Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust


# Effect of Diabetes Care on Surgical Outcomes

## or Peri-operative Glucose Control - Is it Important?

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# Data from Public Health England

- People with diabetes are
  - Less likely to be offered day case surgery
  - More likely to have emergency surgery
  - Have a longer LOS following surgery
  - Have higher rates of 28-day readmissions following surgery

Variation in Inpatient Activity: Diabetes. http://www.yhpho.org.uk/resource/view.aspx?RID=105866

Last accessed 20th Sept 2015

# Do Peri-Operative High Glucose Levels Cause Harm?

- High pre-operative glucose or HbA1c has been related to adverse outcomes following
  - spinal surgery
  - vascular surgery
  - colorectal surgery
  - cardiac surgery
  - trauma
  - mastectomies
  - foot and ankle
  - neurosurgery
  - transplant surgery
  - HBP surgery
  - cholecystectomy
  - cardiac surgery

Walid MS et al J Hosp Med 2010;5:E10-E14
O'Sullivan CJ et al Europ J of Vasc Endovasc Surg 2006;32:188-197
Gustafsson UO et al Brit J Surg 2009;96:1358-1364
Halkos ME et al Ann of Thorac Surg 2008;86:1431-1437
Kreutziger J et al J Trauma 2009;67(4):704-8
Vilar-Compte et al Am J Infect Control 2008;36(3):192-198
Park C et al Transplantation 2009;87(7):1031-1036
Ambiru S et al J Hosp Infect 2008;68(3):230-233
Chaung SC et al J Formos Med Ass 2004;103(8):607-612
Shibuya N et al J Foot Ankle Surg 2013;52(2):207-211

# Excess Mean Length of Stay in Diabetes Inpatients Aged 18 – 60 Years

## 269,265 Diabetes Discharges and 4,411,593 Matched Controls

| | Mean LOS (days) | | | Excess LOS (days) | | n | | |
|---|---|---|---|---|---|---|---|---|
| | E10 | E11 | C | E10 | E11 | E10 | E11 | C |
| Surg. | 5.4 (0.1) | 5.1 (0.1) | 4.2 (0.2) | 1.2 | 0.9 | 18,032 | 32,135 | 1,501,453 |
| T &O | 4.8 (0.1) | 5.3 (0.2) | 4.6 (0.1) | 0.2 | 0.7 | 8,178 | 12,203 | 885,606 |
| GM | 4.8 (0.2) | 5.4 (0.2) | 4.4 (0.1) | 0.4 | 1.0 | 70,988 | 82,446 | 1,709,553 |
| Card. | 4.2 (0.1) | 4.2 (0.1) | 3.8 (0.1) | 0.4 | 0.4 | 5,307 | 15,009 | 229,784 |
| MFE | 4.8 (0.2) | 5.6 (0.2) | 4.7 (0.1) | 0.1 | 0.1 | 2,444 | 4,549 | 85,197 |

E10 = Type 1 diabetes  E11 = Type 2 diabetes  c = controls

English Hospitals, 4 consecutive years of discharges 2000-2004

Sampson MJ et al Diabetes Research & Clinical Practice 2007;77(1):92-98

# Day Case Avoidance

| | Admissions for males with diabetes | Admissions per 1000 males with diabetes | Admissions per 1000 males without diabetes | Diabetes admissions/non-diabetes admissions | Excess admissions in diabetes |
|---|---|---|---|---|---|
| 0-15 | 956 | 99 | 50 | 1.99 | 475 |
| 16-24 | 1,633 | 51 | 43 | 1.20 | 274 |
| 25-34 | 3,289 | 70 | 57 | 1.24 | 627 |
| 35-44 | 10,014 | 93 | 79 | 1.18 | 1,511 |
| 45-54 | 27,487 | 122 | 118 | 1.04 | 994 |
| 55-64 | 60,788 | 210 | 203 | 1.04 | 2,148 |
| 65-74 | 87,207 | 241 | 355 | 0.68 | -41,187 |
| 75+ | 77,832 | 328 | 413 | 0.79 | -20,344 |
| All male | 269,206 | 205 | 123 | 0.82 (age adjusted) | -55,501 |

| | Admissions for females with diabetes | Admissions per 1000 females with diabetes | Admissions per 1000 females without diabetes | Diabetes admissions/non-diabetes admissions | Excess admissions in diabetes |
|---|---|---|---|---|---|
| 0-15 | 975 | 106 | 40 | 2.63 | 604 |
| 16-24 | 1,986 | 58 | 62 | 0.94 | -136 |
| 25-34 | 3,708 | 79 | 91 | 0.87 | -567 |
| 35-44 | 10,390 | 190 | 118 | 1.61 | 3,942 |
| 45-54 | 23,708 | 172 | 160 | 1.08 | 1,736 |
| 55-64 | 42,589 | 202 | 207 | 0.97 | -1,184 |
| 65-74 | 61,743 | 233 | 288 | 0.81 | -14,657 |
| 75+ | 62,924 | 213 | 279 | 0.76 | -19,748 |
| All female | 208,023 | 197 | 137 | 0.87 (age adjusted) | -30,011 |
| Total (male and female) | 477,229 | 202 | 130 | 0.85 (age-adjusted) | -85,512 |

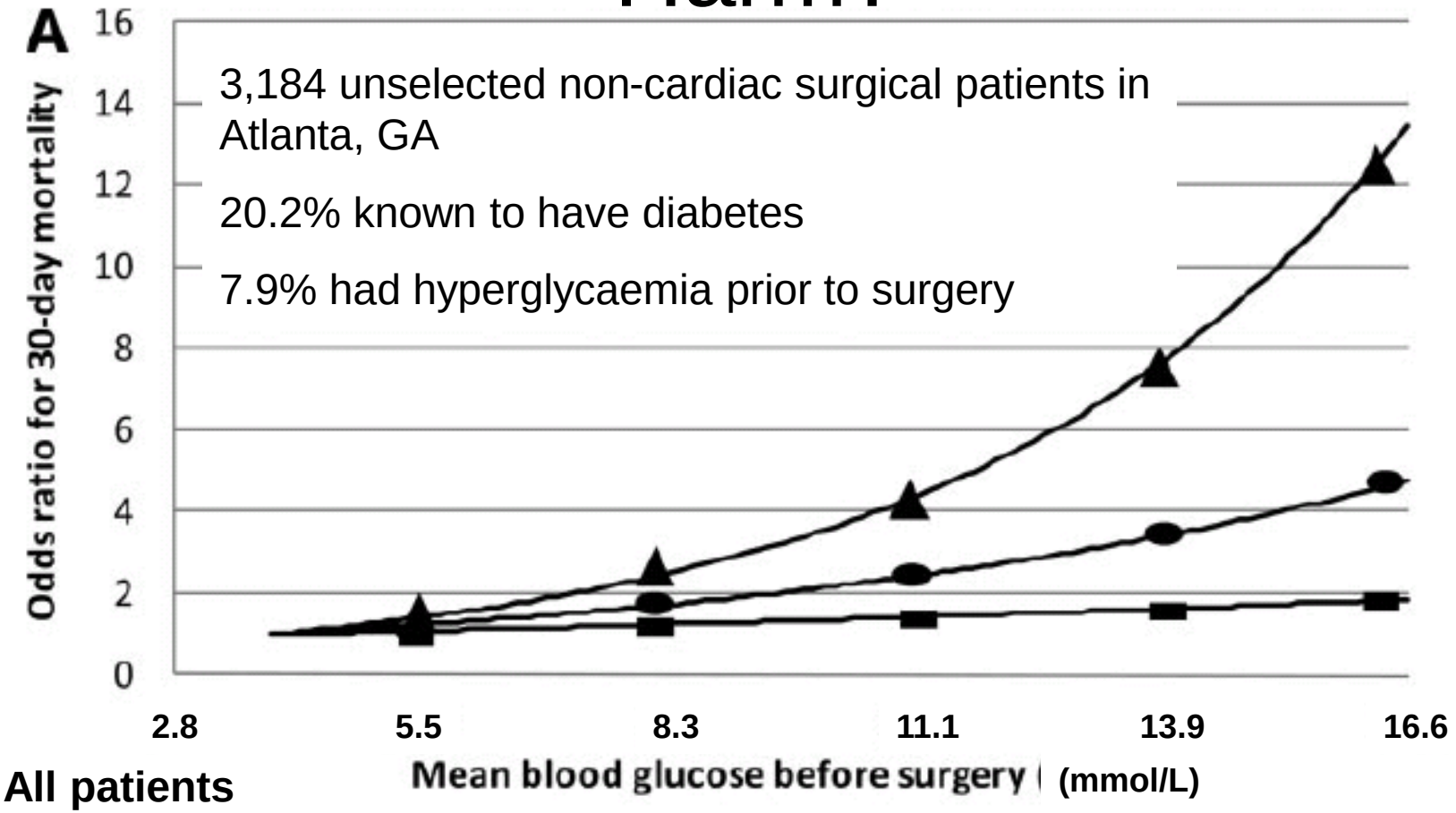
Men

In 2009-10, 85,512 people with diabetes were denied day case surgery. If 1 bed day costs £300, then this equates to £25.6m

