Inpatient Diabetes in the 21st Century: CSI or CSII

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Association of British Clinical Diabetologists

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Disclosures

ME has received speaker/ writers fees, travel support, & research support from:

Abbott Diabetes Care, AstraZeneca, Dexcom, Eli Lilly, Medtronic, Cellnovo, Novo Nordisk, Roche, Boehringer Ingelheim, Sanofi Aventis.

National Diabetes Inpatient Audit
Hospital characteristics, 2018

NHS Digital

England and Wales

9 May 2019

Key facts

Participation in NaDIA Hospital Characteristics dipped in 2018 with over 20 sites failing to return a survey

Inpatient staffing levels for almost all diabetes professions have increased substantially since 2017

One fifth of hospitals still have no diabetes inpatient specialist nurses (DISNs)

Use of electronic prescribing and electronic patient records continues to rise slowly. Almost 65% of NaDIA sites still do not fully utilise electronic prescribing technology

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Solutions for the 2020s?

- Research based evidence!
- Glucose monitoring
- IT monitoring and decision support
- Automated insulin delivery

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Diabetes Clinical Studies Groups (CSGs)

Working together to improve the lives of people with diabetes through research.

Self-management, acute care & long-term care

CSG 4 Acute care

CSG 5 Long-term self-management & glycaemic control

Prevention & management of complications

CSG 6 Microvascular & macrovascular complications

Cause, prevention & cure

CSG 1 Causes of diabetes

CSG 2 Prevention, targets & therapies for Type 1 diabetes

CSG 3 Prevention, targets & therapies for Type 2 diabetes

Children's diabetes

CSG 7 Children's diabetes sub-group (in partnership with BSPED/NIHR CRN)

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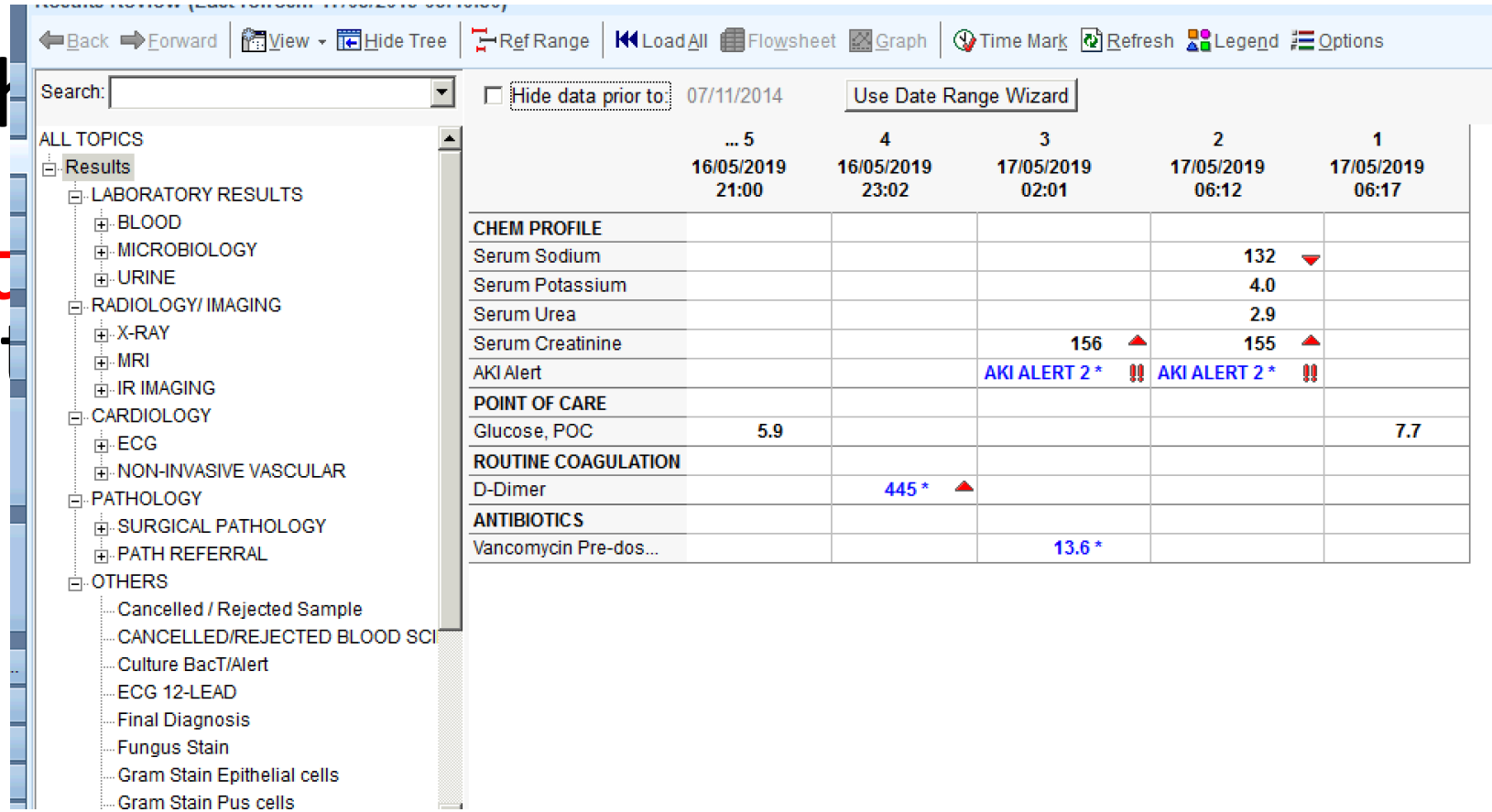
Solutions for the 2020s?

- Research
- Glucose
- IT monit
- Automat



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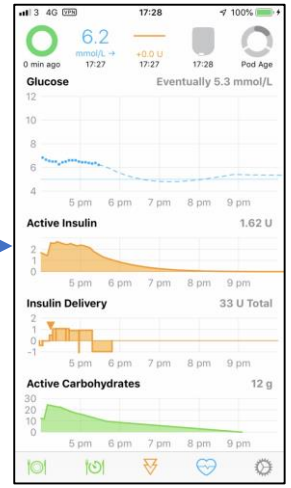
CSII and Inpatients

DTN UK
collaborate · evolve · support

CLINICAL GUIDELINE:
Guidelines for managing continuous subcutaneous insulin infusion (CSII, or 'insulin pump') therapy in hospitalised patients

1



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3

4

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Closed-Loop Insulin Delivery for Glycemic Control in Noncritical Care

Lia Bally, Ph.D., Hood Thabit, Ph.D., Sara Hartnell, B.Sc., Eveline Andereggen, R.N., Yue Ruan, Ph.D., Malgorzata E. Wilinska, Ph.D., Mark L. Evans, M.D., Maria M. Wertli, Ph.D., Anthony P. Coll, M.B., B.S., Christoph Stettler, M.D., and Roman Hovorka, Ph.D.

