Picture This: DKA – Current Management and Future Challenges

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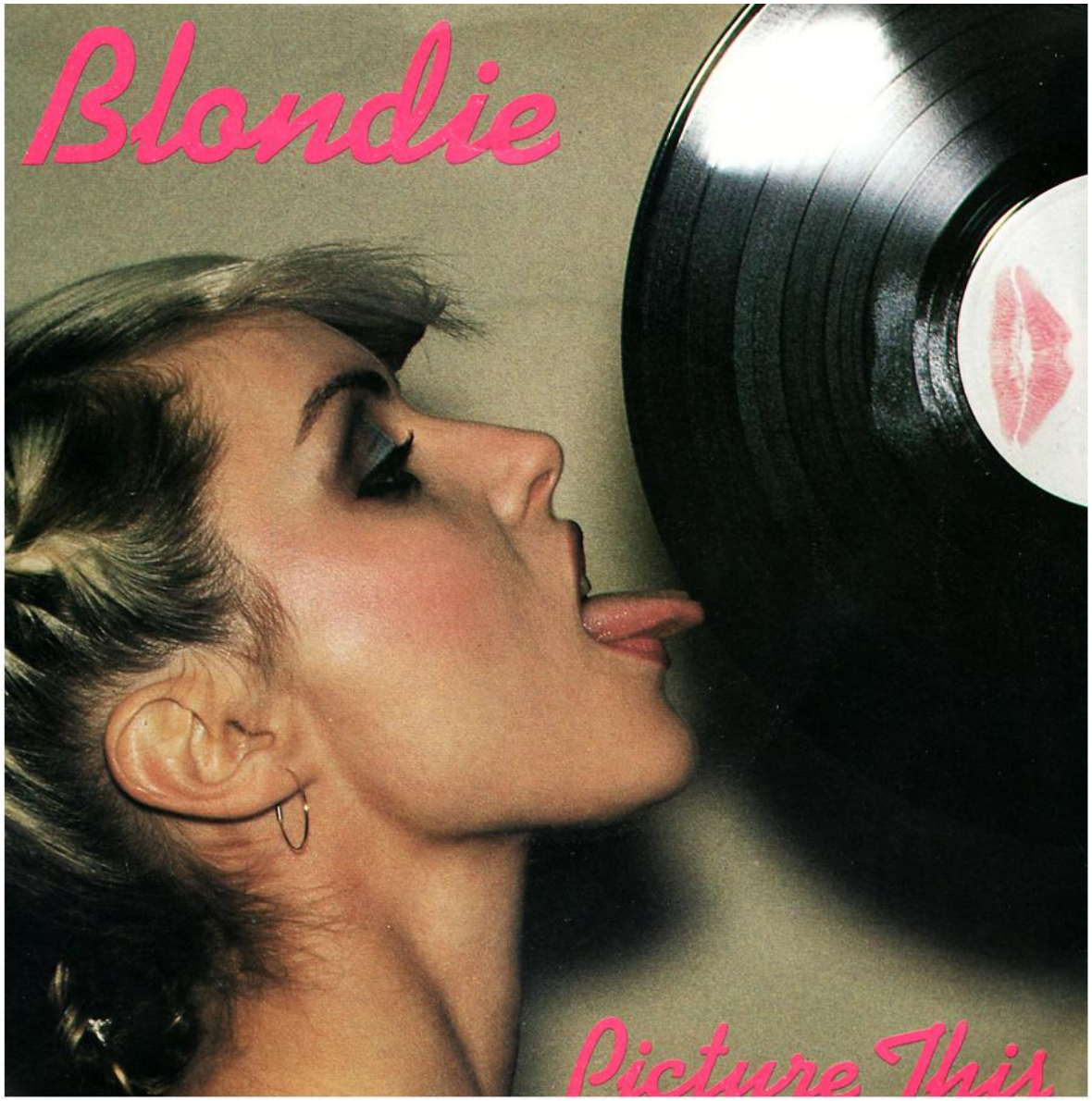
Blondie
Picture This

Overview

- Why I think the ADA is wrong
- The pathogenesis of DKA
- A bit of history (where we have been)
- Where we are now
- What is going on
- Where do we want to be

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Diagnostic Criteria - ADA and JBDS

	DKA		
	Mild (plasma glucose >250 mg/dl)	Moderate (plasma glucose >250 mg/dl)	Severe (plasma glucose >250 mg/dl)
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10
Urine ketone*	Positive	Positive	Positive
Serum ketone*	Positive	Positive	Positive
Effective serum osmolality†	Variable	Variable	Variable
Anion gap‡	>10	>12	>12
Mental status	Alert	Alert/drowsy	Stupor/coma

DIAGNOSIS:
Ketonaemia $\geq$ 3.0mmol/L **or** significant ketonuria (more than 2+ on standard urine sticks)
Blood glucose > 11.0mmol/L or known diabetes mellitus **(200mg/dl)**
Bicarbonate ($HCO3^-$) < 15.0mmol/L **and/or** venous pH < 7.3

Kitabchi AE et al Diabetes Care 2009;32(7):1335-1343
http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm

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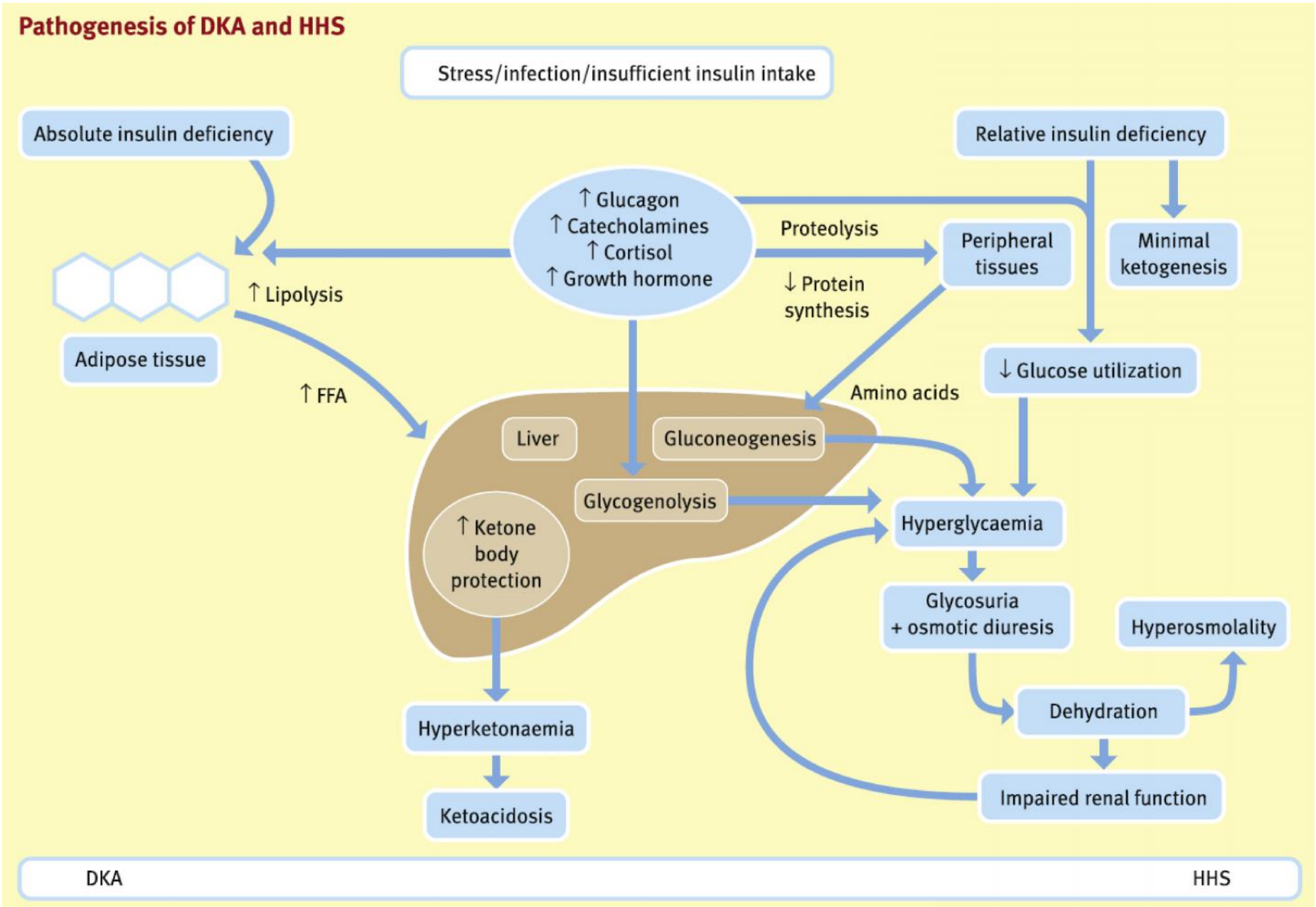

English P et al Postgrad Med J 2004;80:253-261

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A Brief History

Howard Root in Boston reports reduction in mortality from 12% to 1.6% between 1940 and 1944 – using up to 1770 units of insulin in the 1st 24h after admission

Malins and Black in Birmingham used between 140 and 1400 units of insulin in the first 24h depending on severity in 170 consecutive cases

1922

1945

1949

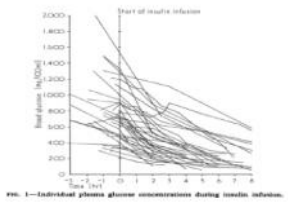
1948

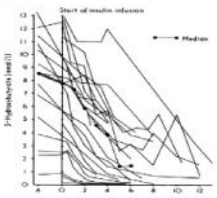
1973

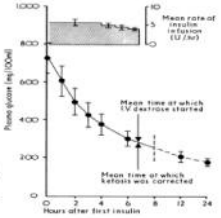
Type 1 diabetes universally fatal

In 1925 Joslin reports that 31 out of 33 patients with DKA survive – with gentle fluid replacement

Micks in Dublin used 100 units for those in 'pre-coma' and 100 units every 15 minutes - between 500 and 2000 units depending on severity of coma







RD Lawrence advocates very aggressive fluid management

3 consecutive papers in the BMJ showed that low dose insulin infusions (5-6 units/hr) work just as well as high dose in lowering glucose & ketones