Women

Kerr M, *'Inpatient Care for People with Diabetes: the Economic Case for Change'*. NHS Diabetes 2012

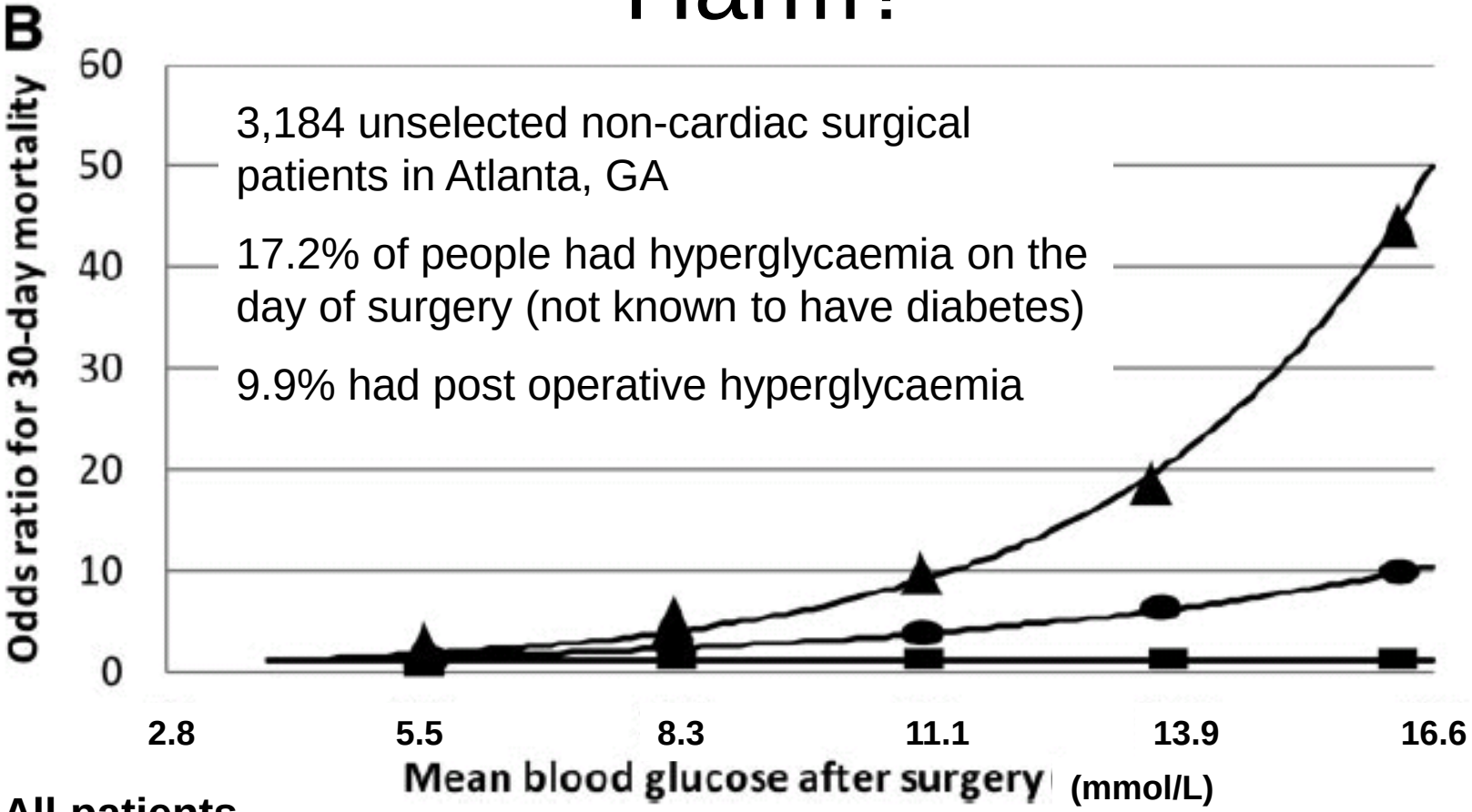
# Do High Glucose Levels Cause Harm?




- All patients
- Patients with diabetes
- Patients without diabetes

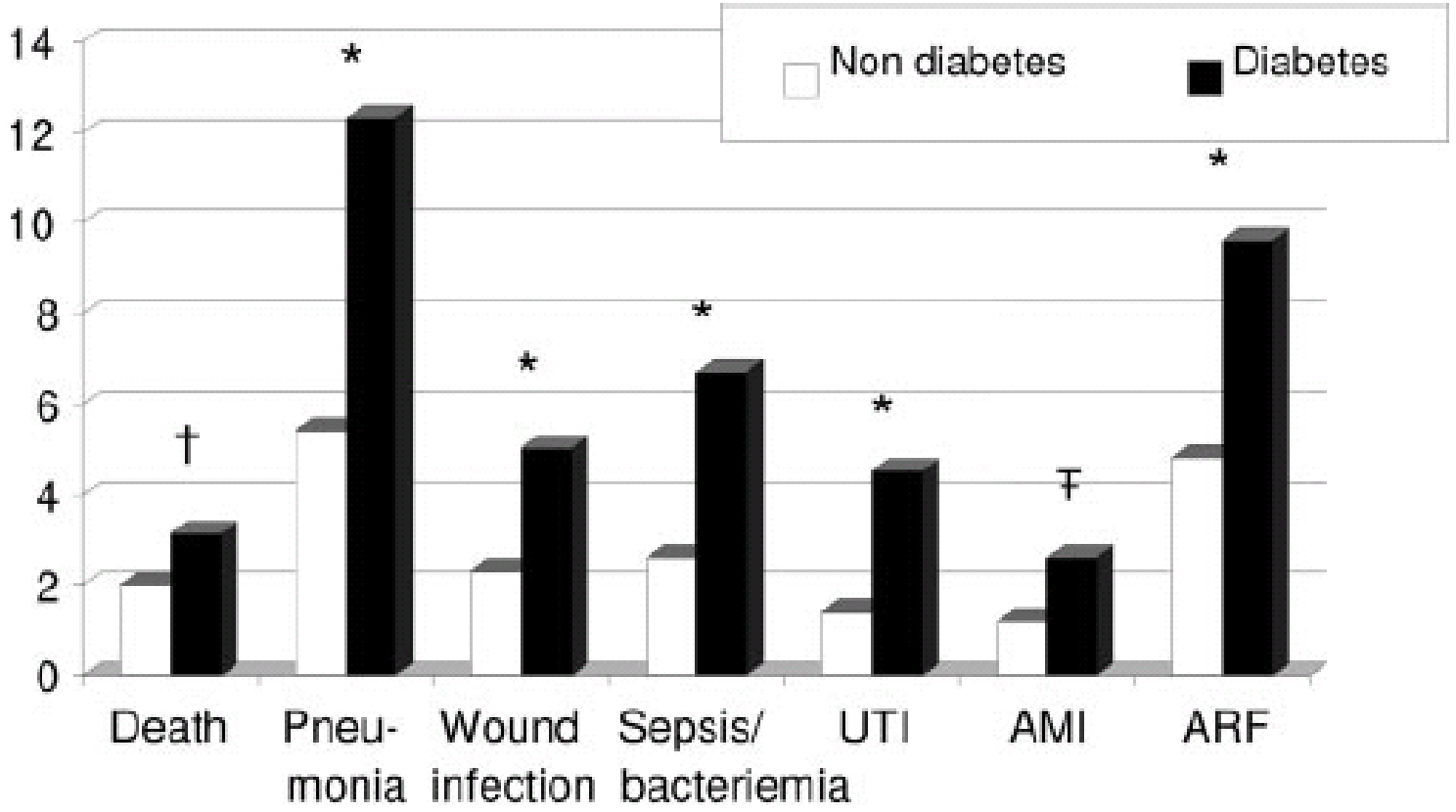
Frisch A et al Diabetes Care 2010;33(8):1783-1788