NEJM
Aug 9 2018

CAD (Control Algorithm Device)
(containing control algorithm)

Navigator II
Receiver
(CGM) or similar
CE-marked

DANA Diabecare R
or similar
CE-marked
insulin pump

Navigator
Transmitter
(CGM) or similar
CE-marked device

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Study Population

	Closed-Loop N = 70	Control N = 66
Gender (M/F)	50/20	43/23
Age (yrs)	68 ± 10	68 ± 14
BMI (kg/m^2)	32.7 ± 8.2	32.1 ± 8.1
HbA1c (%)	8.1 ± 1.9	8.0 ± 1.9
Duration of diabetes (yrs)	17 ± 11	16 ± 11
Duration on insulin (yrs)	10 ± 9	8 ± 9
Total daily insulin dose (U/24h)	64 (59)	51 (39)

Data presented as mean ± SD

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Results – Overall Glucose Control

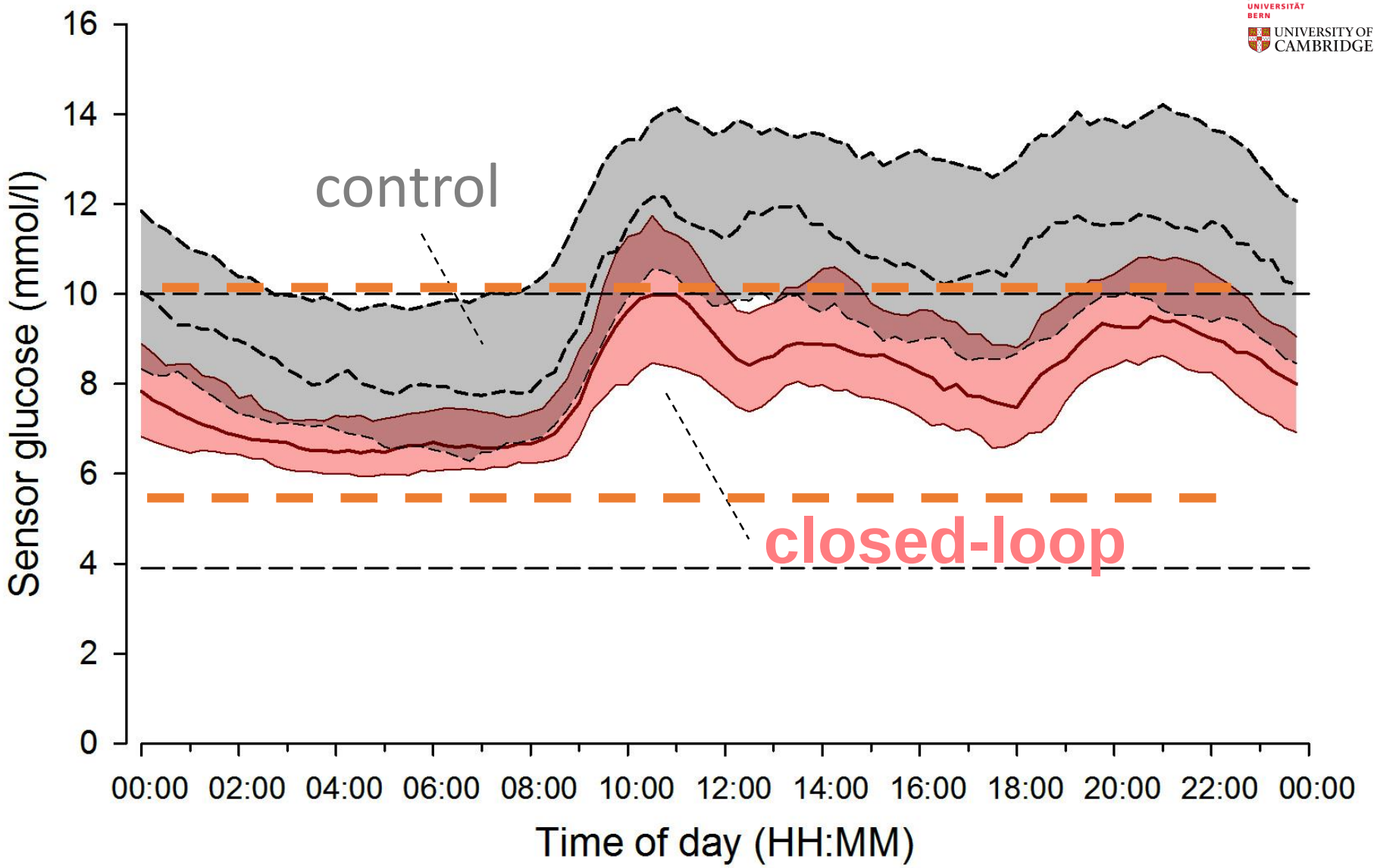
Analysis by intention to treat

	Closed loop N = 70	Control N = 66	P
*Time in target 5.6-10 mmol/l (%)	66 (18)	39 (15)	<0.001
Mean glucose (mmol/l)	8.5 (1.6)	10.5 (2.4)	<0.001
SD of glucose (mmol/l)	2.6 (1.0)	3.3 (1.1)	<0.001
Between days CV of glucose (%)	15.6 (8.0)	21.7 (12.2)	0.001
Time > 10 mmol/l (%)	23.6 (16.6)	49.5 (22.8)	<0.001
Time < 5.6 mmol/l (%)	10.6 (6.7)	9.0 (13.2)	0.37
Time < 3.0 mmol/l (%)	0.0 (0.0 – 0.1)	0.0(0.0 – 0.0)	0.80
AUC < 3.0 mmol/l (mmol/l x mins)	0.0 (0.0 – 17.1)	0.0 (0.0 – 0.0)	0.63

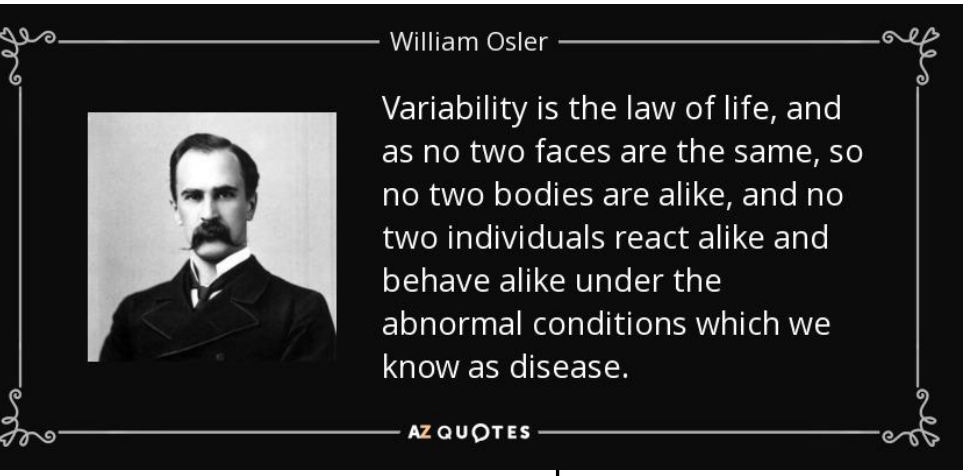
* Primary endpoint
Data are presented as mean (SD) or median (IQR)