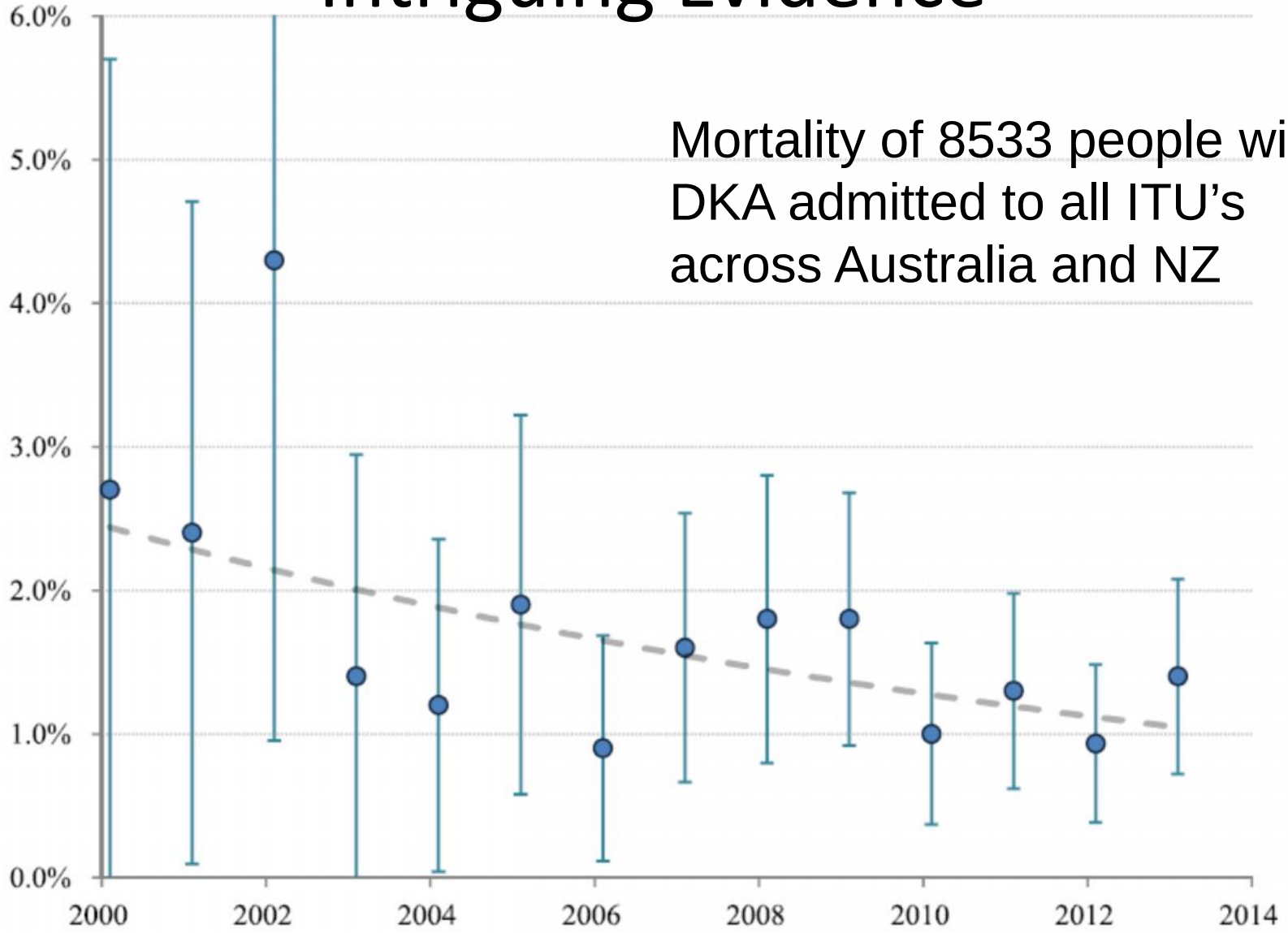
People Were Still Dying

Author (yr)	Age <50 yr No. (% mortality)	Age ≥50 yr No. (% mortality)
Diabetic ketoacidosis		
Fitzgerald et al. (1961)[6]	104 (7%)	56 (21%)
Beigelman (1971)[7]	415 (3%)	67 (29%)
Soler et al. (1973)[8]	207 (4%)	31 (16%)
Keller et al. (1975)[9]	26 (4%)	32 (22%)
Gale et al. (1981)[10]	206 (3%)	111 (43%)
Sheppard and Wright (1982)[11]	239 (2%)	113 (12%)
This study* (1982)	109 (4%)	77 (26%)

- Given 0.1u/kg/hr and 1-2 L of fluid on admission then 1 L every 3-4 hours, and giving potassium 20-40mmol/hour

Carroll P et al Diabetes Care 1983;6(6):579-585

Intriguing Evidence

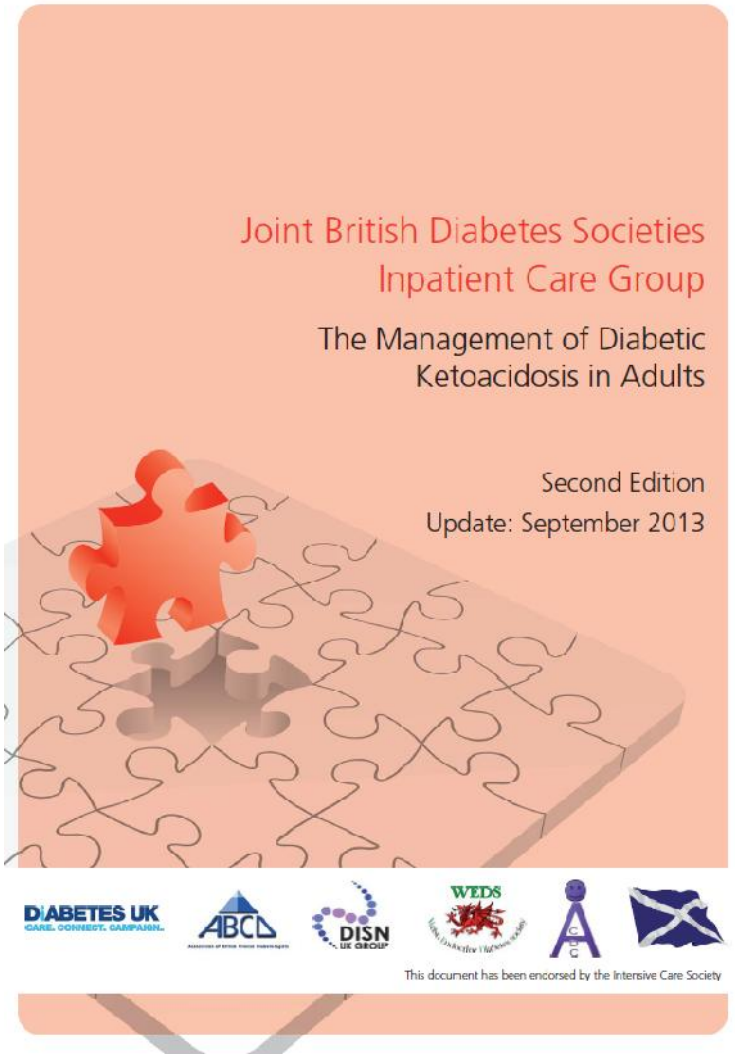


Mortality of 8533 people with DKA admitted to all ITU's across Australia and NZ

Venkatesh B et al Critical Care 2016;1:451

A Question

- How do we know that what we are doing is correct?



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

Overview

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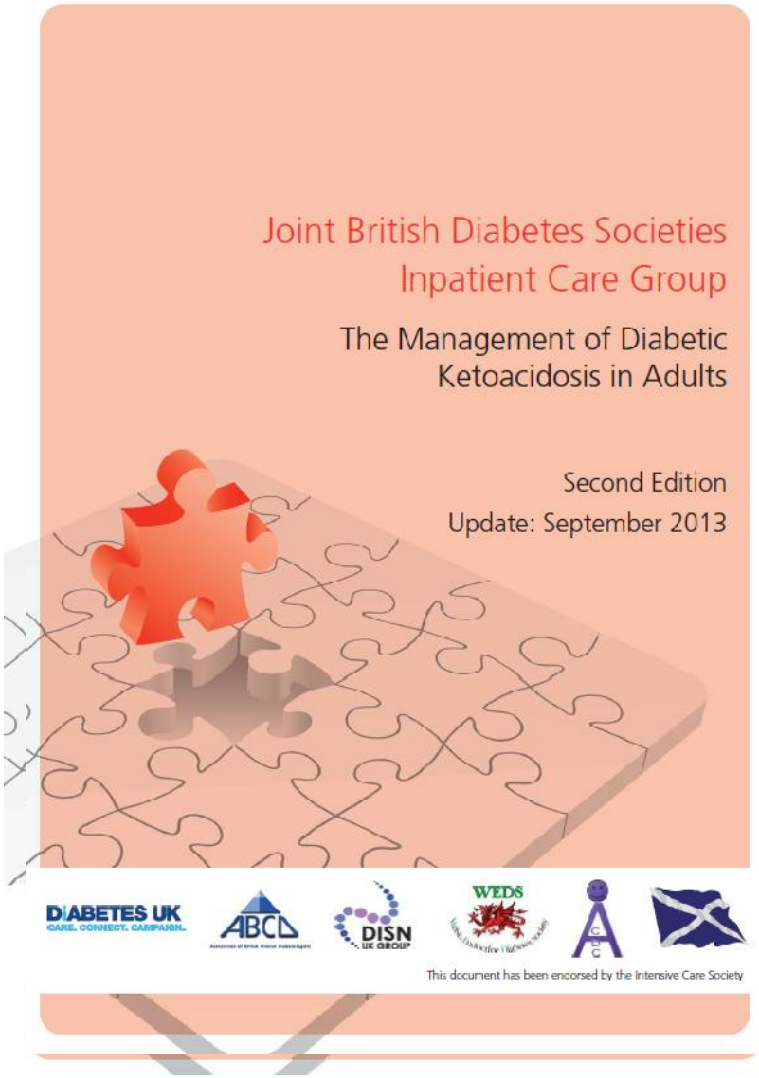
Where Are We Now?

- In 2010 the JBDS produced a guideline on the management of DKA
- With > 20,000 hard copies given out or downloaded
- An updated guideline was published in late 2013
- A national survey was conducted in Autumn 2014



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

What Was Done?

Joint British Diabetes Societies Inpatient Care Group

Data collection tool for the Management of Diabetic Ketoacidosis (DKA) in Adults

(Admission to Discharge)

Name of Hospital: Your grade ☐ Consultant ☐ SpR ☐ CMT ☐ DISN ☐ Other.....

Year diabetes diagnosed?		Age	Gender: ☐ Male ☐ Female

1. Ethnicity ☐ Not stated

White	Mixed	Asian / British Asian	Black / Black British	Other
☐ a) British ☐ b) Irish ☐ c) Any other white background	☐ d) White /Black Caribbean ☐ e) White / Black African ☐ f) White and Asian ☐ g) Any other mixed background	☐ h) Indian ☐ i) Pakistani ☐ j) Bangladeshi ☐ k) Any other Asian	☐ l) Caribbean ☐ m) African ☐ n) Any other Black background	☐ o) Chinese ☐ p) Any other ethnic group

2. Date / time of Admission: (dd/mm/yy hh:mm) 3. Date / time of Discharge: (dd/mm/yy hh:mm)

4. Did this episode of DKA occur in someone who was already an inpatient? ☐ Yes ☐ No ☐ Not recorded

5. How many previous admissions for DKA have they had in the last 12 months?..... 6. Date of death .....(dd/mm/yy)

7. Cause(s) of death: 1)..... 2)..... 3).....

Diagnosis of DKA (Where appropriate please put a x in the box)

8) Was the diagnosis confirmed according to diagnostic criteria? ☐ Yes ☐ No ☐ N/A

a) Blood ketones ..... mmol/L b) Urine ketones ..... c) Blood glucose .....mmol/L	**DIAGNOSIS of DKA (JBDS):** Ketonaemia > 3.0mmol/L or significant ketonuria (more than 2+ on standard urine sticks) Blood glucose > 11.0mmol/L or known diabetes mellitus Bicarbonate (HCO3-) < 15.0mmol/L and/or venous pH < 7.3	**10. Was treatment area?** a) ☐ Level 1? (eg general ward area) b) ☐ Level 2? (eg high dependency area) c) ☐ Level 3? (eg ITU) d) ☐ Acute medical unit? e) ☐ A&E f) ☐ Other? (please state) .....
d) pH ..... e) Bicarbonate .....mmol/L	**9. If you use different diagnostic criteria for diagnosing DKA – please list them here** Ketones .....mmol/L Glucose.....mmol/L pH..... Other.....	**11. Do you use the JBDS DKA guidelines?** a) ☐ Yes b) ☐ No

Joint British Diabetes Societies Inpatient Care Group

Institutional Standards for the Management of Diabetic Ketoacidosis (DKA) in Adults
(Complete one per Institution)

Name of Hospital:		Date form completed:	
Form completed by		Grade	

(Put N/A= not applicable or NR = not recorded)

1. Guidelines	Yes	No	Don't know
a) Do you have a DKA **treatment pathway**?			
b) Do you have **local guidelines for managing DKA**?			
c) Do you have an **Integrated Care Plan (ICP)** for DKA?			
d) Are your guidelines **current and valid**?			
e) What are your guidelines based on? ☐ i) Joint British Diabetes Societies guidance? ☐ ii) Other..... *(please state)*			

2. Staffing	Yes	No	Don't know
a) In the clinical areas where patients with DKA are initially cared for, do you have **trained health care professionals** available to measure blood ketone levels 24 hours per day?			
b) Do you have **dedicated inpatient diabetes specialist nurses** at a staffing level of 1WTE per 300 beds? If the answer is **NO** – what is your current DISN staffing level per 300 beds?.....WTE			
c) Do you have a **clinical lead** responsible for the implementation & audit of DKA guidelines?			

