pre-mixed insulin regime, patients usually need 60% of the total insulin requirement at breakfast and the remaining 40% with the evening meal
- **Step 3- Review response to any new insulin regime prior to discharge**
    - o CBG should be checked one hour after discontinuing VRIII, at least four-hourly for the first 24 hours after VRIII has been discontinued, and between two and four times a day for all in-patients on subcutaneous insulin
    - o Adjust the doses of insulin according to blood glucose measurements. A target of 6.0-10.0 mmol/L is appropriate for most in-patients, but patients with significant co-morbidities may benefit from less stringent targets (4.0-12.0 mmol/L)
    - o Ensure the patient and carers are confident in using the insulin delivery device prior to resuming self-management. Refer to the inpatient diabetes team for education and support

Method A: Calculating estimated insulin dose from patient's weight

Insulin requirements for an adult patient can be calculated from a weight-based formula (see worked example).

- Frail elderly patients, renal failure (CKD stage 4 or 5), severe hepatic failure, newly diagnosed Type 1 diabetes:

  Total daily insulin dose = 0.3 x body weight in kg

- All other adult patients: Total daily insulin dose = 0.5 x body weight in kg

Worked Example using method A:

Patient with CKD Stage 4 weighs 100 kg	100 kg
Total daily insulin requirement (TDD) = 0.3 x body weight	0.3 x 100 **= 30 units**
Basal bolus insulin regime (MDI)* Give half of TDD as basal insulin and divide the remainder by three for bolus doses with each meal	Basal dose: 30 ÷ 2 **= 15 units** Bolus dose: 15 ÷ 3 = **= 5 units with each meal**
Twice-daily pre-mixed insulin regime* Give 60% of total daily requirement (TDD) with breakfast and 40% with evening meal	Breakfast dose: 60% **= 18 units** Evening Meal: 40% **= 12 units**

*For specific insulin brands to be used- see local protocols and stock lists or seek advice of your local diabetes team

Method B: Calculating estimated insulin dose from insulin requirements during the VRIII

An estimate of the daily insulin requirement can be estimated from the last 6 hours of the VRIII as follows:

Divide the total dose of insulin administered in last 6 hours of the VRIII by 6 to calculate average hourly dose of insulin. Multiply this by 20 (not 24, to reduce risk of hypoglycaemia) to estimate the patient's total daily insulin requirement. A further correction may be needed in some patients, depending on individual insulin sensitivity, previous degree of glycaemic control and severity of intercurrent illness.

Worked example using method B:

Total dose of insulin administered in last 6 hours (6 times hourly rate)	12 units
Divide by 6 to calculate hourly dose	12 ÷ 6 = 2 units
Multiply by 20 (not 24 to reduce risk of hypoglycaemia) to estimate **total daily insulin requirement TDD**	2 x 20 **= 40 units**
Basal bolus insulin regime (MDI)* Give half of TDD requirement as basal insulin and divide the remainder by three for bolus doses with each meal	Basal dose: 40 ÷ 2 **= 20 units** Bolus dose: 20 ÷ 3 **= 7 units with each meal**
Twice-daily pre-mixed insulin regime* Give 60% of TDD with breakfast and 40% with evening meal	Breakfast dose: 60% **= 24 units** Evening Meal: 40% **= 16 units**

*For specific insulin brands to be used- see local protocols and stock lists or seek advice of your local diabetes team

Patients on continuous subcutaneous insulin infusion (CSII, insulin pump)

- The inpatient diabetes team should be involved with all patients on a CSII, to give individual advice
- In most patients, the previous basal subcutaneous insulin regime should be restarted via the CSII. Continue the VRIII for at least 30 minutes after CSII is restarted to avoid rebound hyperglycaemia
- It is not always necessary to wait until a mealtime to switch back to CSII. Avoid restarting CSII at bedtime because of the risk of rebound hyperglycaemia overnight
- The CSII should not be recommenced until the patient is capable of managing it. Consult the patient about their pump management as patients are usually very knowledgeable about their device

Appendix 3. Management of hyper - and hypoglycaemia following discontinuation of the VRIII

Hyperglycaemia post VRIII

Capillary Blood Glucose (CBG) should be checked one hour after discontinuing VRIII and at least four times for the next 24 hours to ensure that there is no rebound hyperglycaemia i.e. pre-meal and pre-bed.