Bally L et al, N Engl J Med. 2018

Glucose profile



Bally L et al, N Engl J Med. 2018



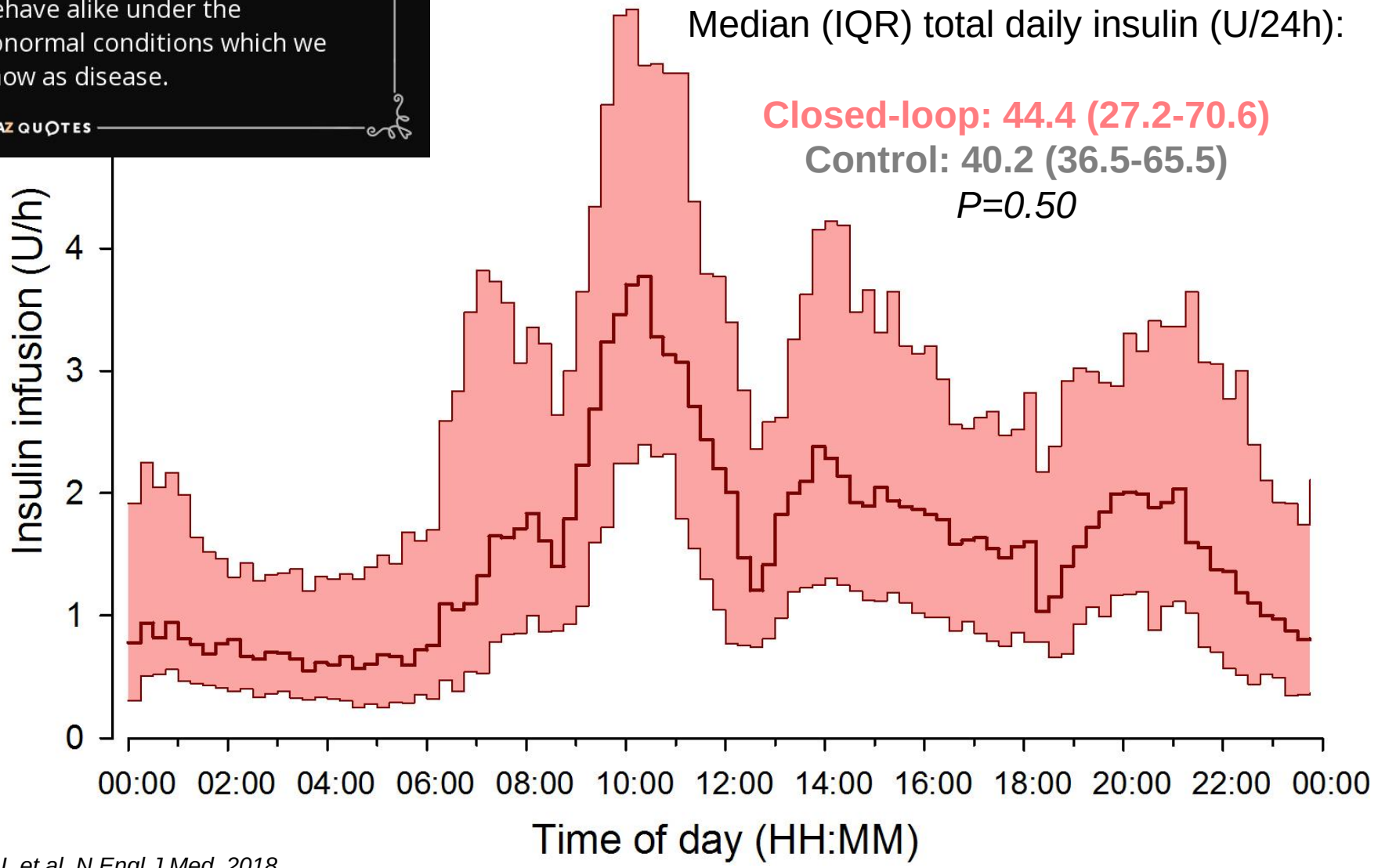
Insulin profile

Median (IQR) total daily insulin (U/24h):

Closed-loop: 44.4 (27.2-70.6)

Control: 40.2 (36.5-65.5)