3. Monitoring	Yes	No	Don't know
a) In the clinical areas where patients with DKA are initially cared for, do you have the facility to **measure blood ketones** in your Trust?			
b) Do you have **blood glucose testing meters that are centrally connected** in your Trust?			

4. Audit / Education	Yes	No	Don't know
a) Do you have **a quality assurance scheme** in place for both glucose and ketone meters?			
b) Have you **audited the outcomes** of your patients admitted with DKA the last past?			
c) Do you **monitor against performance indicators** eg those listed in the JBDS guideline?			
d) Do you have a **rolling educational programme** for medical staff?			
e) Do you have a **rolling educational programme** for nursing staff?			

5. Patients	Yes	No	Don't know
a) Do your patients have access to the specialist diabetes **team within 24 hours of admission?**			
b) Do your patients have the choice to **self-manage their diabetes**?			

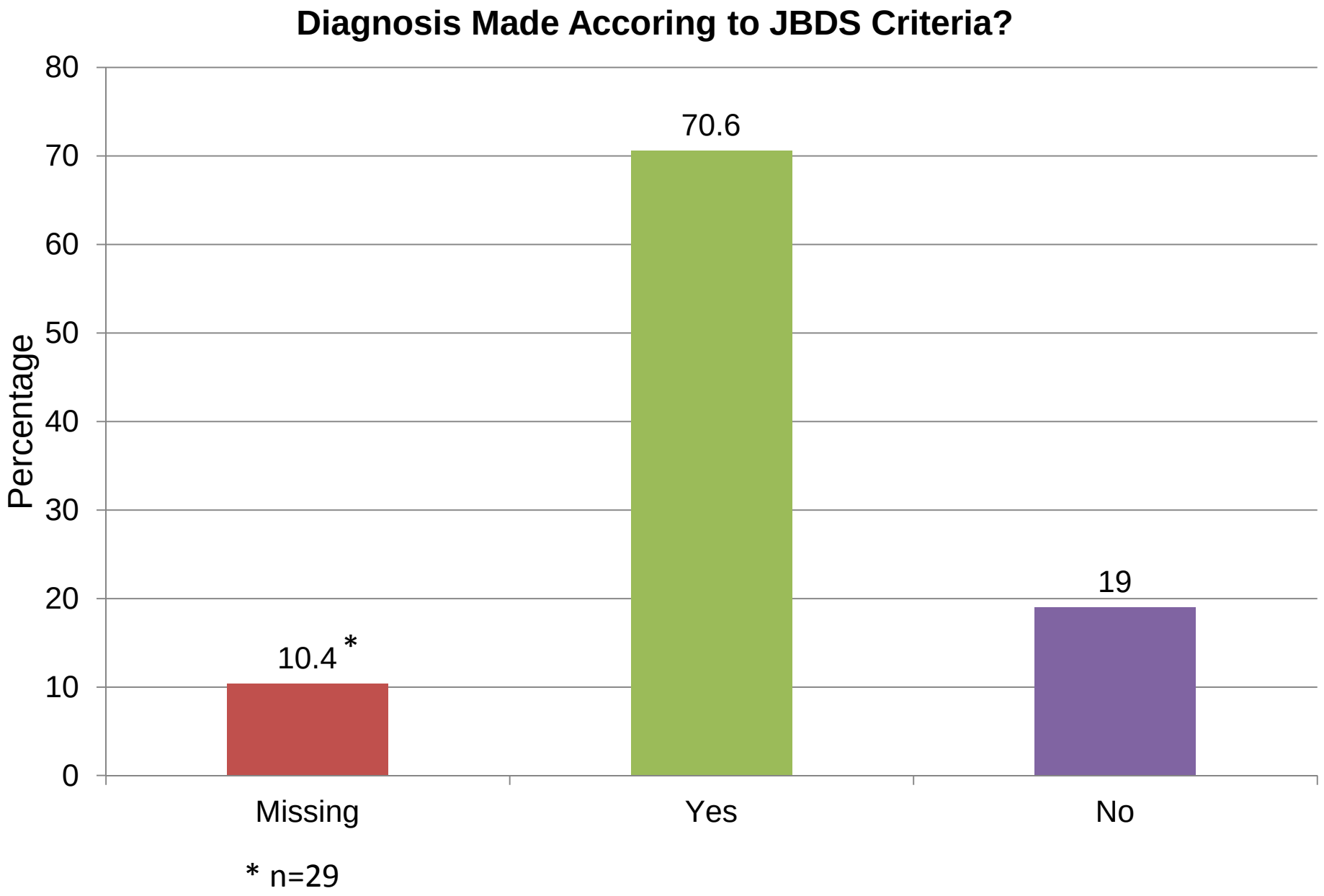
Results

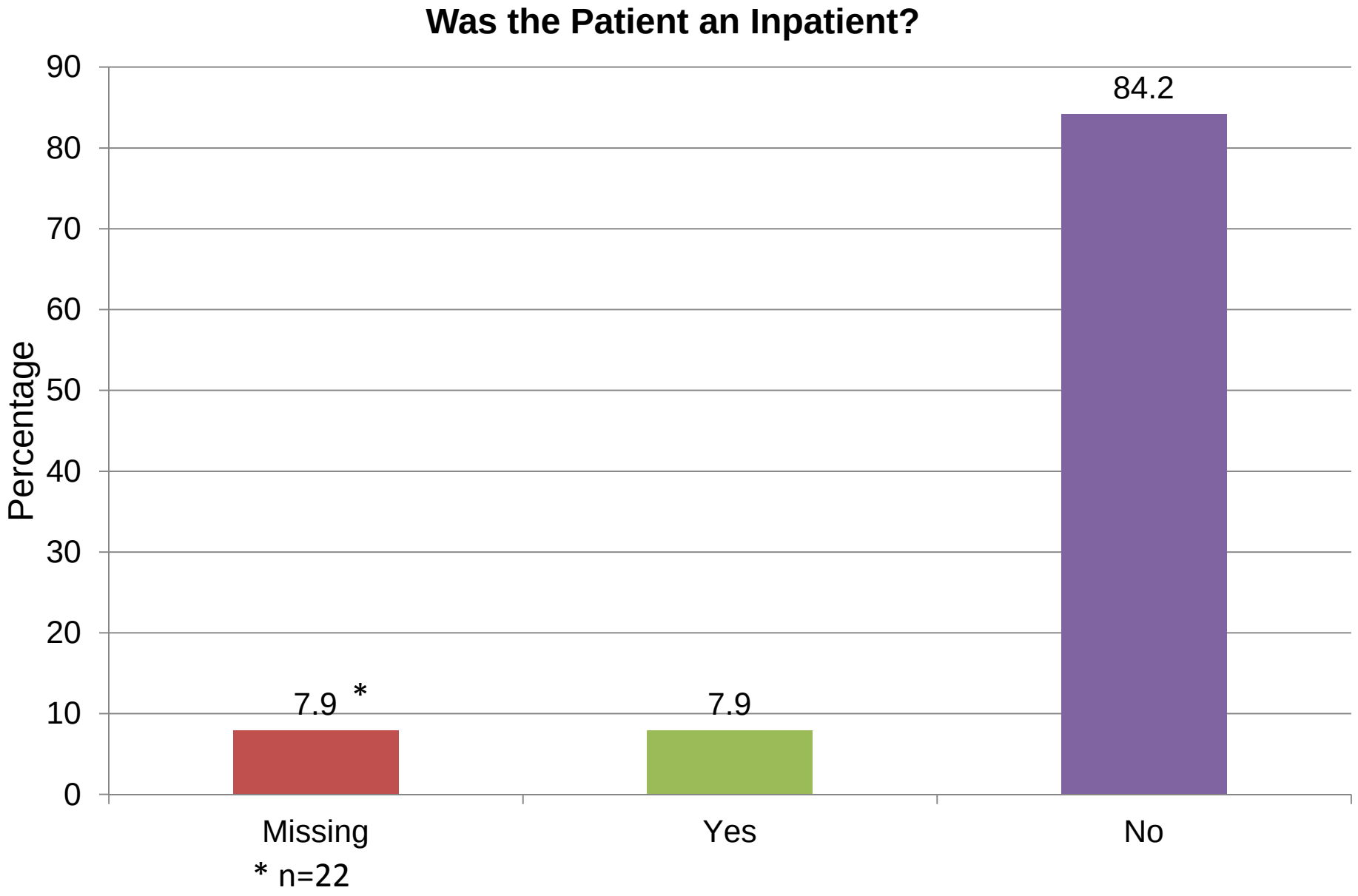
- 283 forms were received from 72 hospitals between May and November 2014
- Here is a flavour of the results

Times (Median)

- Admission to diagnosis - 35.5 min
- Admission to starting 09% NaCl - 41.5 min
- Admission to starting FRIII - 60 min
- Admission to resolution - 18.7 hours
- To hospital discharge - 2.6 days

Dhatariya K et al Diabetic Medicine 2016;33(2):252-260


Diagnosis Made Accoring to JBDS Criteria?
Percentage
80
70
60
50
40
30
20
10
0
70.6
19
10.4 *
Missing
Yes
No
* n=29



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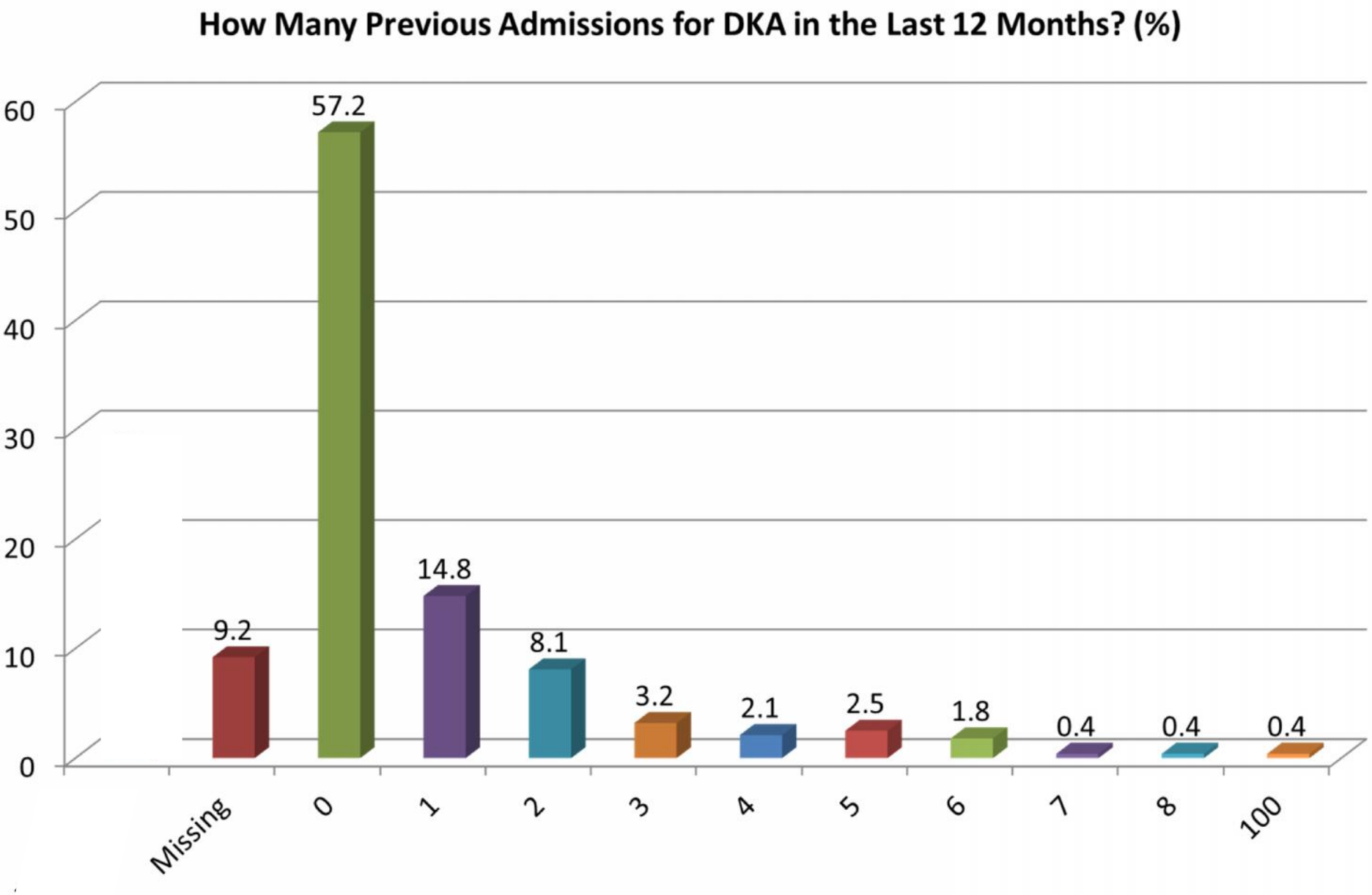