# Do High Glucose Levels Cause Harm?




Frisch A et al Diabetes Care 2010;33(8):1783-1788

# Do High Glucose Levels Cause Harm?




Frisch A et al Diabetes Care 2010;33(8):1783-1788

# More Observational Data

- Observational data from 55 US hospitals over 5 years looked at the outcomes of 18,278 patients 11,633 of whom who had a BG measured pre op, on day 1 post op or day 2 post op
- 55.4 ± 15.3 years
- 65.7% women

Kwon S et al Ann Surgery 2013;257(1):8-14

# Hyperglycaemic Individuals

- Were more likely to be
  - Older
  - Heavier
  - More comorbidities
  - Have longer operations
  - Have diabetes (but not always)

Kwon S et al Ann Surgery 2013;257(1):8-14

# Outcomes

**TABLE 2.** Adjusted Multivariate Logistic Regression Analysis on the Effect of Perioperative Hyperglycemia (>180 mg/dL at Any Point on the Day of Surgery, Postoperative Day 1, or Postoperative Day 2) on Outcomes Presented as Odds Ratio and 95% Confidence Intervals (Within Parenthesis)

| | Composite Infections (n = 491) | Deaths (n = 48) | Reoperative Interventions (n = 257) | Anastomotic Failures (n = 43) | Myocardial Infarctions (n = 13) |
|---|---|---|---|---|---|
| Hyperglycemia | 2.0 (1.63–2.44) | 2.71 (1.72–4.28) | 1.8 (1.41–2.3) | 2.43 (1.38–4.28) | 1.15 (0.43–3.1) |
| Diabetes[§] | | | | | |
| Noninsulin-dependent | 0.51 (0.37–0.69) | 0.48 (0.25–0.93) | 0.63 (0.44–0.9) | 0.45 (0.21–0.99) | 0.77 (0.15–4.08) |
| Insulin-dependent | 0.52 (0.35–0.76) | 0.78 (0.36–1.68) | 0.54 (0.35–0.85) | 0.49 (0.18–1.32) | 1.66 (0.26–10.71) |

High glucose levels were associated with poor outcomes

But – having diabetes was protective (?increased vigilance)

Kwon S et al Ann Surgery 2013;257(1):8-14

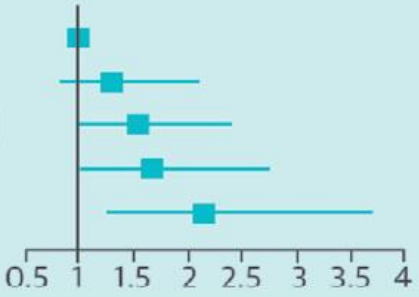
# Cardiac Surgery?

- 352 patients (150 without diabetes)
- Randomised to 5.6-7.8 vs 7.9-10 mmol/l post CABG
- 90 day outcomes (death, infections, etc)
- Most benefit achieved in those without diabetes on the intensive treatment arm (p=0.008)

Umpierrez G et al Diabetes Care 2015;38(9):1665-1672

# HbA1c and Outcome Post CABG

| Death + MACE | | | |
|---|---|---|---|
| ≤7.0 (Ref) | 29/358 | 81 [56 - 116] | 1.00 |
| 7.1 - 8.0 | 76/993 | 76 [61 - 96] | 1.34 [0.82 - 2.21] |
| 8.1 - 9.0 | 122/1,588 | 77 [64 - 92] | 1.59 [1.00 - 2.54] |
| 9.1 - 10.0 | 64/796 | 80 [63 - 103] | 1.73 [1.03 - 2.90] |
| >10.0 | 43/355 | 121 [90 - 163] | 2.25 [1.29 - 3.94] |

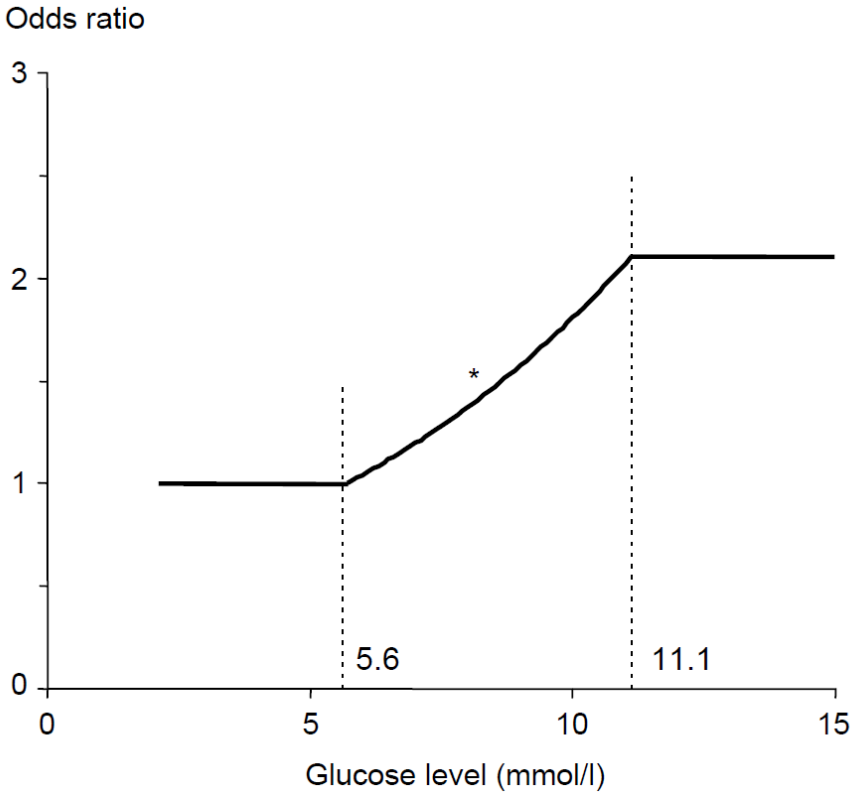



- 764 patients with T1DM undergoing CABG between 1997-2012 in Sweden
- For every 1% (9mmol/mol) rise in pre-operative HbA1c above 7% (53mmol/mol), there was an 18% increase in mortality or MACE

Nyström T et al. JACC 2015;66(5):535-543

# In Addition…..

- Other data has confirmed the harm of high pre-operative glucose levels in non-cardiac, non vascular surgery




30 day mortality rates for 989 patients with diabetes – for each mmol/L increase in blood glucose, OR for mortality rose by 1.19 (CI 1.1 - 1.3)

Noorddij PG et al EJE 2007;156(1):137-142

# Benefits of Glucose Control Extend to Those Without Diabetes

- 2383 people undergoing cardiac surgery randomised to tight peri- or post-operative glycaemic control (4.4-6.1 mmol/l)
- Those without diabetes had the greatest benefit in reductions complications
  - CV
  - Pulmonary
  - Neurological
  - GI
  - Renal

Blaha J et al J Clin Endo Metabol 2015;100(8):3081-3089

# Thus….

- Whilst there is data to show that poor glycaemic control is associated with poor outcomes
- There is no consistent data to show that improving control also improves outcomes