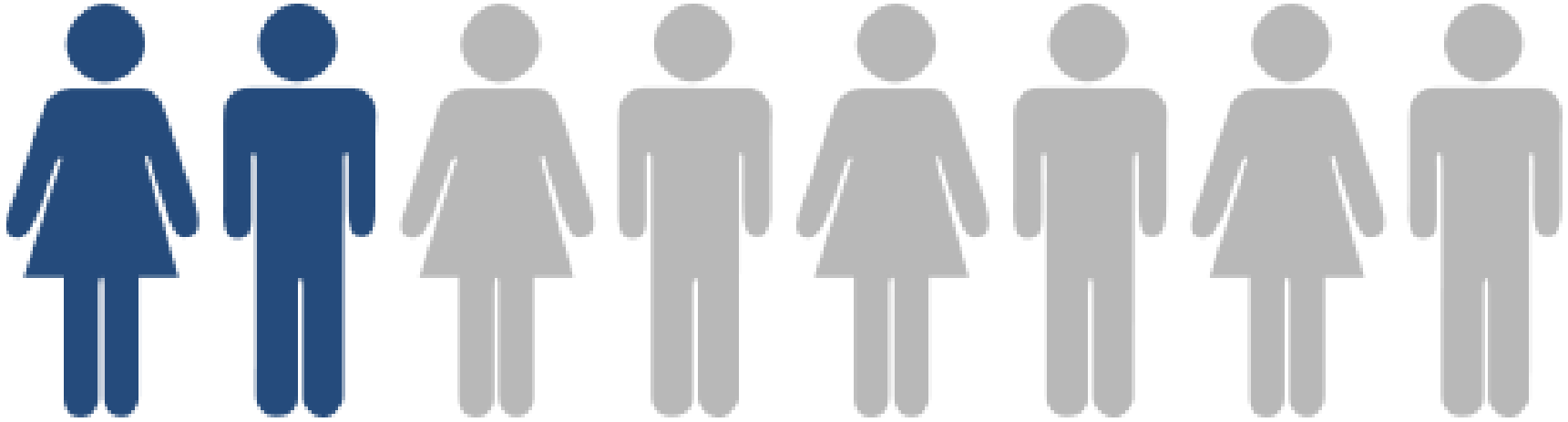
P=0.50



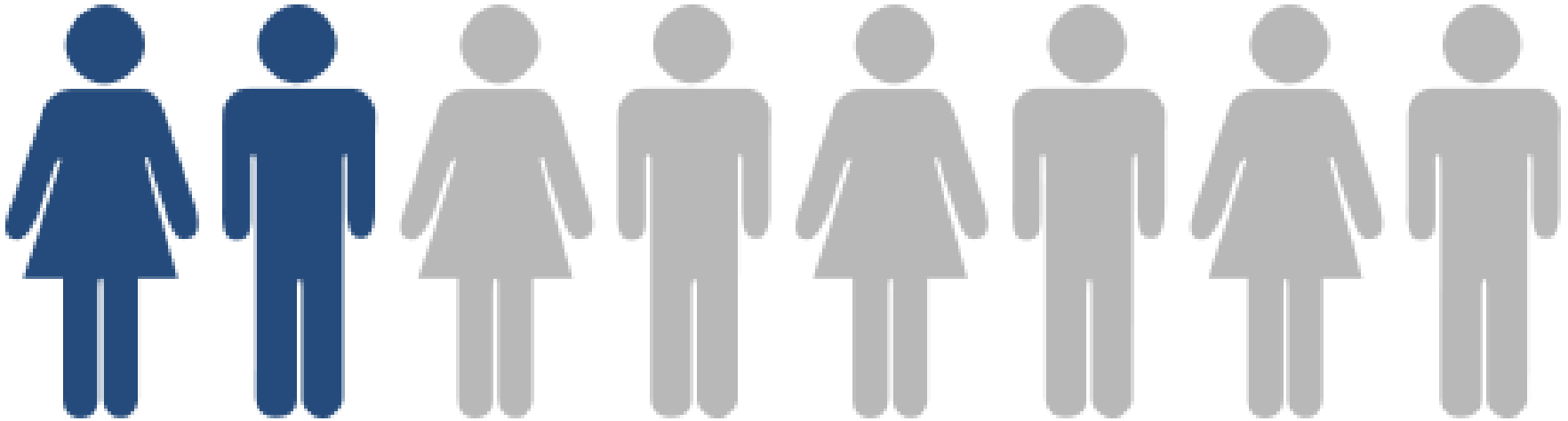
Bally L et al, N Engl J Med. 2018

Safety Evaluation

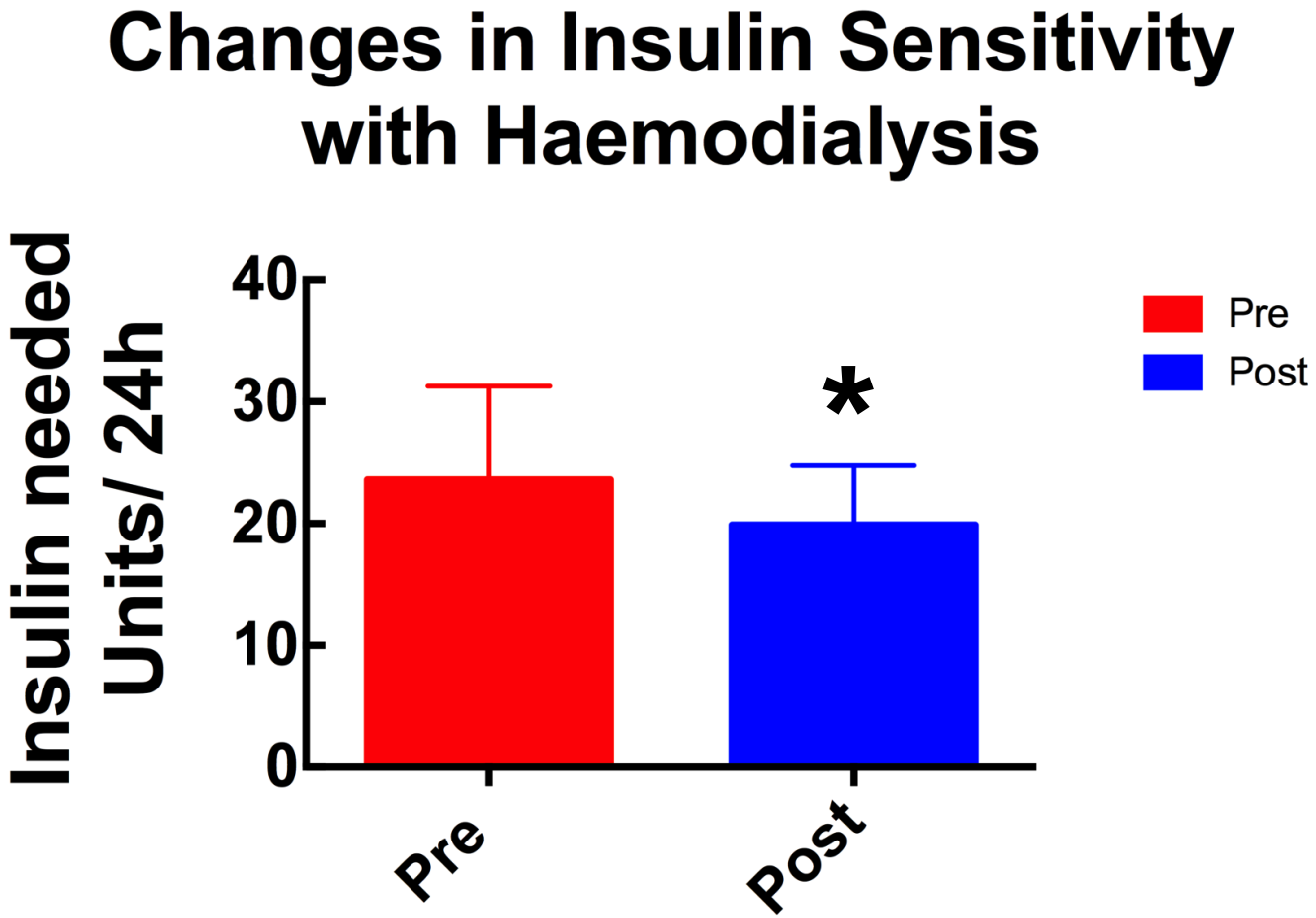
- **No severe hypoglycaemic episodes** in either period
- **No hyperglycaemia with ketosis** in either period



Who benefits the most ??



Haemodialysis patients?