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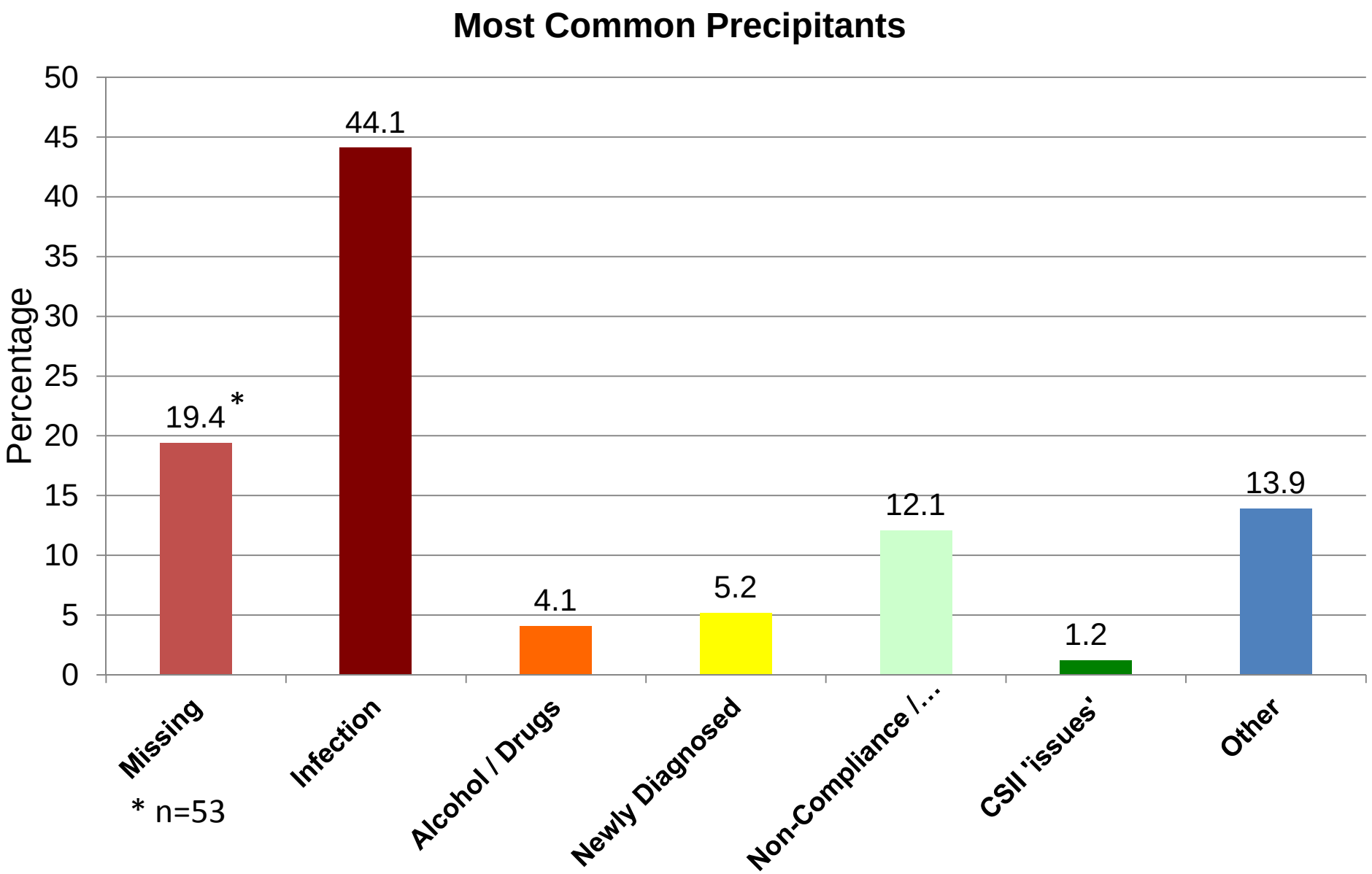

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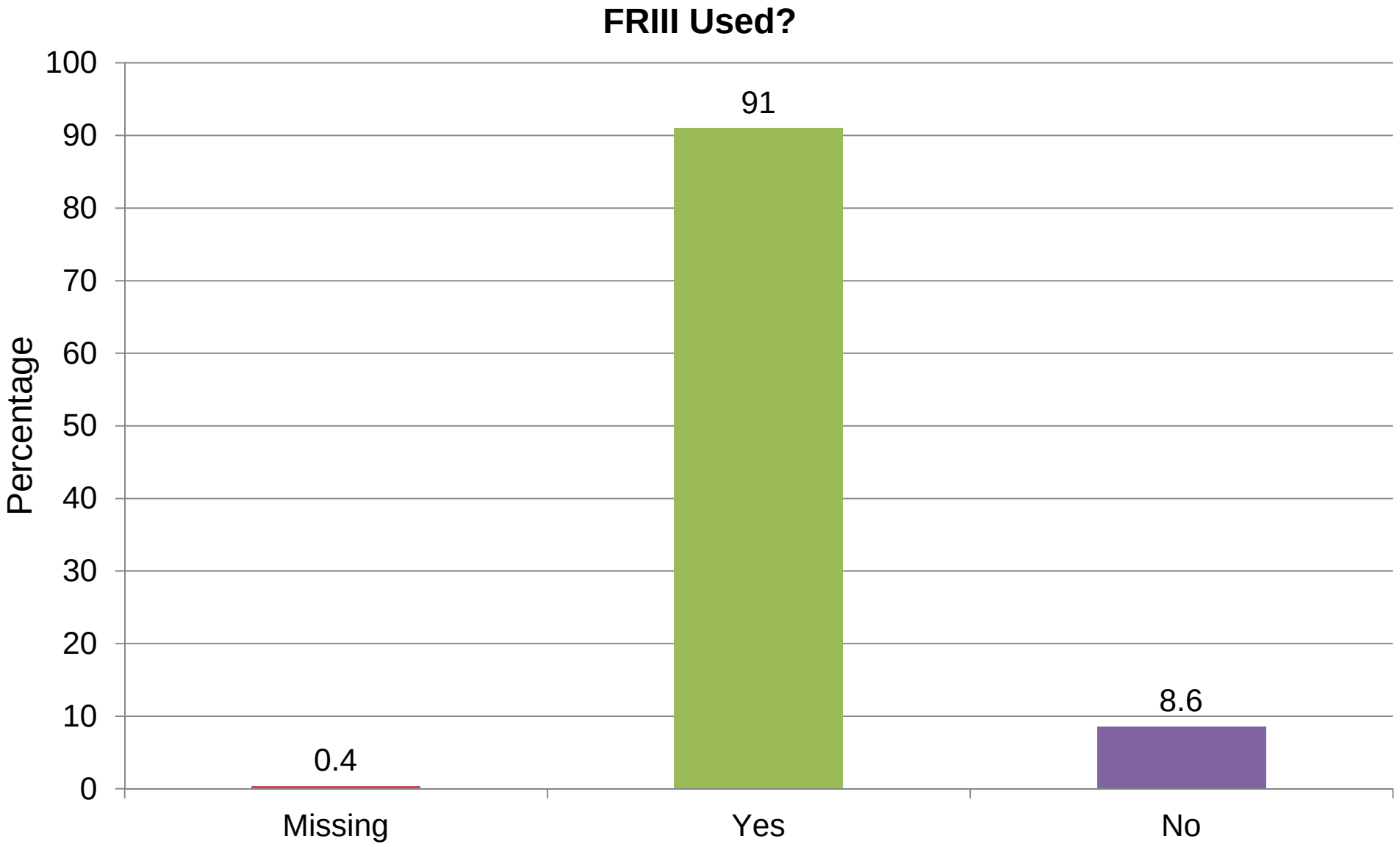

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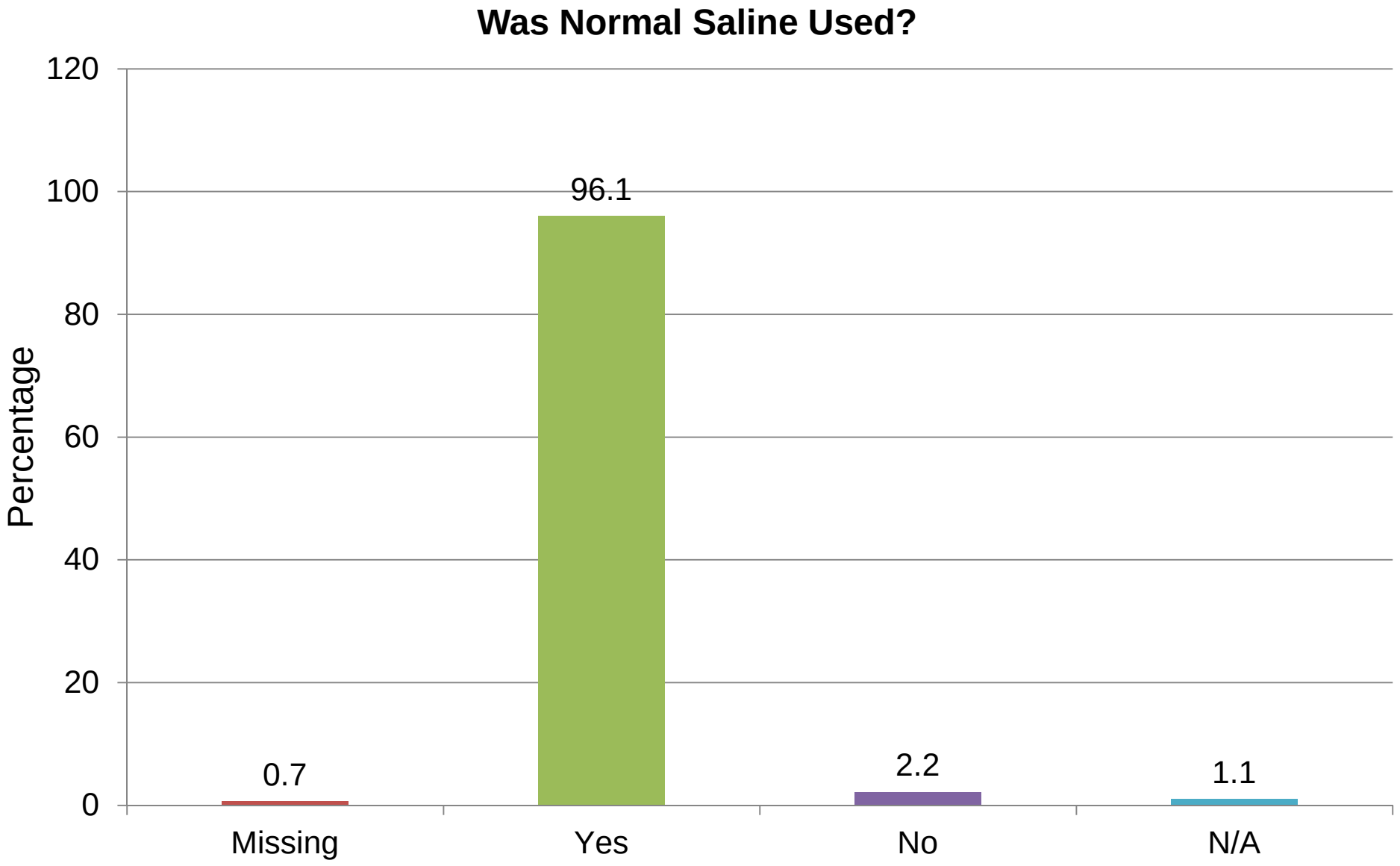