DO NOT recommence the VRIII if hyperglycaemia recurs unless the patient is clinically unwell.

General Guidance

1. Ensure that VRIII was discontinued appropriately with usual medication recommenced. Risk of rebound hyperglycaemia and possible ketoacidosis if intravenous access is lost unexpectedly or VRIII is stopped inappropriately.
2. If patient was previously on a basal insulin ensure this was continued with no gap in administration during VRIII.

   If basal insulin was omitted in error this must be restarted before the VRIII is discontinued. If the basal insulin is not due for several hours, give half the usual dose of basal insulin, along with a meal and bolus insulin. This will provide essential background insulin until the usual dose can be recommenced.
3. Be aware that diabetes control may have been suboptimal control prior to admission. Check HbA1c and consider adjusting usual medication. Seek advice from the diabetes team for optimisation of their diabetes medication and ongoing management.

Specific Guidance

Blood glucose greater than 12.0 mmol/L with blood ketones less than 3.0 mmol/L or urine ketones no more than ++

Type 1 diabetes: give subcutaneous rapid acting analogue insulin *. Assume that 1 unit will drop blood glucose by 3 mmol/L BUT wherever possible take advice from the patient about the amount of insulin normally required to correct high blood glucose.

Recheck the blood glucose 1 hour later to ensure it is falling. Repeat the subcutaneous insulin dose after 2 hours if the blood glucose is still above 12.0 mmol/L. In this situation the insulin dose selected should take into account the response to the initial dose – consider increasing the dose if the response is inadequate. Recheck the blood glucose after 1 hour. If it is not falling consider re-introducing VRIII.

Type 2 diabetes: give 0.1 units/kg of subcutaneous rapid acting analogue Insulin *, and recheck blood glucose 1 hour later to ensure it is falling.

Repeat the subcutaneous insulin after 2 hours if the blood glucose is still above 12.0 mmol/L. In this situation the insulin dose selected should take into account the response to the initial dose – consider doubling the dose if the response is inadequate.

Repeat the blood glucose after another hour. If it is not falling consider re-introducing VRIII.

** (rapid acting analogue insulin eg Novorapid®, Humalog®, Apidra®)*

Hypoglycaemia post VRIII

- VRIII is not indicated for treatment of hypoglycaemia
- Should hypoglycaemia occur following discontinuation of VRIII follow JBDS treatment of hypoglycaemia guidelines available at: http://www.diabetologistsabcd.org.uk/subsite/JBDS_IP_Hypo_Adults_Revised.pdf
- Establish cause of hypoglycaemia
- Consider adjusting usual medication especially if patient's dietary intake is reduced from pre-admission
- Patients with severe (less than 3.0 mmol/L) or recurrent hypoglycaemia must be referred to the diabetes team

Appendix 4. Quick reference tool for the use of a VRIII

Absolute Indications

1. NBM Type 1 diabetes >1 missed meal
2. Type 1 diabetes with recurrent vomiting (exclude DKA)
3. Type 1 or 2 diabetes and severe illness with need to achieve good glycaemic control e.g. sepsis

Special circumstances: For ACS, stroke, TPN/enteral feeding/steroids and pregnancy, follow local guidelines and seek advice from the diabetes team

Aim

CBG in range 6.0-10.0 mmol/L
(4.0-12.0 mmol/L acceptable)
Avoid hypoglycaemia (CBG <4.0 mmol/L)
Limit use to < 24 hours where possible
Try to avoid using in those patients able to eat and drink