Sobngwi et al Diabetes Care 2010

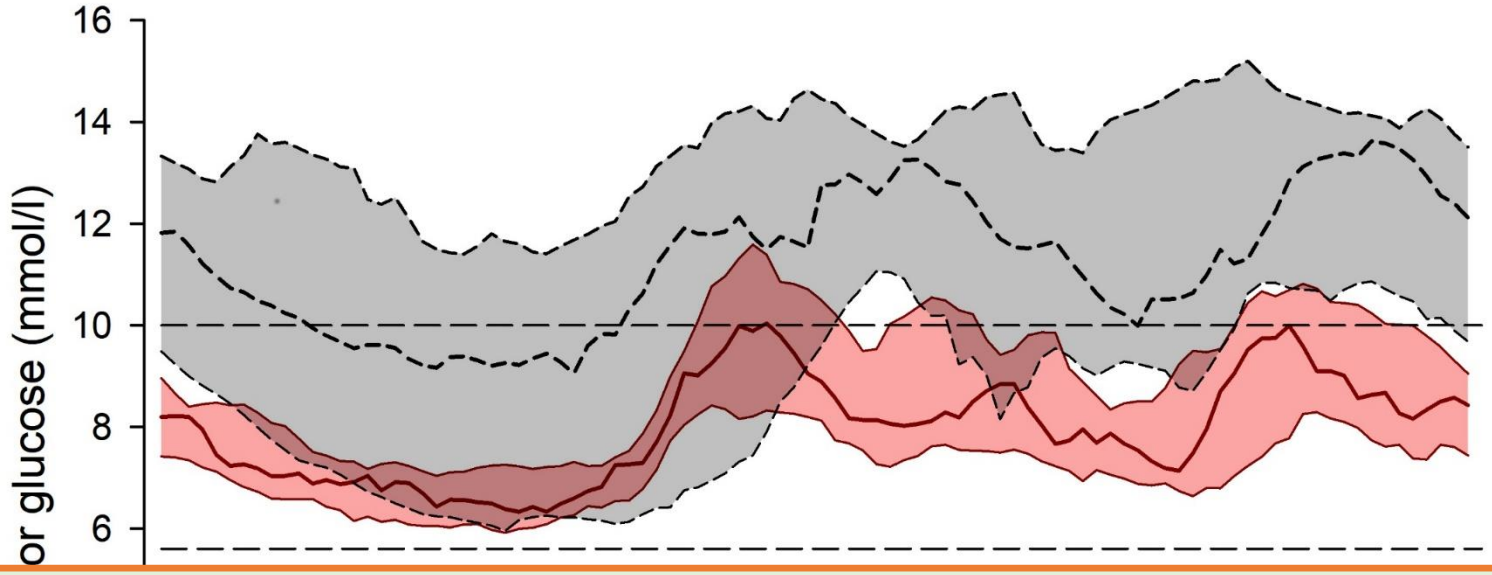
Haemodialysis patients

- Closed-loop (**n=9**), control (**n=8**)
- Number of haemodialysis sessions:

  4.2±1.5 (CL) and 3.6±2.5 (control)
- Study duration: 8.0±3.1 (CL) and

  7.7±4.8 days (control)

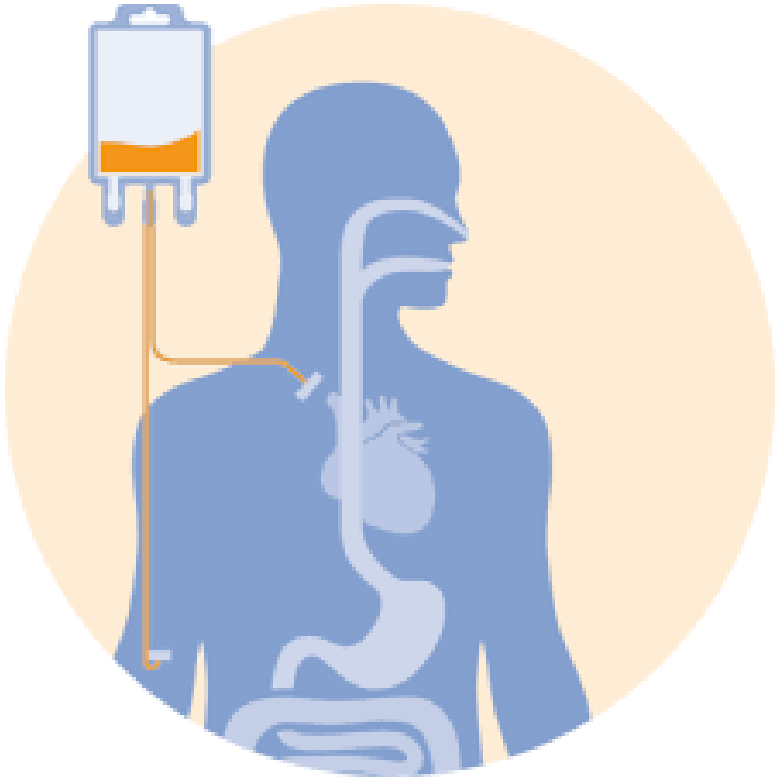
Glucose profile in dialysis patients



- 38% more time spent in target (95% confidence interval 24.4 to 50.8; p<0.001)
- 37% less time above target (p=0.001)
- No difference in hypoglycaemia (p=0.82)
- Similar amounts of insulin delivered (p=0.42)

Bally L et al, Kidney International 2019

Glucose management during nutrition support



- Hyperglycaemia during nutrition support
  - Up to 88% of patients receiving parenteral nutrition
  - Up to 30% of patients receiving enteral nutrition
- Adverse effects on patient morbidity and mortality

Fully closed-loop insulin delivery in inpatients receiving nutritional support: a two-centre, open-label, randomised controlled trial

Charlotte K Boughton, Lia Bally*, Franco Martignoni, Sara Hartnell, David Herzig, Andreas Vogt, Maria M Wertli, Malgorzata E Wilinska, Mark L Evans, Anthony P Coll, Christoph Stettler, Roman Hovorka*

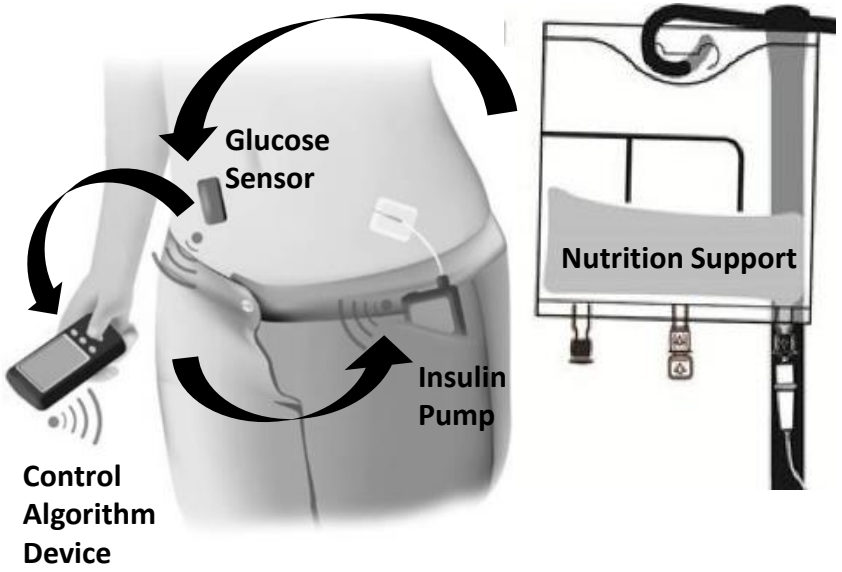
Lancet Diabetes Endocrinol 2019; 7: 368–77

Published Online March 29, 2019

Summary

Background Glucose management is challenging in patients who require nutritional support in hospital. We aimed to assess whether fully closed-loop insulin delivery would improve glycaemic control compared with conventional subcutaneous insulin therapy in inpatients receiving enteral or parenteral nutrition or both.