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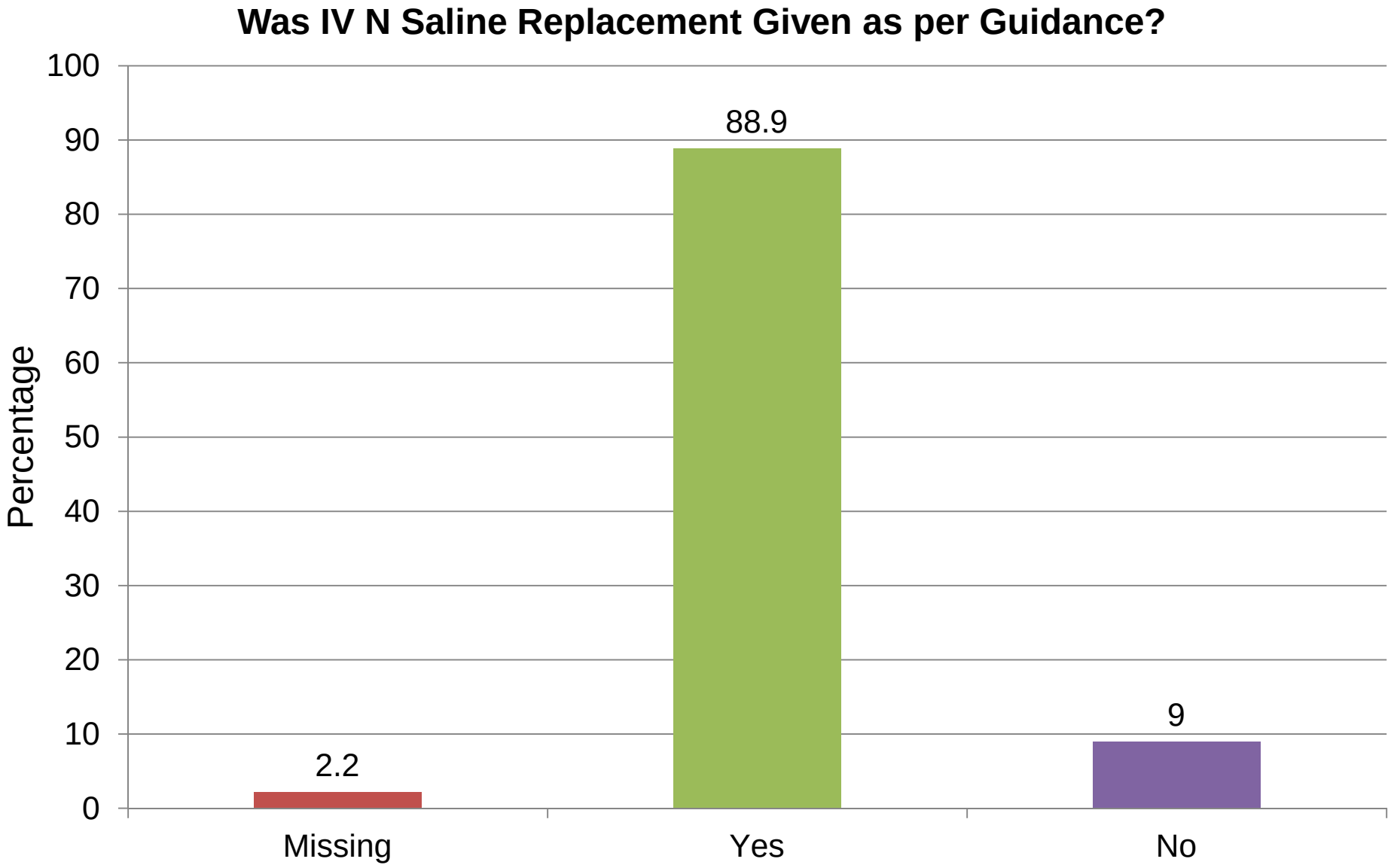

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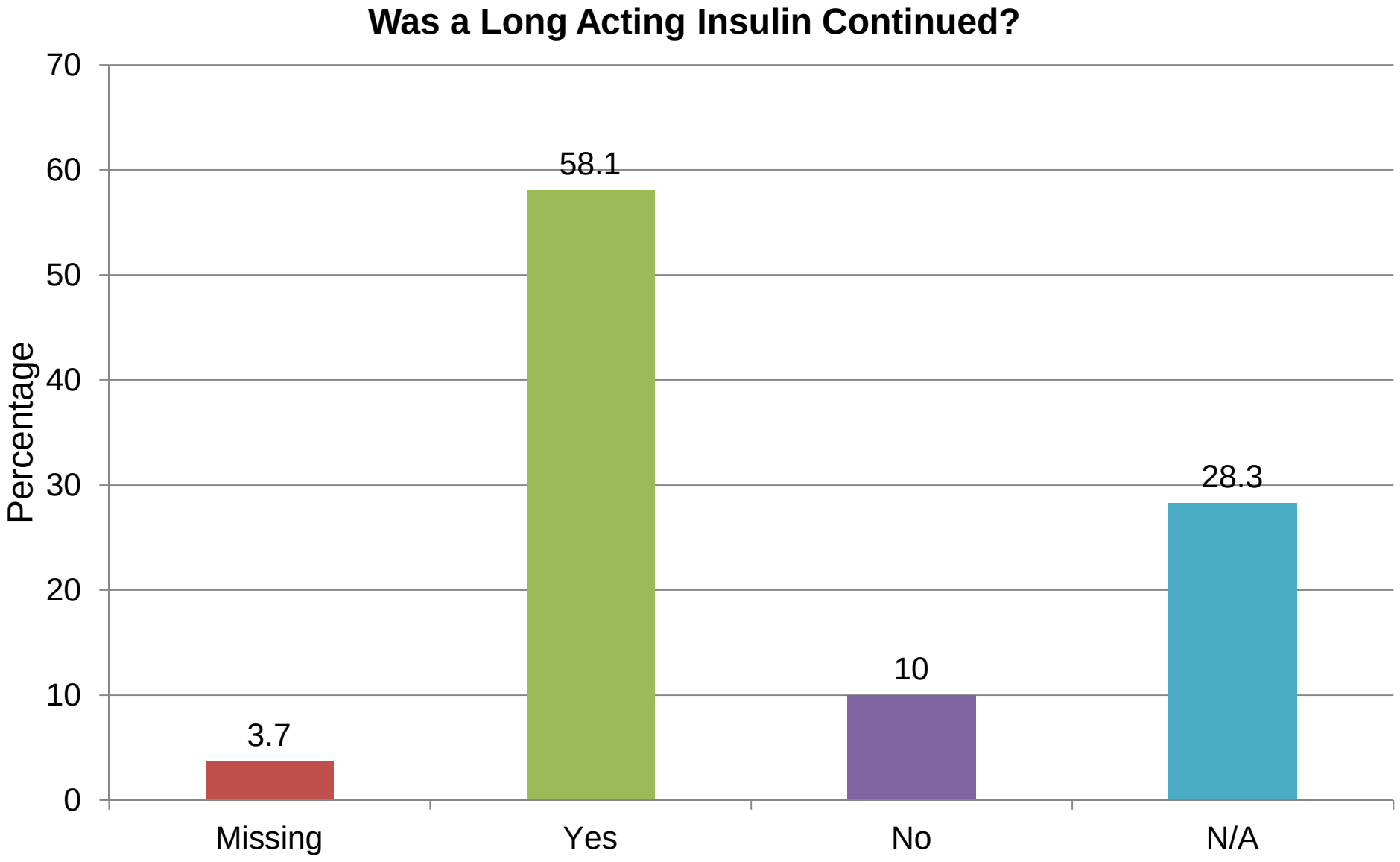