(A bit like diabetes care in general until the mid 1990's)

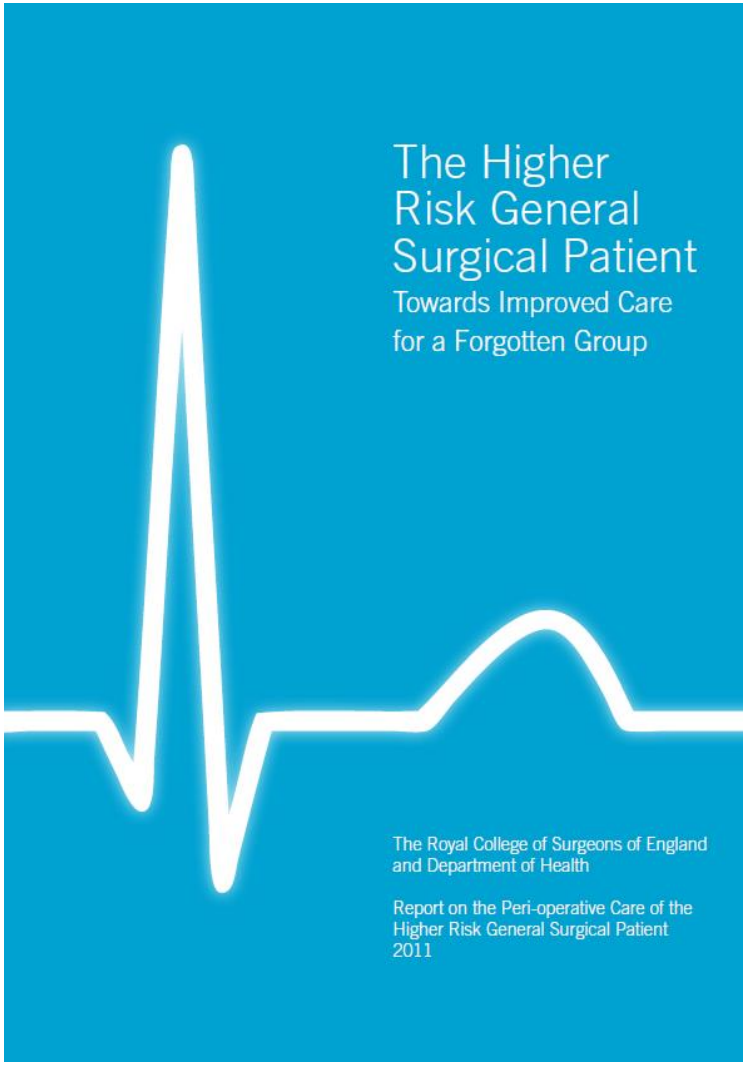
# The ITU Story

- 2001 Leuven (Surgical) 1548 Positive
  Van den Berghe G et al NEJM 2001;345:1359-1367
- 2006 Leuven (Medical) 1200 Neutral / Positive
  Van den Berghe G et al NEJM 2006;354:449-461
- 2008 VISEP (Septic) 537 Stopped early
  Brunkhorst FM et al NEJM 2008;358:125-139
- 2008 De la Rosa (General) 504 Neutral
  De La Rosa G et al Critical Care 2008;12:R120
- 2009 GluControl 1078 Stopped early / Neutral
  Preiser J-C et al Intensive Care Medicine 2009 35:1738-1748
- 2009 Leuven (PICU) 700 Positive
  Vlasselaers D et al Lancet 2009;373:547-556
- 2009/12/15 NICE-SUGAR 6104 Harmful (especially hypos) / Neutral (TBI)
  The NICE-SUGAR Study Investigators NEJM 2009;360:1283-1297
  NEJM 2012;367:1108-1118
  Intensive Care Medicine 2015;41(6):1037-1047
- 2012 Boston Children's 980 Neutral
  Agus MS et al NEJM 2012;367(13):1208-1219
- 2014 CHiP (PICU) 1369 Neutral (hypos)
  Macrae D et al NEJM 2014;370(2):107-108
- 2014 CGAO–REA 2684 Neutral (hypos)
  Kalfon P et al Intensive Care Med 2014;40(2):171-181
  Canotti R et al Critical Care 2014;18:498

"The jury is still out"

Van den Berghe G Intensive Care Med 2013;39(5):823-825

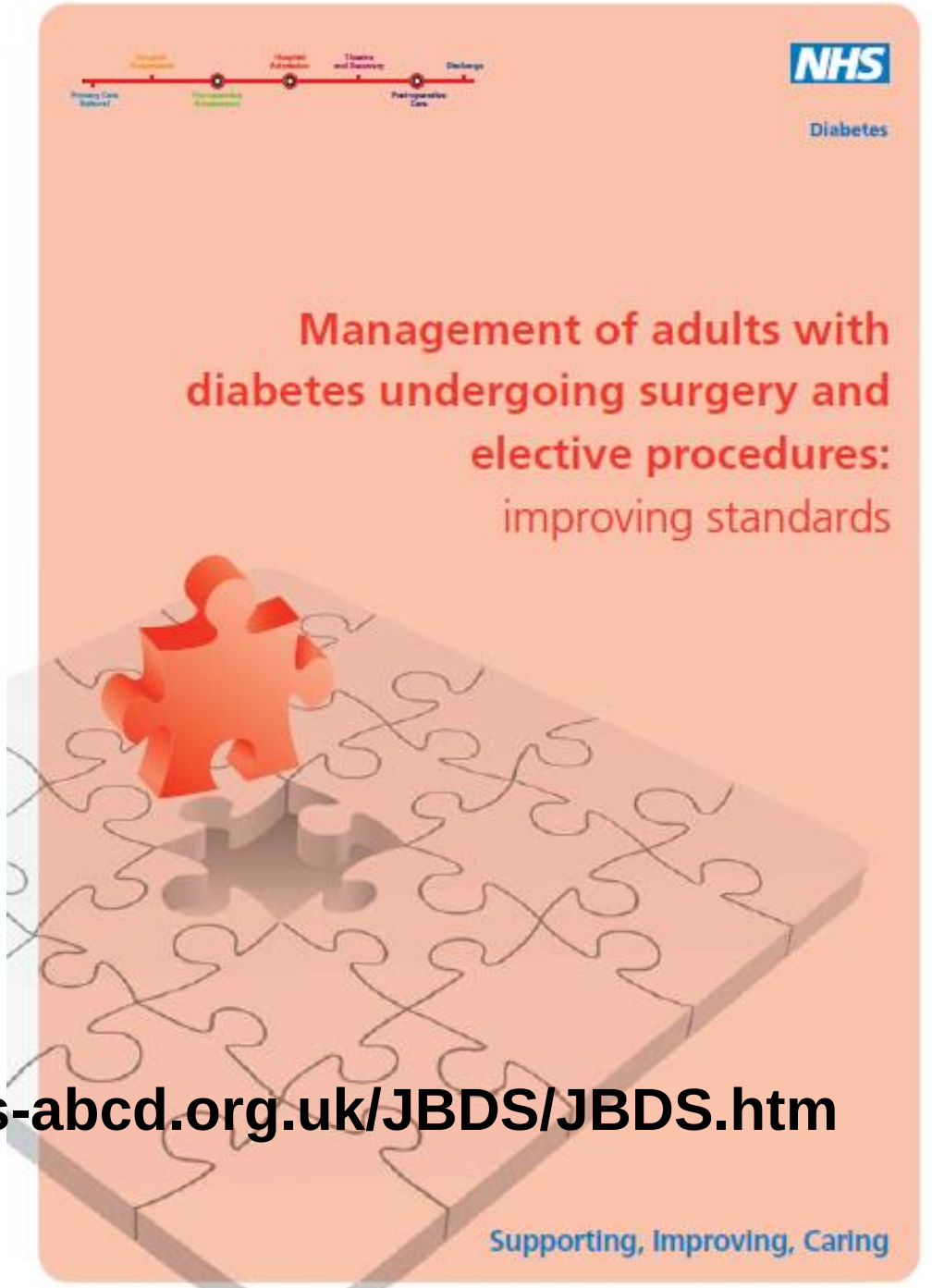
# Something Some of You May Have Seen




- Disappointingly, the word ‘diabetes’ appears only once, ‘hyperglycaemia’ and ‘glucose’ do not appear at all in this document