Closing the loop on nutrition support



- Two-centre RCT
- Inpatients on parenteral and/or enteral nutrition requiring s.c. insulin therapy
- Efficacy and safety of fully automated closed-loop insulin delivery with Fiasp vs. conventional s.c. insulin therapy
- Up to 15 days or until hospital discharge

Study population

	Closed-Loop N = 21	Control N = 22
Male sex – no./total no [%]	14/21 [67]	17/22 [77]
Age (yrs)	66 (14)	69 (10)
BMI (kg/m^2)	27.0 (4.3)	29.3 (5.1)
HbA1c (%)	7.3 (1.6)	7.4 (1.8)
Duration of diabetes (yrs)	11 (14)	7 (8)
Duration on insulin (yrs)	3 (9)	3 (6)
Total daily insulin dose (U/kg/24h)	0.6 (0.4)	0.6 (0.3)

Data presented as mean ± SD

Admission reasons

	Closed-loop N = 21	Control N = 22
Infection/Sepsis	3 (14)	2 (9)
Renal	1 (5)	2 (9)
Malignancy	6 (29)	9 (41)
Gastrointestinal	8 (38)	6 (27)
Respiratory	1 (5)	0 (0)
Neurological	3 (14)	2 (9)
Medical/surgical	7/14	8/14
Emergency/elective	13/8	12/10
Charlson Comorbidity Score	8 (4)	6 (2)

Data presented as N (%). CCI P=0.010

Nutrition regimens

	Closed-loop N = 21	Control N = 22
# patients on PN	6	7
# patients on EN	14	12
# patients on PN + EN	1	3
Daily CHO received as PN (g/24h)	131 (55)	145 (73)
Daily CHO received as PN (g/24h)	176 (65)	182 (75)
Daily CHO received as oral intake (g/24h)	53 (45)	36 (38)
Total carbohydrate (g/24h)	207 (57)	210 (76)

Data presented as mean ± SD. PN, parenteral nutrition; EN, enteral nutrition; CHO, carbohydrate

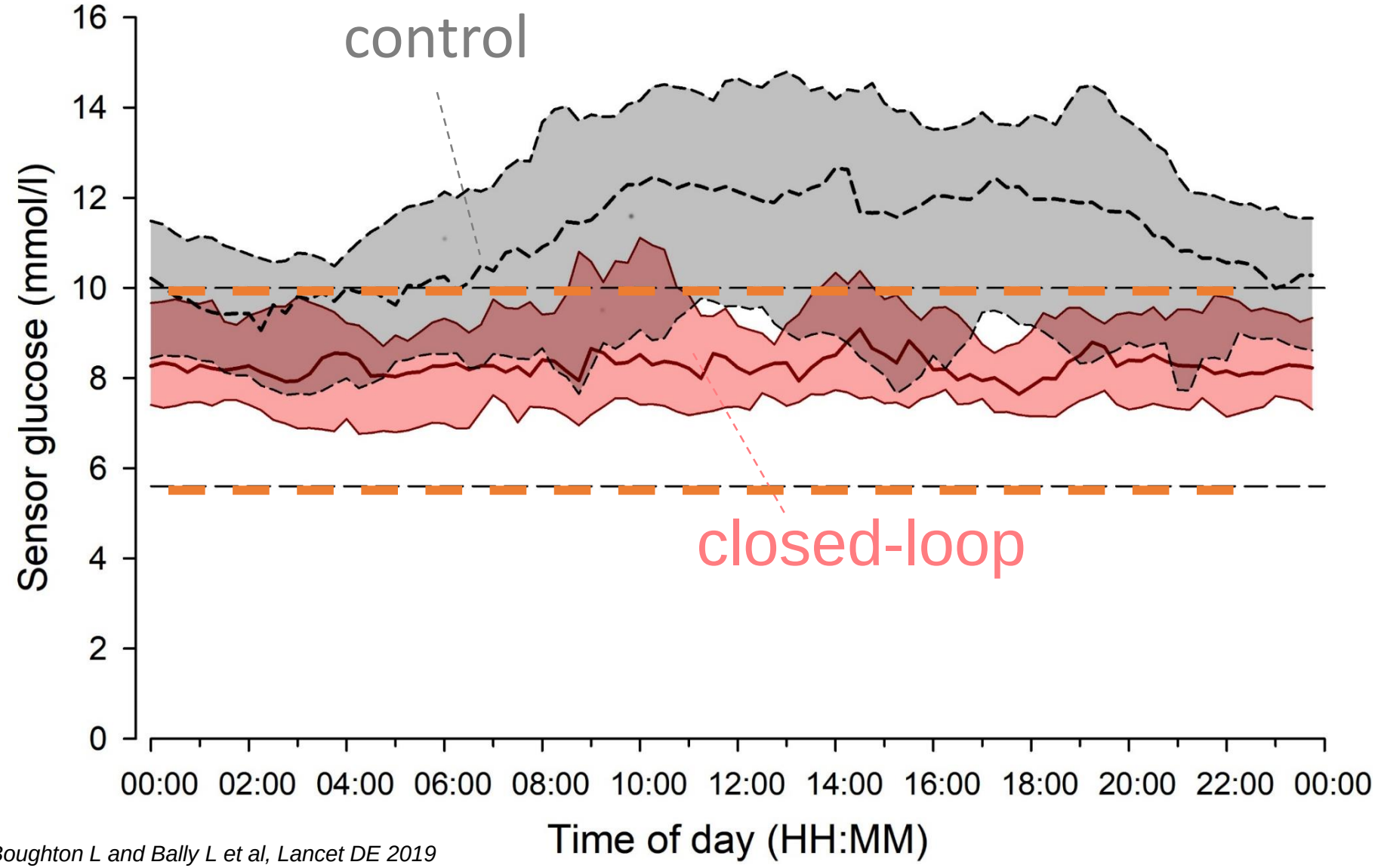
Results - overall glucose control

Analysis by intention to treat

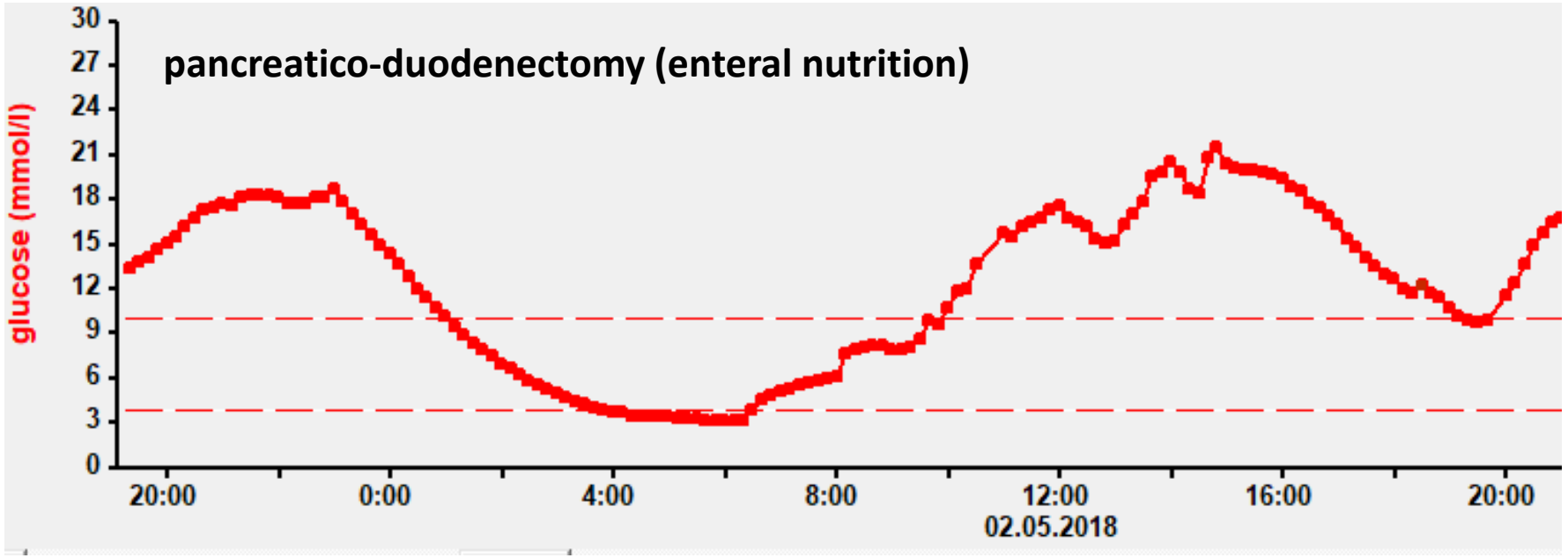
	Closed-loop N = 21	Control N = 22	P
*Time in target 5.6–10.0 mM (%)	68.5 (15.5)	36.4 (26.6)	<0.001
Mean glucose (mM)	8.5 (1.2)	11.4 (3.4)	0.001
SD of glucose (mM)	2.3 (0.8)	3.4 (1.4)	0.003
Time > 10 mM (%)	22.2 (15.7)	54.8 (29.7)	<0.001
Time < 5.6 mM (%)	9.3 (6.3)	8.7 (10.3)	0.82
Time < 3.0 mM (%)	0.0 (0.0 – 0.2)	0.0 (0.0 – 0.8)	0.37
AUC < 3.0 mM (mM x mins)	0.0 (0.0 – 4.4)	0.0 (0.0 – 20.1)	0.39
Total daily insulin dose (U)	54 (26 – 83)	40 (29 – 53)	0.41