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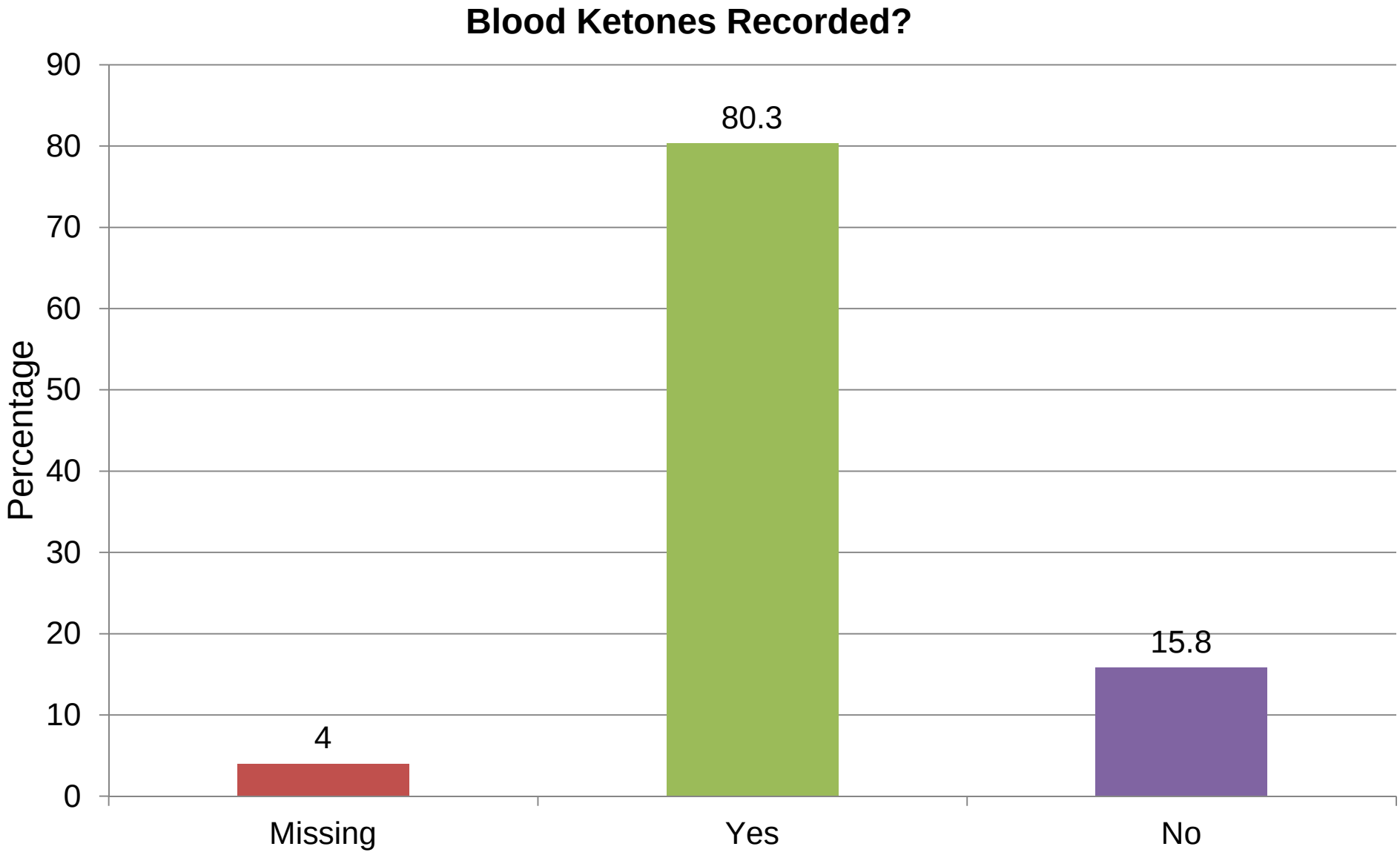
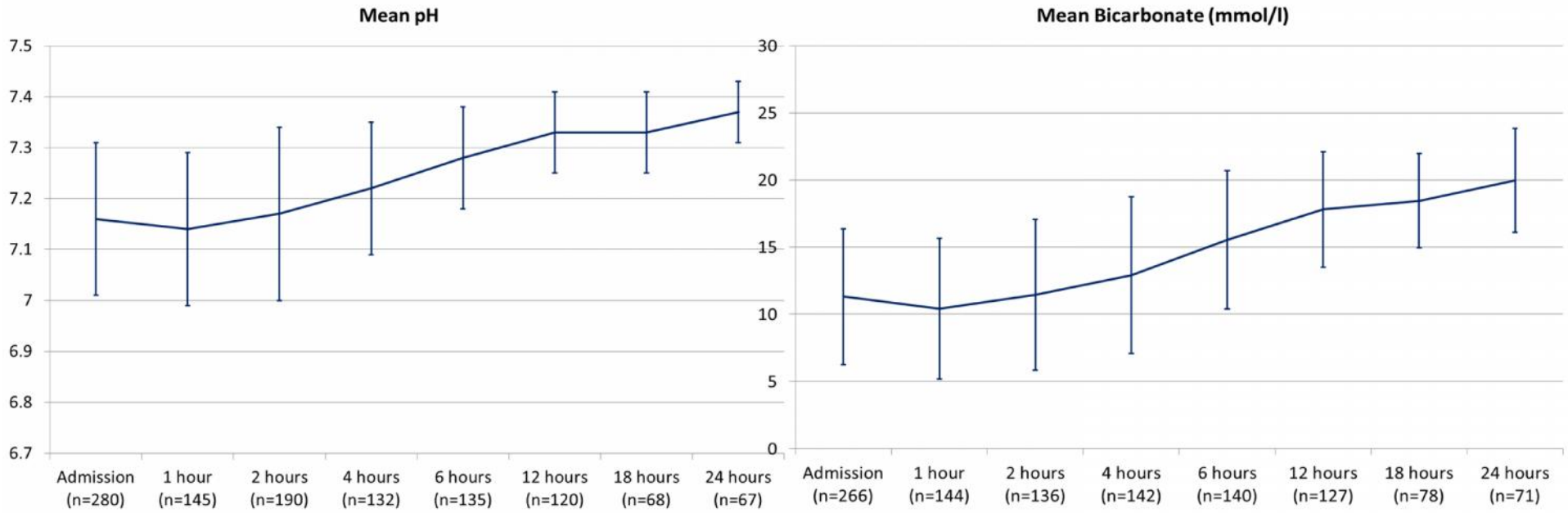


Dhatariya K et al Diabetic Medicine 2016;33(2):252-260

Fixed Rate Intravenous Insulin

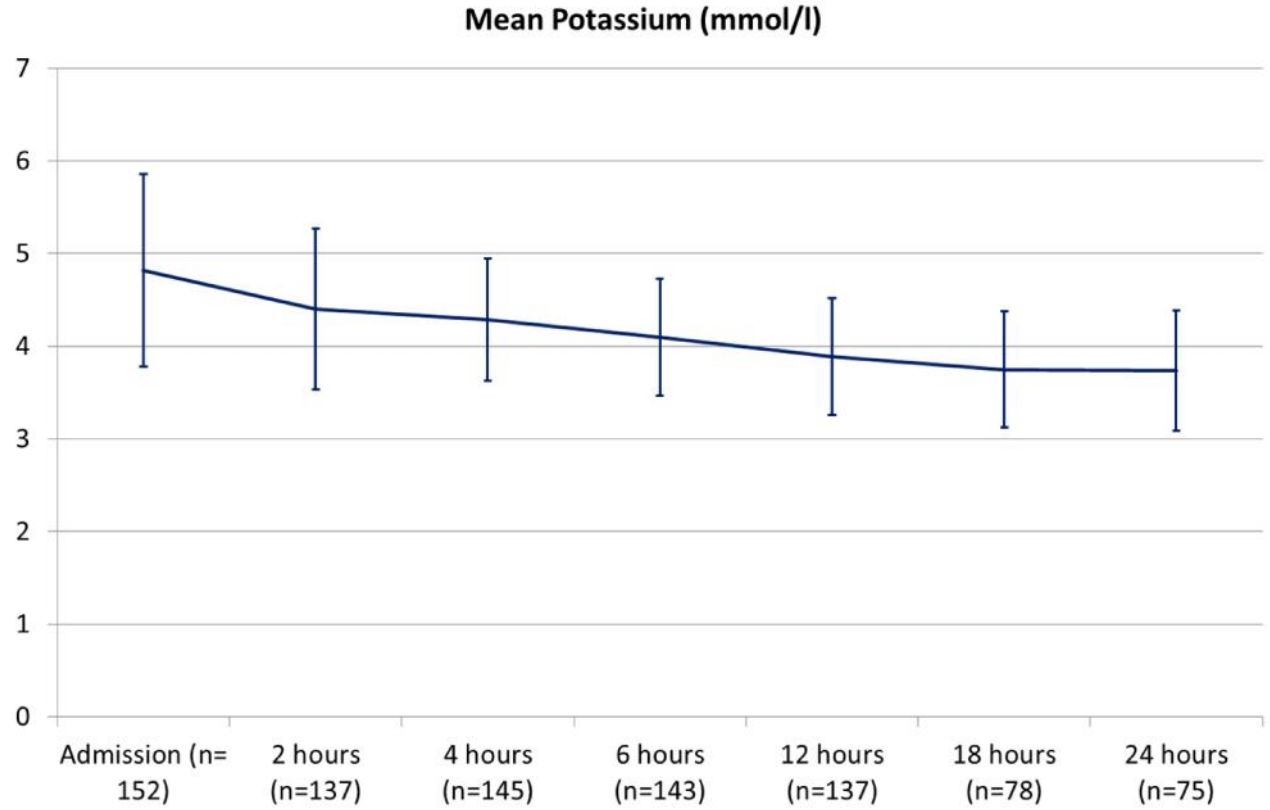
- The use of 0.1units/kg/hr led to excellent rises in pH and bicarbonate – so DKA resolved by 18.77 hours



Dhatariya K et al Diabetic Medicine 2016;33(2):252-260

Potassium

- But despite an aggressive potassium replacement regimen – more than 50% of patients became hypokalaemic



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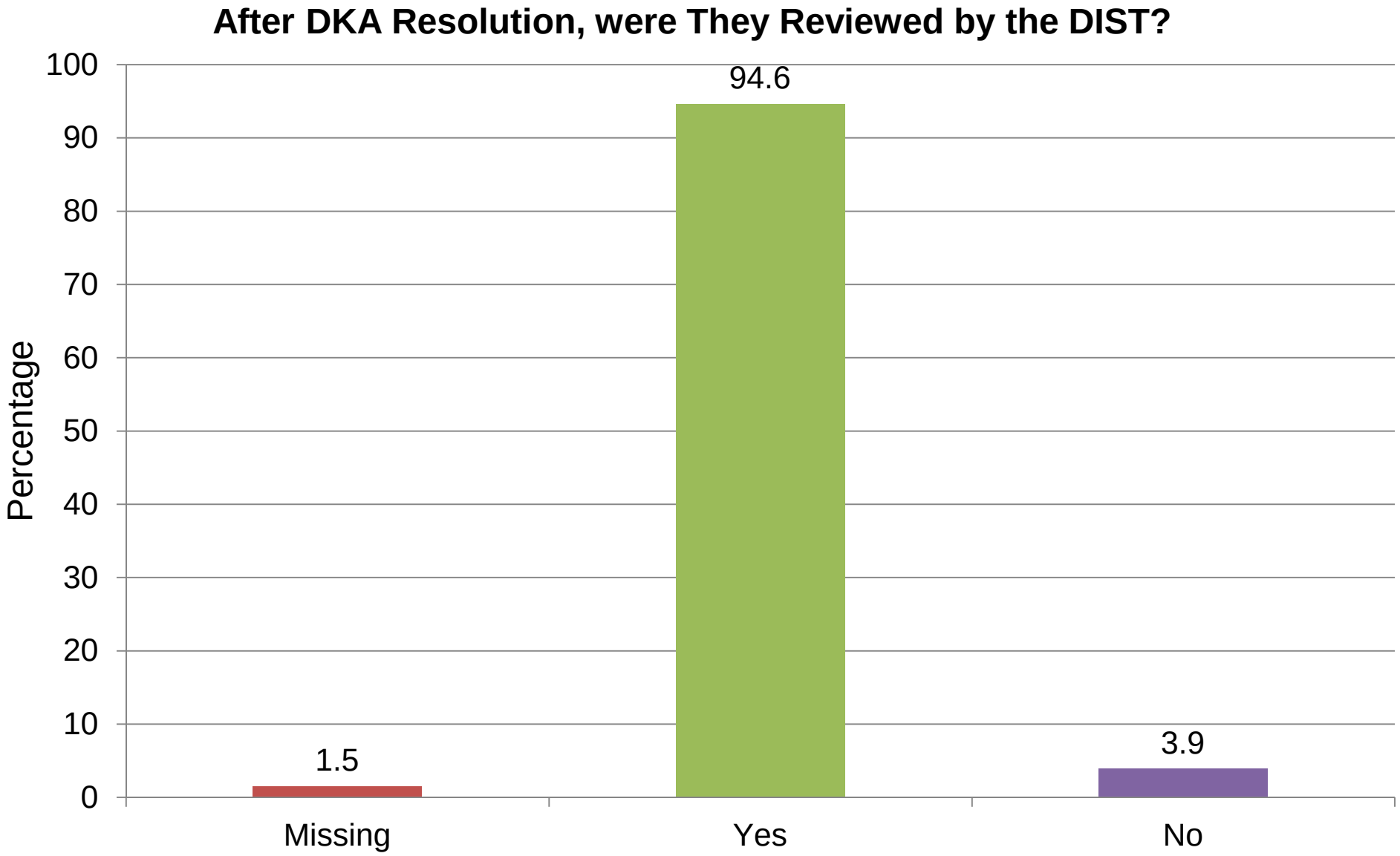