http://www.rcseng.ac.uk/publications/docs/higher-risk-surgical-patient/

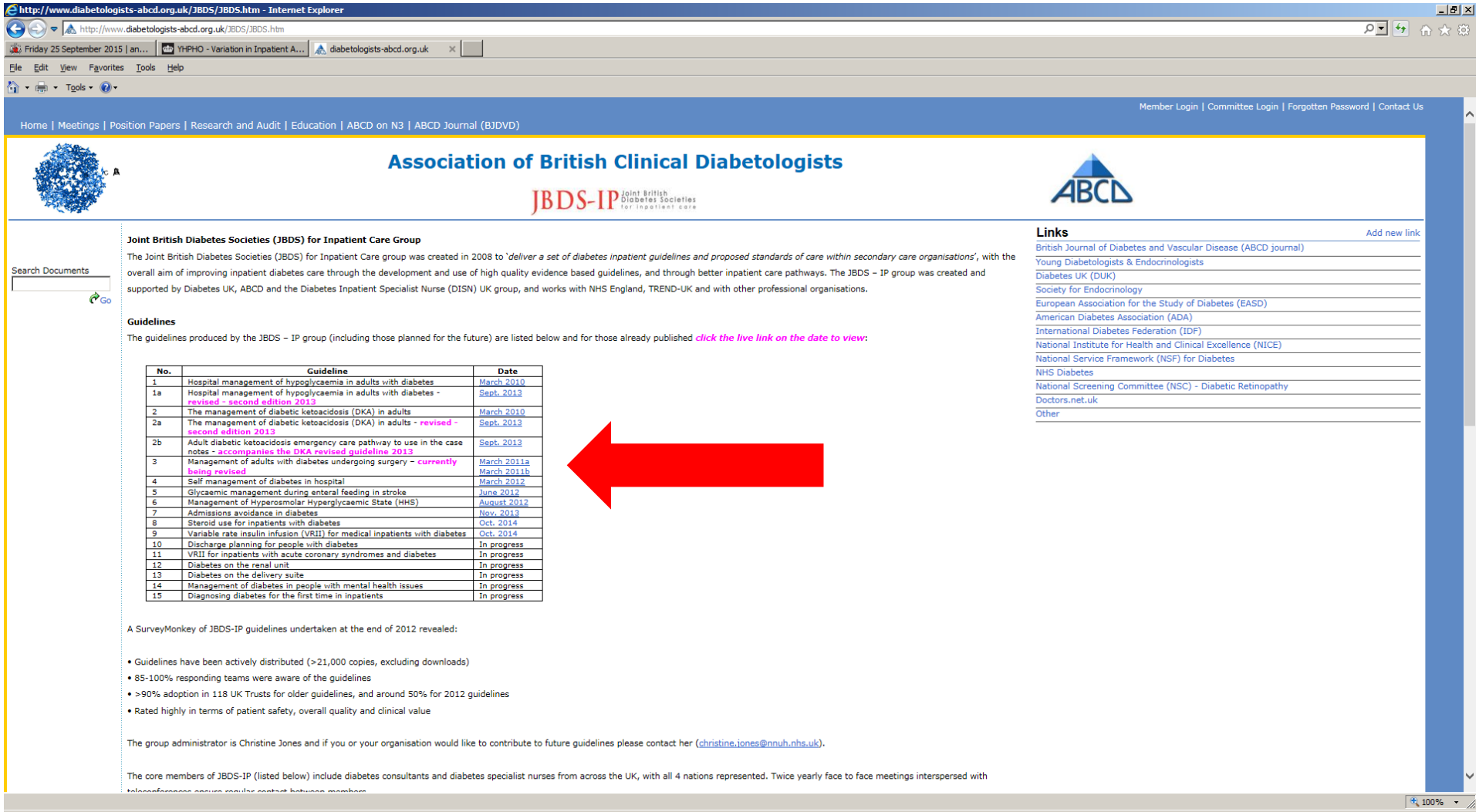
# In 2011 Along Came This…..




**http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm**

# How to Access This

- Open your search engine of choice
- Type in ‘ABCD’ and ‘JBDS’
- Click on the first link



http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm - Internet Explorer

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

Friday 25 September 2015 | an... | YHPHO - Variation in Inpatient A... | diabetologists-abcd.org.uk

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Association of British Clinical Diabetologists

JBDS-IP Joint British Diabetes Societies for Inpatient care

ABCD

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**Joint British Diabetes Societies (JBDS) for Inpatient Care Group**

The Joint British Diabetes Societies (JBDS) for Inpatient Care group was created in 2008 to '*deliver a set of diabetes inpatient guidelines and proposed standards of care within secondary care organisations*', with the overall aim of improving inpatient diabetes care through the development and use of high quality evidence based guidelines, and through better inpatient care pathways. The JBDS – IP group was created and supported by Diabetes UK, ABCD and the Diabetes Inpatient Specialist Nurse (DISN) UK group, and works with NHS England, TREND-UK and with other professional organisations.

**Guidelines**

The guidelines produced by the JBDS – IP group (including those planned for the future) are listed below and for those already published ***click the live link on the date to view***:

| No. | Guideline | Date |
|---|---|---|
| 1 | Hospital management of hypoglycaemia in adults with diabetes | March 2010 |
| 1a | Hospital management of hypoglycaemia in adults with diabetes - **revised - second edition 2013** | Sept. 2013 |
| 2 | The management of diabetic ketoacidosis (DKA) in adults | March 2010 |
| 2a | The management of diabetic ketoacidosis (DKA) in adults - **revised - second edition 2013** | Sept. 2013 |
| 2b | Adult diabetic ketoacidosis emergency care pathway to use in the case notes - **accompanies the DKA revised guideline 2013** | Sept. 2013 |
| 3 | Management of adults with diabetes undergoing surgery – **currently being revised** | March 2011a<br>March 2011b |
| 4 | Self management of diabetes in hospital | March 2012 |
| 5 | Glycaemic management during enteral feeding in stroke | June 2012 |
| 6 | Management of Hyperosmolar Hyperglycaemic State (HHS) | August 2012 |
| 7 | Admissions avoidance in diabetes | Nov. 2013 |
| 8 | Steroid use for inpatients with diabetes | Oct. 2014 |
| 9 | Variable rate insulin infusion (VRII) for medical inpatients with diabetes | Oct. 2014 |
| 10 | Discharge planning for people with diabetes | In progress |
| 11 | VRII for inpatients with acute coronary syndromes and diabetes | In progress |
| 12 | Diabetes on the renal unit | In progress |
| 13 | Diabetes on the delivery suite | In progress |
| 14 | Management of diabetes in people with mental health issues | In progress |
| 15 | Diagnosing diabetes for the first time in inpatients | In progress |

A SurveyMonkey of JBDS-IP guidelines undertaken at the end of 2012 revealed:

- Guidelines have been actively distributed (>21,000 copies, excluding downloads)
- 85-100% responding teams were aware of the guidelines
- >90% adoption in 118 UK Trusts for older guidelines, and around 50% for 2012 guidelines
- Rated highly in terms of patient safety, overall quality and clinical value

The group administrator is Christine Jones and if you or your organisation would like to contribute to future guidelines please contact her (christine.jones@nnuh.nhs.uk).