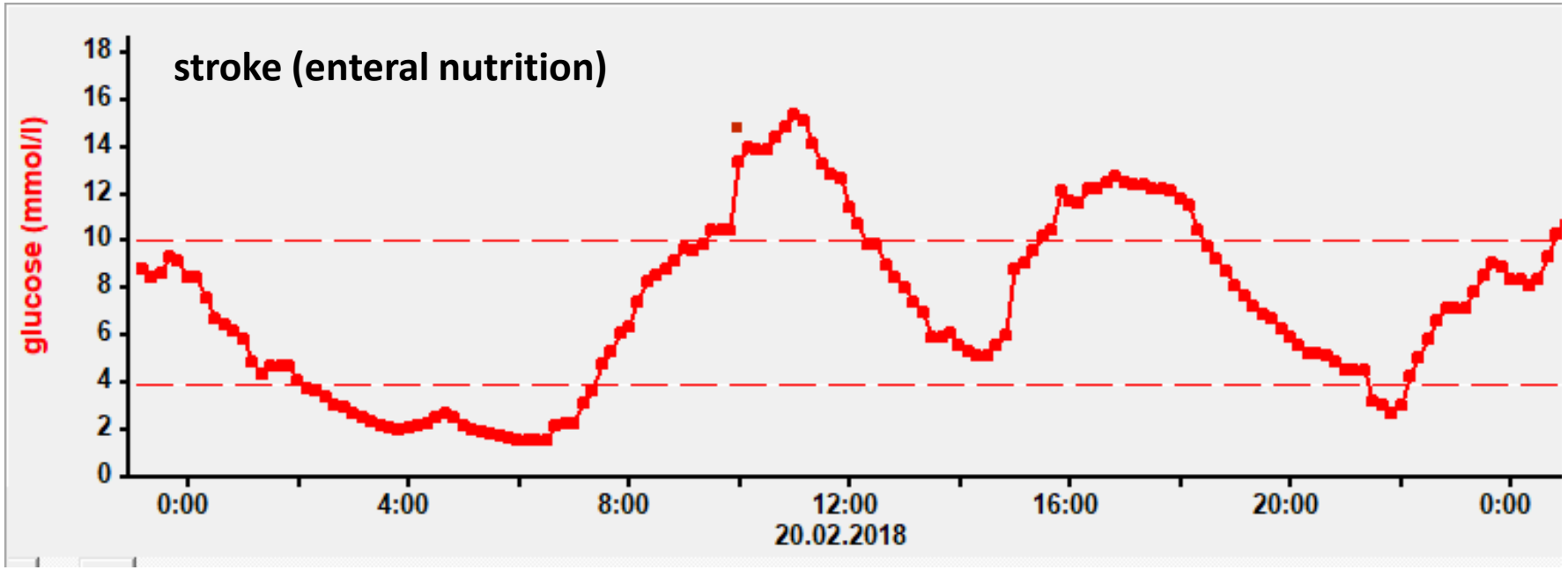
* Primary endpoint
Data presented as mean (SD) or median (IQR)

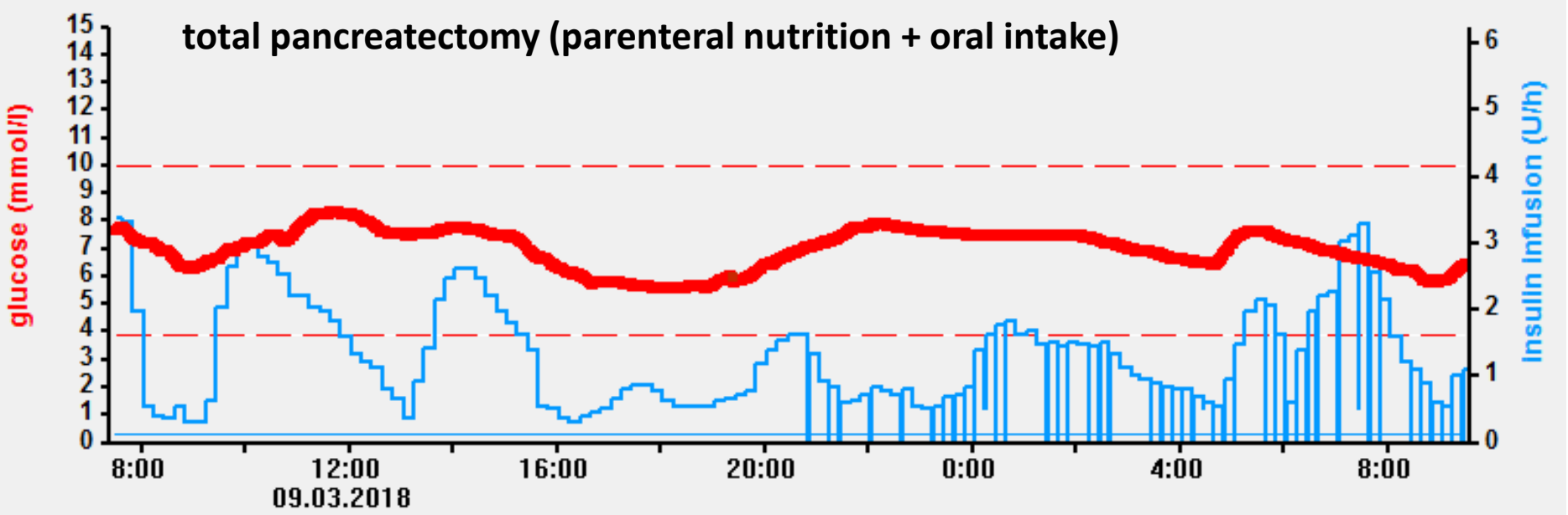
Glucose profile in patients receiving nutrition support