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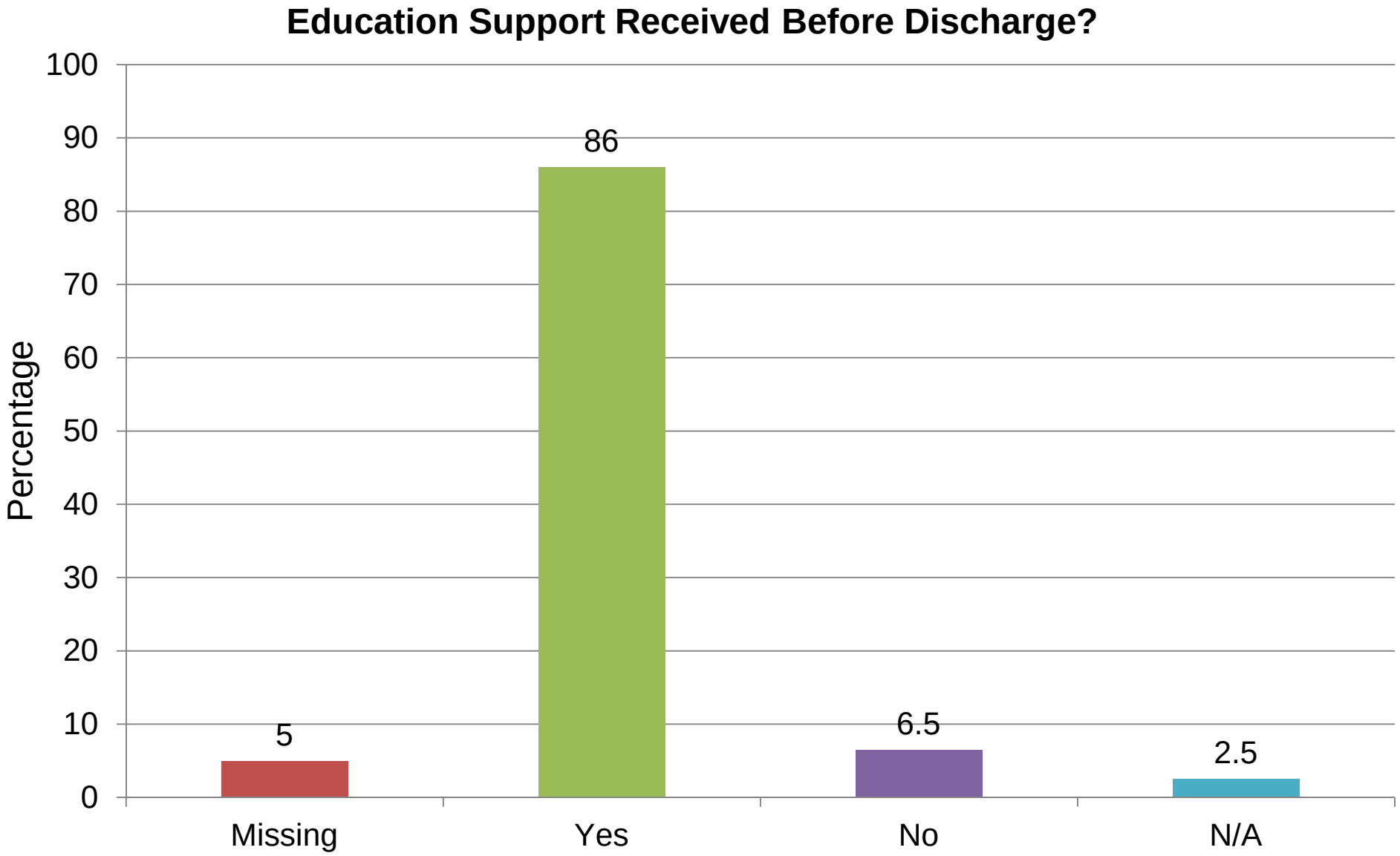

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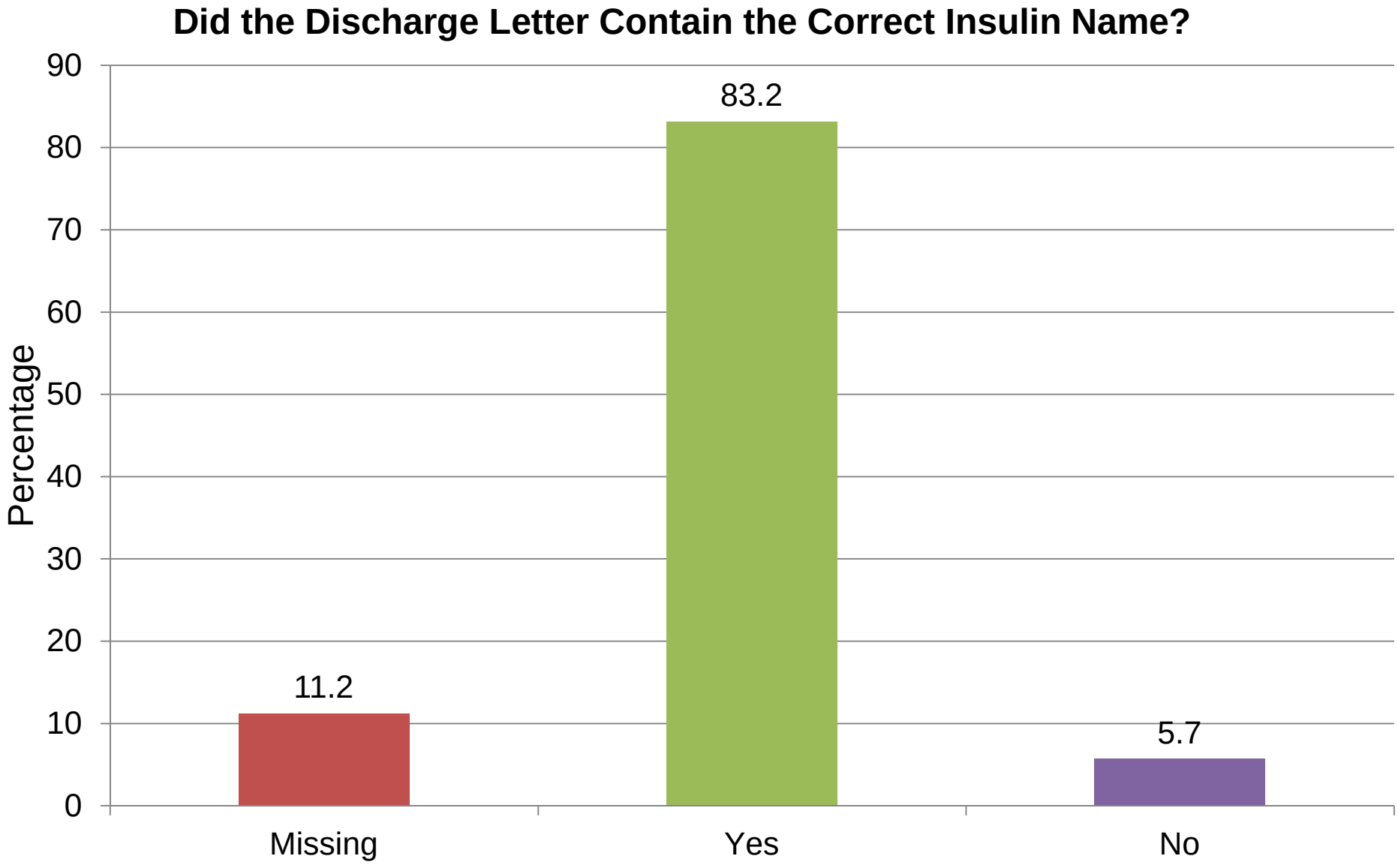

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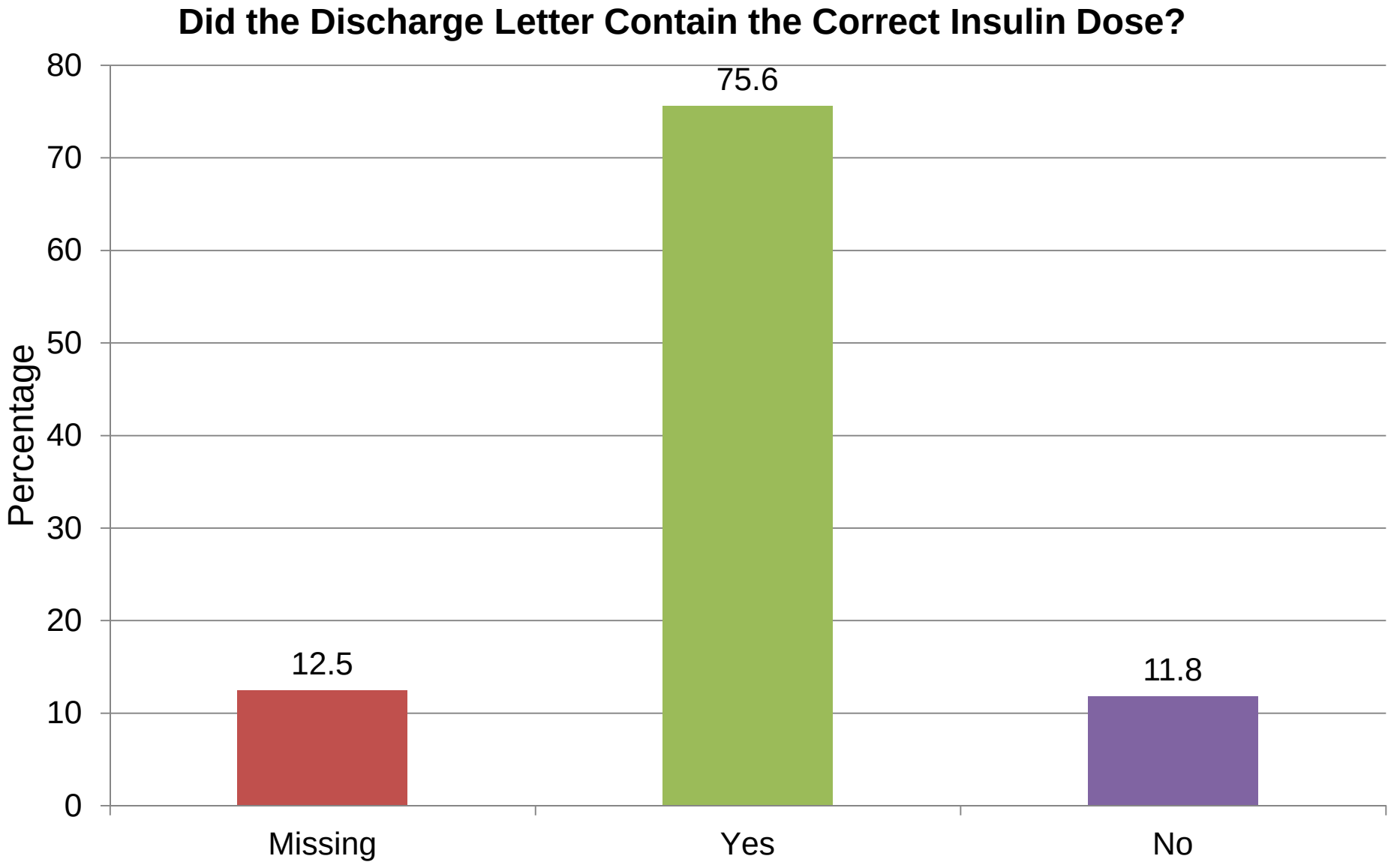

Dhatariya K et al Diabetic Medicine 2016;33(2):252-260

Timeline

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Type 1 diabetes universally fatal

In 1925 Joslin reports that 31 out of 33 patients with DKA survive – with gentle fluid replacement

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Howard Root in Boston reports reduction in mortality from 12% to 1.6% between 1940 and 1944 – using up to 1770 units of insulin in the 1st 24h after admission

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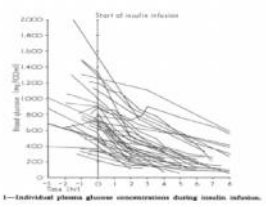

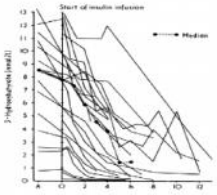

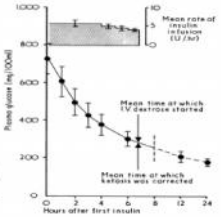

3 consecutive papers in the BMJ showed that low dose insulin infusions (5-6 units/hr) work just as well as high dose in lowering glucose & ketones

2010

The first UK national guideline for managing DKA published

Updated in 2013

2014

Survey of current management

?