The core members of JBDS-IP (listed below) include diabetes consultants and diabetes specialist nurses from across the UK, with all 4 nations represented. Twice yearly face to face meetings interspersed with

**Links** Add new link

- British Journal of Diabetes and Vascular Disease (ABCD journal)
- Young Diabetologists & Endocrinologists
- Diabetes UK (DUK)
- Society for Endocrinology
- European Association for the Study of Diabetes (EASD)
- American Diabetes Association (ADA)
- International Diabetes Federation (IDF)
- National Institute for Health and Clinical Excellence (NICE)
- National Service Framework (NSF) for Diabetes
- NHS Diabetes
- National Screening Committee (NSC) - Diabetic Retinopathy
- Doctors.net.uk
- Other

100%

# And This…..

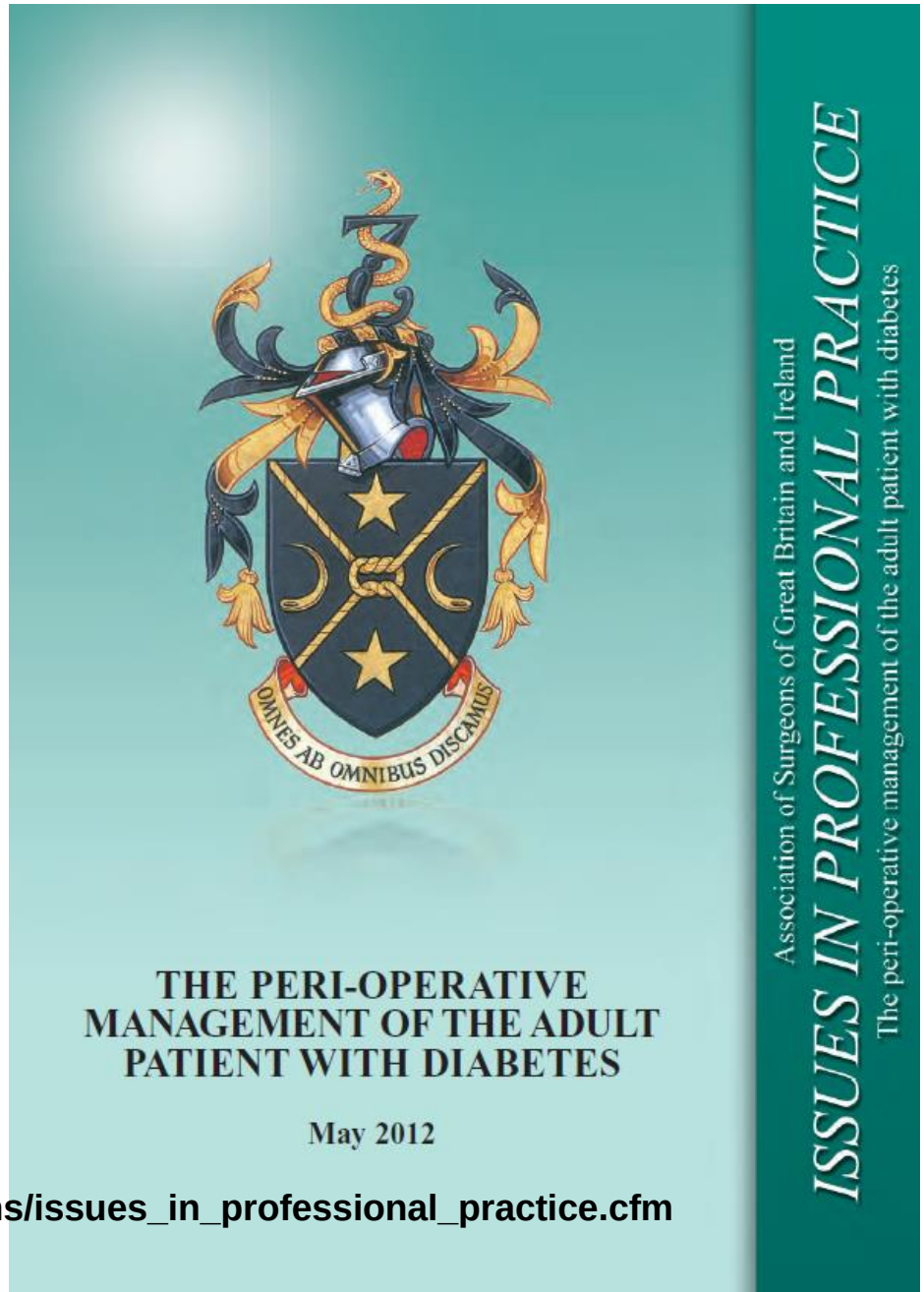
## Diabetes UK Position Statements and Care Recommendations

## NHS Diabetes guideline for the perioperative management of the adult patient with diabetes*

K. Dhatariya[1], N. Levy[2], A. Kilvert[3], B. Watson[4], D. Cousins[5], D. Flanagan[6], L. Hilton[7], C. Jairam[8], K. Leyden[3], A. Lipp[1], D. Lobo[9], M. Sinclair-Hammersley[10] and G. Rayman[11] for the Joint British Diabetes Societies

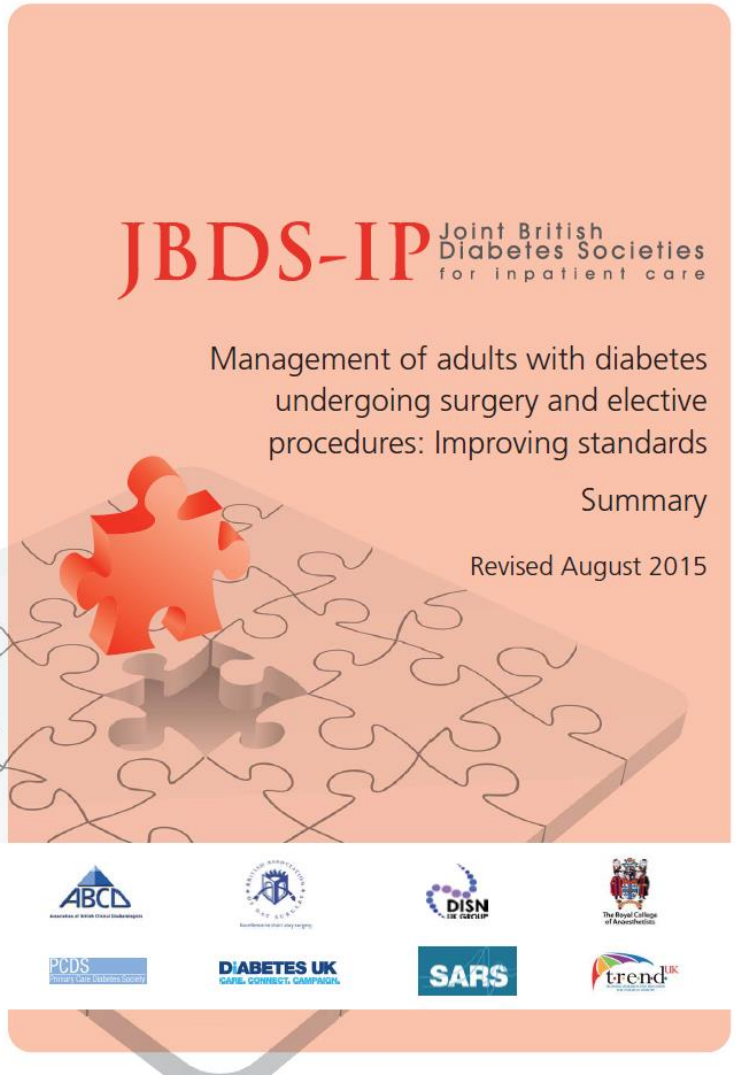
Diabetic Medicine 2012;29(4):420-433

# And This…..



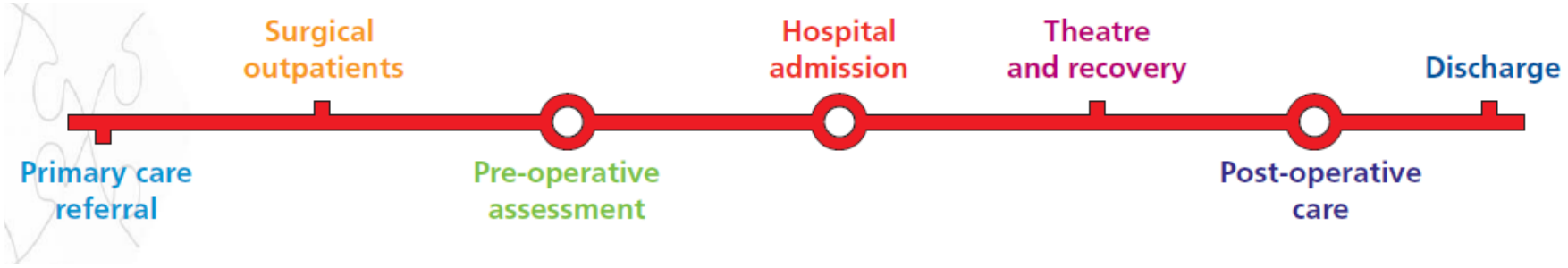

**http://www.asgbi.org.uk/en/publications/issues_in_professional_practice.cfm**

# It Has Now been Updated



# National Guidelines

- Document divided into sections:
  - Primary care
  - Surgical outpatients
  - Pre-operative assessment clinic
  - Hospital admission
  - Theatre and recovery
  - Post-operative care
  - Discharge