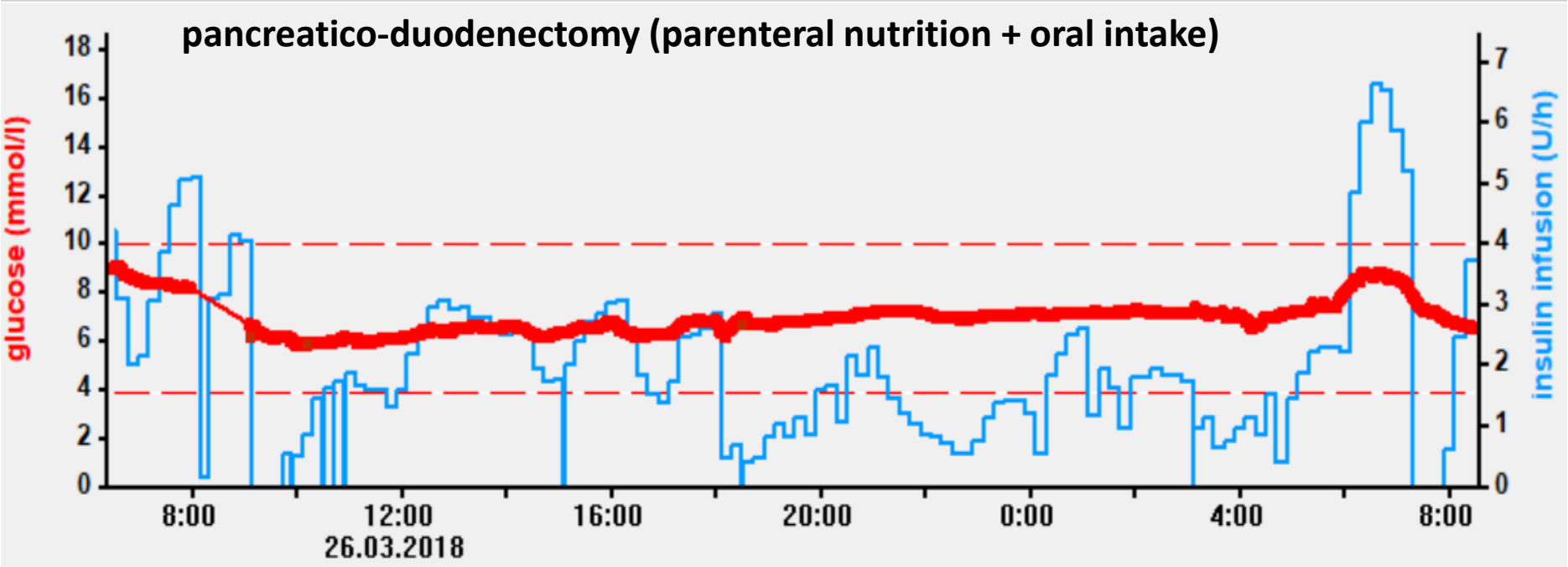


Boughton L and Bally L et al, Lancet DE 2019


pancreatico-duodenectomy (enteral nutrition)
glucose (mmol/l)
30
27
24
21
18
15
12
9
6
3
0
20:00
0:00
4:00
8:00
12:00
02.05.2018
16:00
20:00


stroke (enteral nutrition)
glucose (mmol/l)
18
16
14
12
10
8
6
4
2
0
0:00
4:00
8:00
12:00
20.02.2018
16:00
20:00
0:00


total pancreatectomy (parenteral nutrition + oral intake)
glucose (mmol/l)
Insulin Infusion (U/h)
8:00
12:00
09.03.2018
16:00
20:00
0:00
4:00
8:00


pancreatico-duodenectomy (parenteral nutrition + oral intake)
glucose (mmol/l)
insulin infusion (U/h)
8:00
12:00
26.03.2018
16:00
20:00
0:00
4:00
8:00

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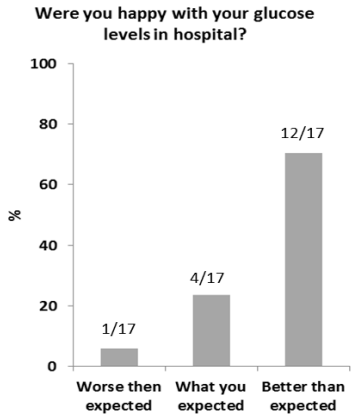
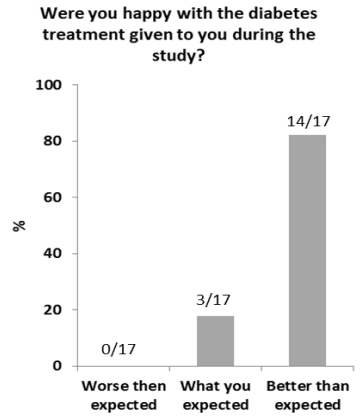
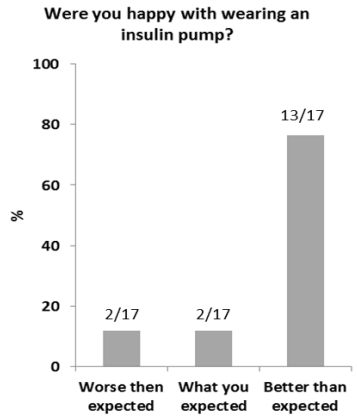
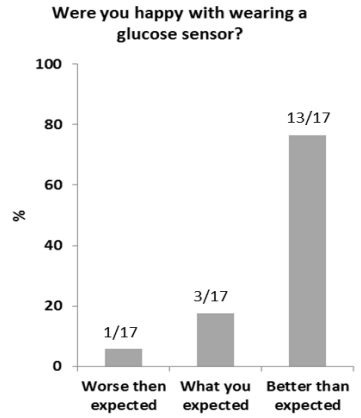
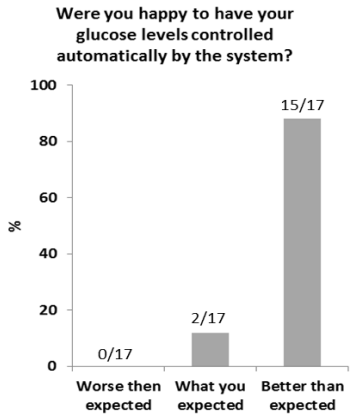
Acceptability outcomes

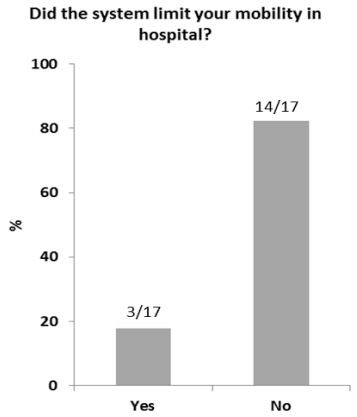


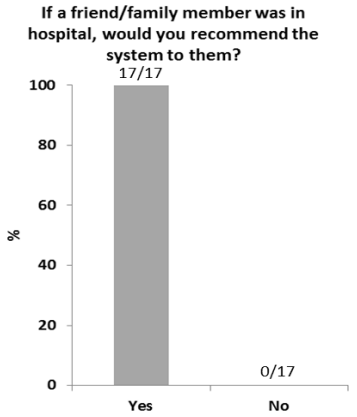












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KNOW DIABETES. FIGHT DIABETES.