VRIII use

1. Withhold usual diabetes treatment during the VRIII **BUT CONTINUE the basal (long-acting) insulin** (see Table 1 overleaf)
2. Prescribe the VRIII + fluids to go with this (see Tables 2 and 3 overleaf)
3. **CBGs must be monitored hourly** whilst the VRIII is in use
4. **Review the patient within 6 hours to make sure that CBGs are in target range.**
    a. If not, ask yourself
        i. Is the infusion running as prescribed? (check lines are patent and the infusion fluid is correct)
        ii. Do I need to adjust the insulin infusion rate?
            1. For CBGs persistently above 12 .0 mmol/L and NOT falling
                a. Upgrade the scale and review again within 6 hours
                b. Check ketones 4 hourly if have Type 1 diabetes, at least once if Type 2
            2. For CBG < 4.0 mmol/L i.e. hypoglycaemia
                a. Stop the VRIII and treat the hypo as per local hypo guidelines
                b. NOTE the VRIII should generally not be stopped for >20 minutes
                c. STEP DOWN to the next scale when the VRIII is restarted – if you are already using the lowest pre prescribed scale, then use the customised section to downgrade further
                d. Review again within 6 hours
5. **Check electrolytes daily** (at risk of hyponatraemia and hypokalaemia)
6. **Review the need for the VRIII at least once daily –** if not sure, ask the diabetes team for help
7. **Review the fluid status daily:** take into account whether your patient is dehydrated or at risk of fluid overload (see Table 3 overleaf)

Stopping the VRIII

8. Ensure the patient is able to eat and drink
    a. CBGs are in the range 6.0-10.0 mmol/L (4.0-12.0 mmol/L acceptable)
    b. That discontinuation takes place at a mealtime (preferably breakfast or lunch but evening meal is acceptable)
9. For
    a. **Insulin treated patients –** Background (long-acting) insulin should have been continued, if not, this MUST be given prior to discontinuation of the VRIII. Give rapid-acting insulin with the meal and then stop the VRIII 30 minutes later
    b. **CSII (insulin pump) treated patients –** involve the diabetes team. Reconnect the CSII, start the normal basal sc regimen, give a bolus dose of insulin with the meal and then stop the VRIII 30 minutes later
    c. **Non insulin treated patients –** restart usual treatment. Ensure that no contra-indications to the previous hypoglycaemic therapy have arisen (see Table 4 overleaf)
10. Check
    a. CBG one hour after discontinuing the VRIII and 4 hourly for the next 24 hours to ensure there is no rebound hyperglycaemia
    b. If the blood glucose rises after the VRIII is discontinued, do not restart the infusion unless the patient is clinically unwell Review the need to change medication or contact the diabetes team for advice at the earliest opportunity

PLEASE CONTACT THE DIABETES TEAM

1. **If you are unable to achieve CBGs within target range**
2. **If your patient requires a VRIII for >24 hours**
3. **If diabetes control was suboptimal prior to admission (i.e. recent pre admission HbA1c >59 mmol/mol)**

Table 1. Examples of long acting or 'background' insulin

Insulin name	Lantus (Glargine), Levemir (Detemir), Degludec, Insulatard, Humulin I, Insuman Basal

Advice on long acting or 'basal' insulin

If the patient is on basal insulin, **this must be continued** alongside the VRIII.

If the basal insulin was omitted in error this must be restarted before the VRIII is discontinued. If the basal insulin is not due for several hours and you want to stop the VRIII, then give half the usual dose of basal insulin along with the meal and dose of rapid acting insulin. This will give essential background insulin until the usual dose can be recommenced.