# The Peri-Operative Management of Diabetes Drugs

# Hypoglycaemic Agents

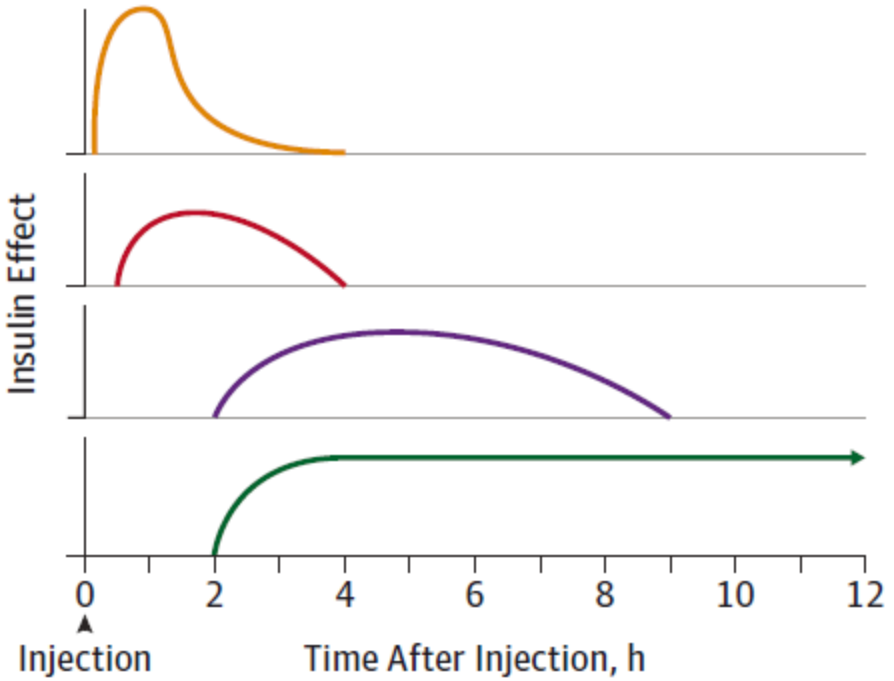
- α glucosidase inhibitors
- Metaglinides
- Metformin
- Sulphonylureas
- Thiazolidindiones
- GLP – 1 analogues
- DPP IV inhibitors
- SGLT2 inhibitors

| Tablets | Day prior to admission | Day of Surgery / whilst on a VRIII | | |
|---|---|---|---|---|
| | | Patient for AM surgery | Patient for PM surgery | If a VRIII is being used* |
| **Acarbose** | Take as normal | Omit morning dose if NBM | Give morning dose if eating | Stop once VRIII commenced, do not recommence until eating and drinking normally |
| **Meglitinide** (e.g repaglinide or nateglinide) | Take as normal | Omit morning dose if NBM | Give morning dose if eating | Stop once VRIII commenced, do not recommence until eating and drinking normally |
| **Metformin** (eGFR is greater than 60ml/min/1.73m$^2$ and procedure not requiring use of contrast media**) | Take as normal | If taken once or twice a day – take as normal<br>If taken three times per day, omit lunchtime dose | If taken once or twice a day – take as normal<br>If taken three times per day, omit lunchtime dose | Stop once VRIII commenced, do not recommence until eating and drinking normally |
| **Sulphonylurea** (e.g glibenclamide, gliclazide, glipizide, etc.) | Take as normal | Once daily am omit<br>Twice daily omit am | Once daily am omit<br>Twice daily omit am and pm | Stop once VRIII commenced, do not recommence until eating and drinking normally |
| **Pioglitazone** | Take as normal | Take as normal | Take as normal | Stop once VRIII commenced, do not recommence until eating and drinking normally |
| **DPP IV inhibitor** (e.g. sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin) | Take as normal | Take as normal | Take as normal | Stop once VRIII commenced, do not recommence until eating and drinking normally |
| **GLP-1 analogue** (e.g. exenatide, liraglutide, lixisenatide, dulaglutide) | Take as normal | Take as normal | Take as normal | Take as normal |
| **SGLT-2 inhibitors** (e.g. dapagliflozin, canagliflozin) | Take as normal | Omit on day of surgery | Omit on day of surgery | Omit on day of surgery |

# Insulin Durations

Figure 1. Insulin Activity Profiles

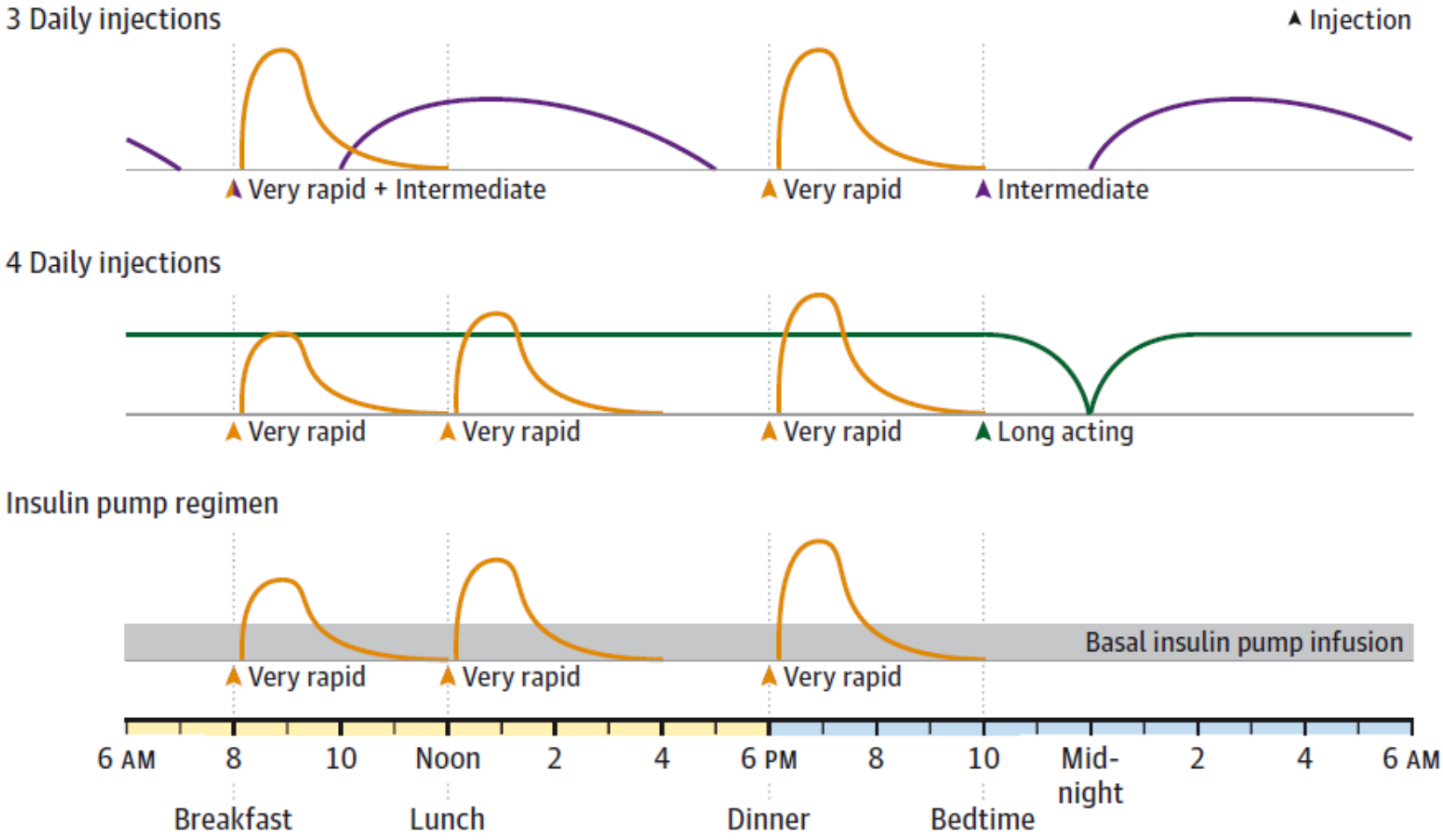
| Insulin | Onset, min | Duration, h |
|---|---|---|
| Very rapid<br>Lispro, aspart, glulisine | 10 | 4 |
| Rapid (regular)<br>CZI | 30 | 4-8 |
| Intermediate<br>NPH | 120 | 8-10 |
| Long acting<br>Glargine, levemir | 120 | 12-24 |