Table 2. Suggested Insulin Infusion Rates

Glucose mmol/L	Insulin Rates (ml/hour) Start on standard rate unless otherwise indicated				
	Reduced rate (for use in insulin sensitive patients e.g. ≤24 units per day	**Standard rate (first choice in most patients)**	**Increased rate (for insulin resistant patients e.g. ≥100 units per day)**	**Customised scale**	**Customised scale**
N.B. if a patient is on basal subcutaneous insulin – continue this alongside the VRIII					
< 4.0	0*	0*	0*		
4.1-8.0	0.5	1	2		
8.1-12.0	1	2	4		
12.1-16.0	2	4	6		
16.1-20.0	3	5	7		
20.1-24.0	4	6	8		
>24.1	6	8	10		

Advice on when to change the scale

1. Review the CBG trend within 6 hours after starting the VRIII

2. Aim to achieve target 6.0-10.0mmol/L (4.0-12.0 mmol/L acceptable)

a. If CBGs within target range i.e. 6.0-10.0 mmol/L (4.0-12.0 mmol/L acceptable) no need to change

b. **If CBGs above target range but still falling**, no immediate need to change, review again within 6 hours

c. **If CBGs above target range and not falling**, upgrade the scale e.g. if the patient is on the standard rate you would upgrade to the increased rate. If the patient is already on the increased rate write up a new (further increased) scale in the customised section. Cross off any previous used scales to avoid confusion.

*If the CBGs have fallen below 4.0 mmol/L i.e. the patient has had a hypo, stop the VRIII and treat the hypoglycaemia. **As soon as the CBG is >4** mmol/L restart the VRIII BUT at a reduced rate e.g. if the patient was on the standard rate when they had their hypo, restart the VRIII at the reduced rate. If the patient was already on the reduced rate scale, write up a new (further reduced) scale in the customised section. N.B. The half-life of intravenous insulin is very short (7-8 minutes) so the VRIII must be started as soon as possible after the CBG rises >4 mmol/L to minimise the risk of ketosis.

Table 3. Choice of infusion fluid

Choice	Serum K level (mmol/L)	Infusion fluid	Infusion rate (ml/hour)
1	3.5-5.5	1 Litre 0.45% NaCl with 5% glucose and 0.3% KCl (40 mmol/L)	125
If infusion fluid 1 is not available use choice 2 as below			
2	3.5-5.5	1 litre 5% glucose with 0.3%KCl (40 mmol/L)	125

Note

If K is >5.5 mmol/L – no K is to be added to the infusion fluid
If K is <3.5 mmol/L – senior review needed as extra potassium needs to be given

Caution in those with eGFR <20 ml/min- may need less K

You must take into account the patient's individual circumstances in terms of fluid requirements (below are suggestions and not a substitute for a thorough clinical assessment)

1. **Dehydrated patient**
   Additional fluid required usually in the form of 0.9% NaCl. This can run alongside the glucose infusion
2. **Frail elderly patient at risk of fluid overload**
   Reduce infusion fluid rate to 83 ml/hr i.e. 2 litres per 24 hours
3. **Patients with severe heart or renal failure**
   May not be able to tolerate standard volumes of fluid. It may be necessary to use 10% glucose instead
   This should be prescribed as 500 ml of 10% glucose with 20 mmol/L KCl to run at 42 ml/hr

Table 4. Ensure no contraindications to restarting 'usual medication'

Considerations	Dose of insulin may need to be reduced if food intake is likely to be less than normal Dose of insulin secretagogues may need to be reduced if food intake is likely to be limited Metformin should only be recommenced when the eGFR is >30 ml/min. Reduce the dose to 500 mg bd if the eGFR is <45 ml/min Review the GLP-1 and DPP4 - inhibitors if the patient was admitted with suspected pancreatitis Review glitazone therapy if the patient was admitted with heart failure or lower limb fracture or has known macular oedema Review dapagliflozin therapy if the patient was admitted with a urogenital infection

Abbreviations

VRIII	Variable rate intravenous insulin infusion
CBG	Capillary blood glucose
CSII	Continuous subcutaneous insulin infusion
SC	Subcutaneous

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