Nathan DM JAMA 2015;314(10):1052-1062

# Insulin Regimens

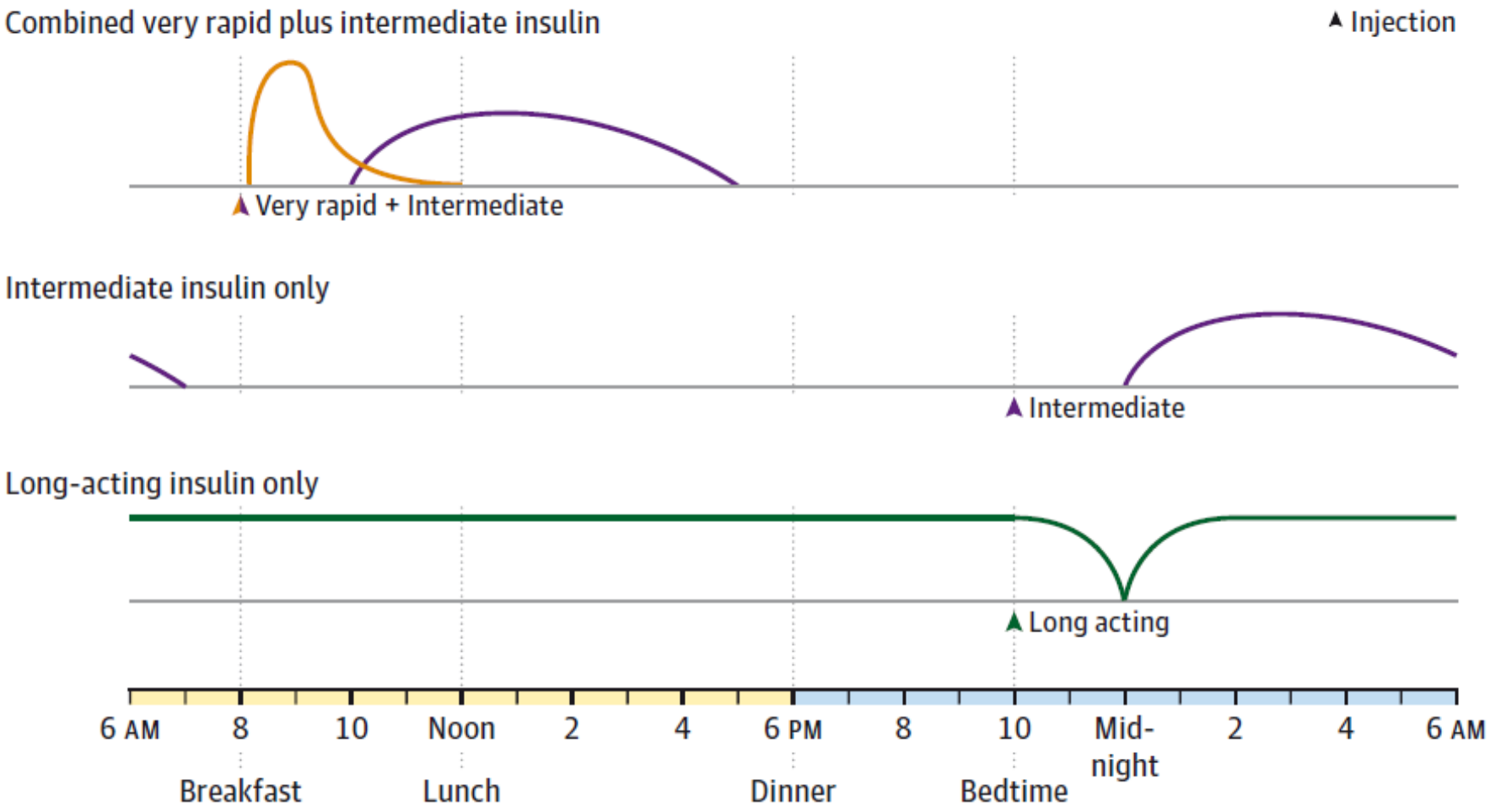
Figure 2. Three Examples of Insulin Regimens for Type 1 Diabetes




Nathan DM JAMA 2015;314(10):1052-1062

# Insulin Regimens

Figure 3. Three Examples of Single Injection Regimens for Type 2 Diabetes




Nathan DM JAMA 2015;314(10):1052-1062

| Insulins | Day prior to admission | Day of Surgery / whilst on a VRIII | | |
|---|---|---|---|---|
| | | Patient for AM surgery | Patient for PM surgery | If a VRIII is being used* |
| **Once daily (evening)** (e.g. Lantus® or Levemir® Tresiba® Insulatard® Humulin I®) Insuman®) | Reduce dose by 20% | Check blood glucose on admission | Check blood glucose on admission | Continue at 80% of the usual dose |
| **Once daily (morning)** (Lantus® or Levemir® Tresiba® Insulatard® Humulin I®) Insuman®) | Reduce dose by 20% | Reduce dose by 20% Check blood glucose on admission | Reduce dose by 20% Check blood glucose on admission | Continue at 80% of the usual dose |
| **Twice daily** (e.g. Novomix 30®, Humulin M3® Humalog Mix 25®, Humalog Mix 50®, Insuman® Comb 25, Insuman® Comb 50 twice daily Levemir® or Lantus®) | No dose change | Halve the usual morning dose. Check blood glucose on admission Leave the evening meal dose unchanged | Halve the usual morning dose. Check blood glucose on admission Leave the evening meal dose unchanged | Stop until eating and drinking normally |
| **Twice daily - separate injections of short acting** (e.g. animal neutral, Novorapid® Humulin S®) Apidra® **and intermediate acting** (e.g. animal isophane Insulatard® Humulin I® Insuman®) | No dose change | Calculate the total dose of both morning insulins and give half as intermediate acting only in the morning. Check blood glucose on admission Leave the evening meal dose unchanged | Calculate the total dose of both morning insulins and give half as intermediate acting only in the morning. Check blood glucose on admission Leave the evening meal dose unchanged | Stop until eating and drinking normally |
| **3, 4 or 5 injections Daily** (e.g. an injection of mixed insulin 3 times a day or 3 meal time injections of short acting insulin and once or twice daily background) | No dose change | **Basal bolus regimens:** omit the morning and lunchtime short acting insulins. Keep the basal unchanged.* **Premixed a.m. insulin:** halve the morning dose and omit lunchtime dose Check blood glucose on admission | Take usual morning insulin dose(s). Omit lunchtime dose. Check blood glucose on admission | Stop until eating and drinking normally |

Norfolk and Norwich University Hospitals NHS
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# Effect of Diabetes Care on Surgical Outcomes

## or Peri-operative Glucose Control - Is it Important?

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