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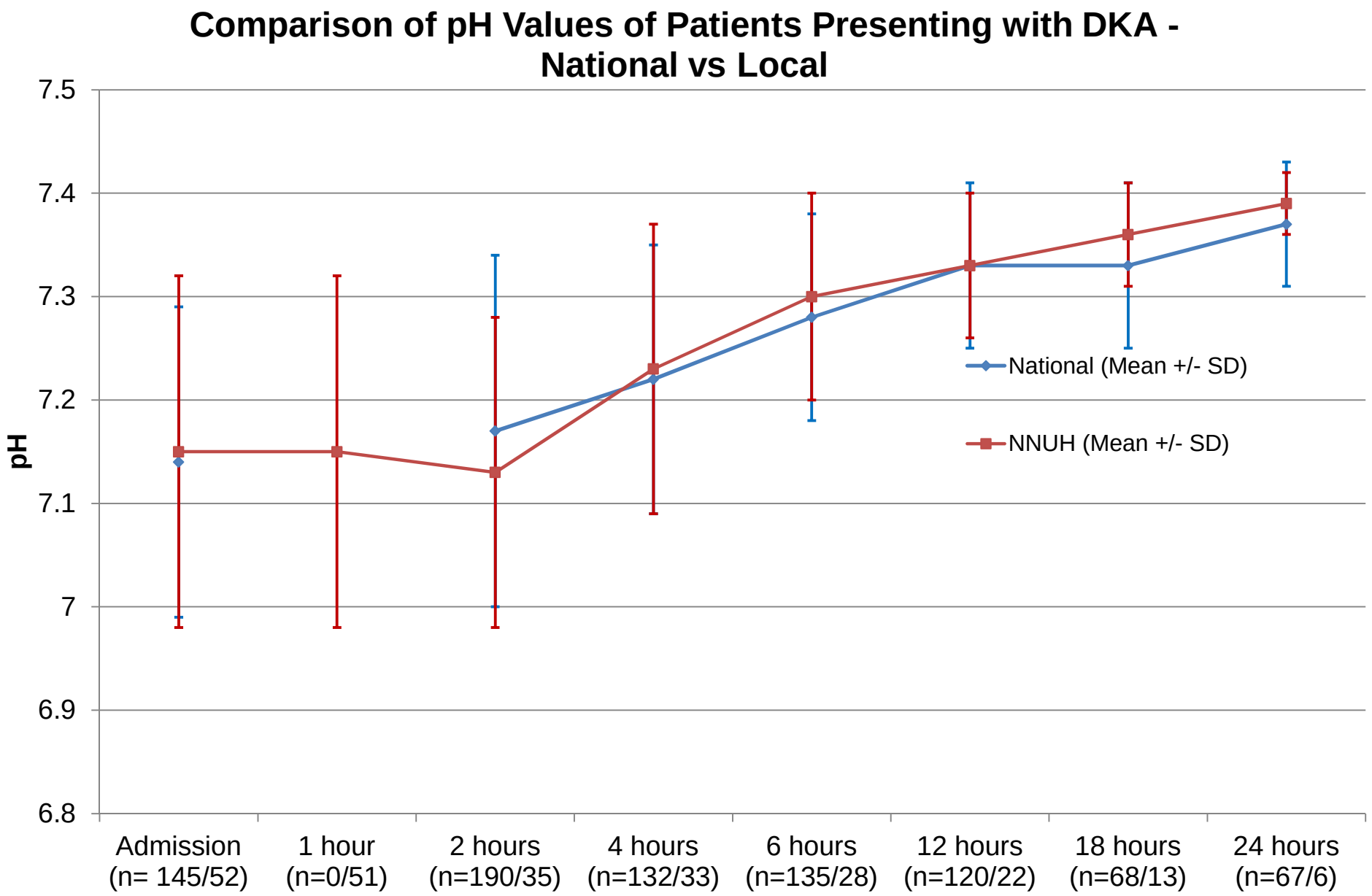
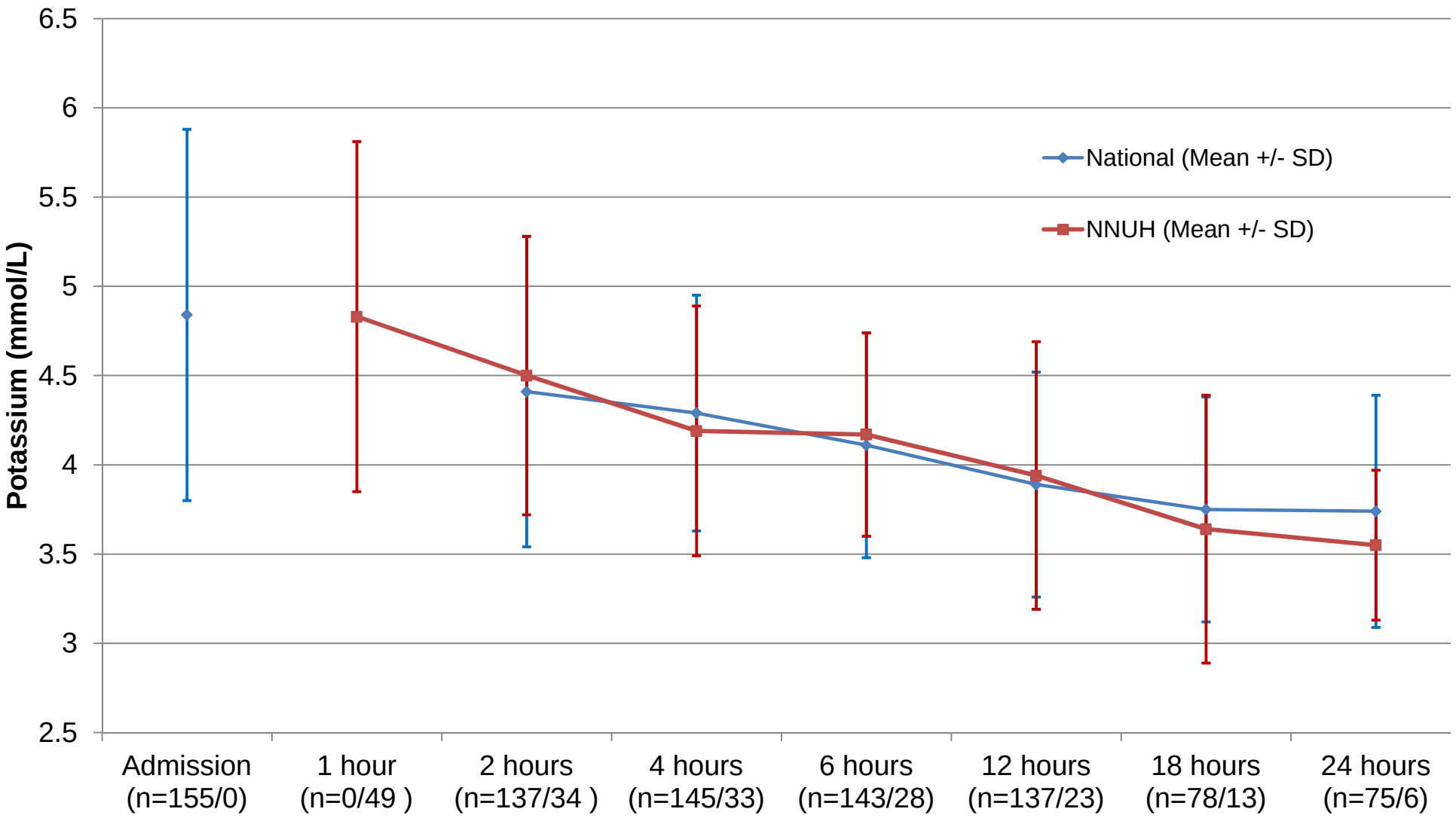
Current Work

- Are the results of a national survey applicable to individual hospitals?


Comparison of pH Values of Patients Presenting with DKA - National vs Local
pH
7.5
7.4
7.3
7.2
7.1
7
6.9
6.8
National (Mean +/- SD)
NNUH (Mean +/- SD)
Admission (n= 145/52)
1 hour (n=0/51)
2 hours (n=190/35)
4 hours (n=132/33)
6 hours (n=135/28)
12 hours (n=120/22)
18 hours (n=68/13)
24 hours (n=67/6)

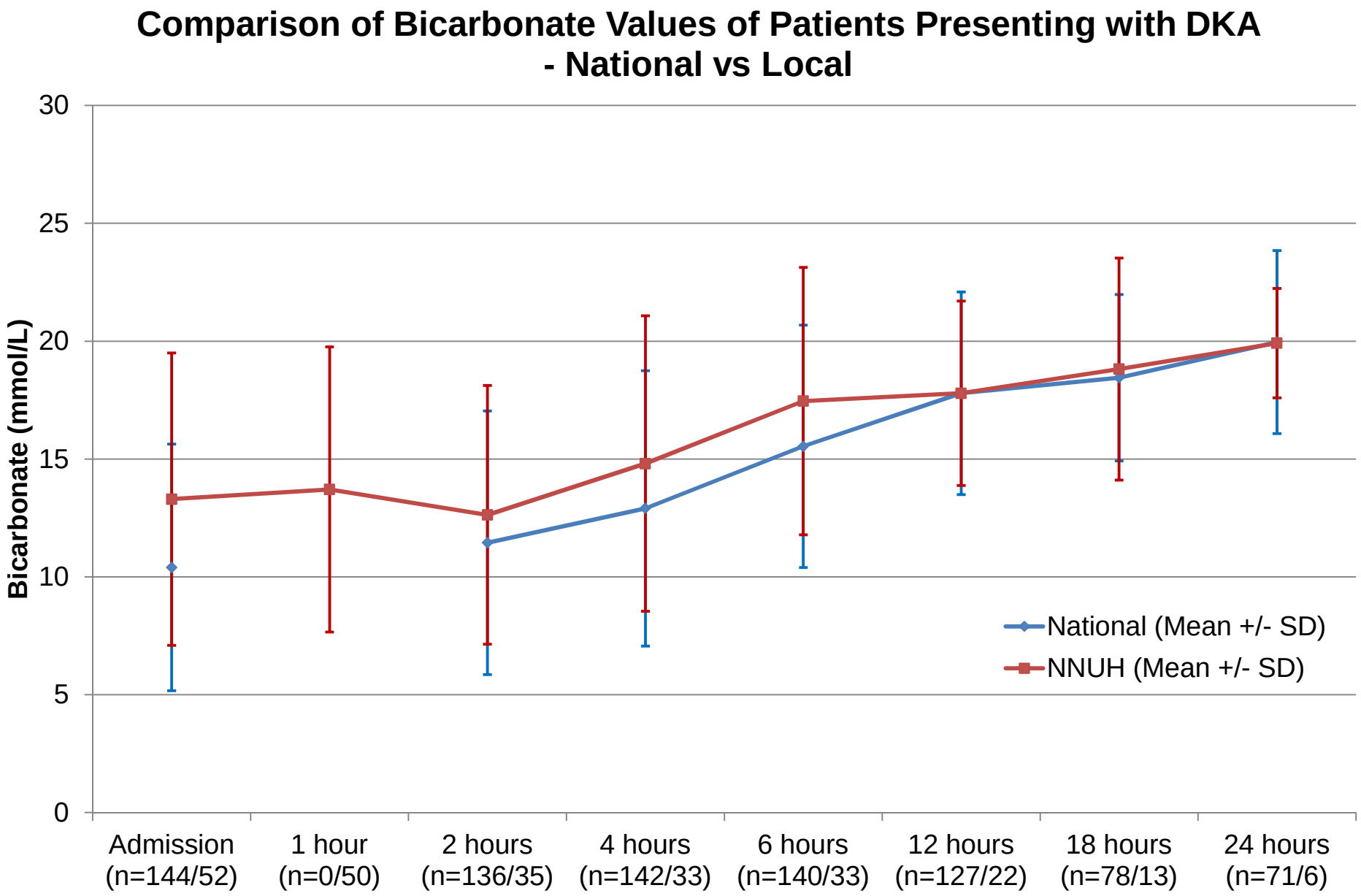
Comparison of Potassium Values of Patients Presenting with DKA - National vs Local

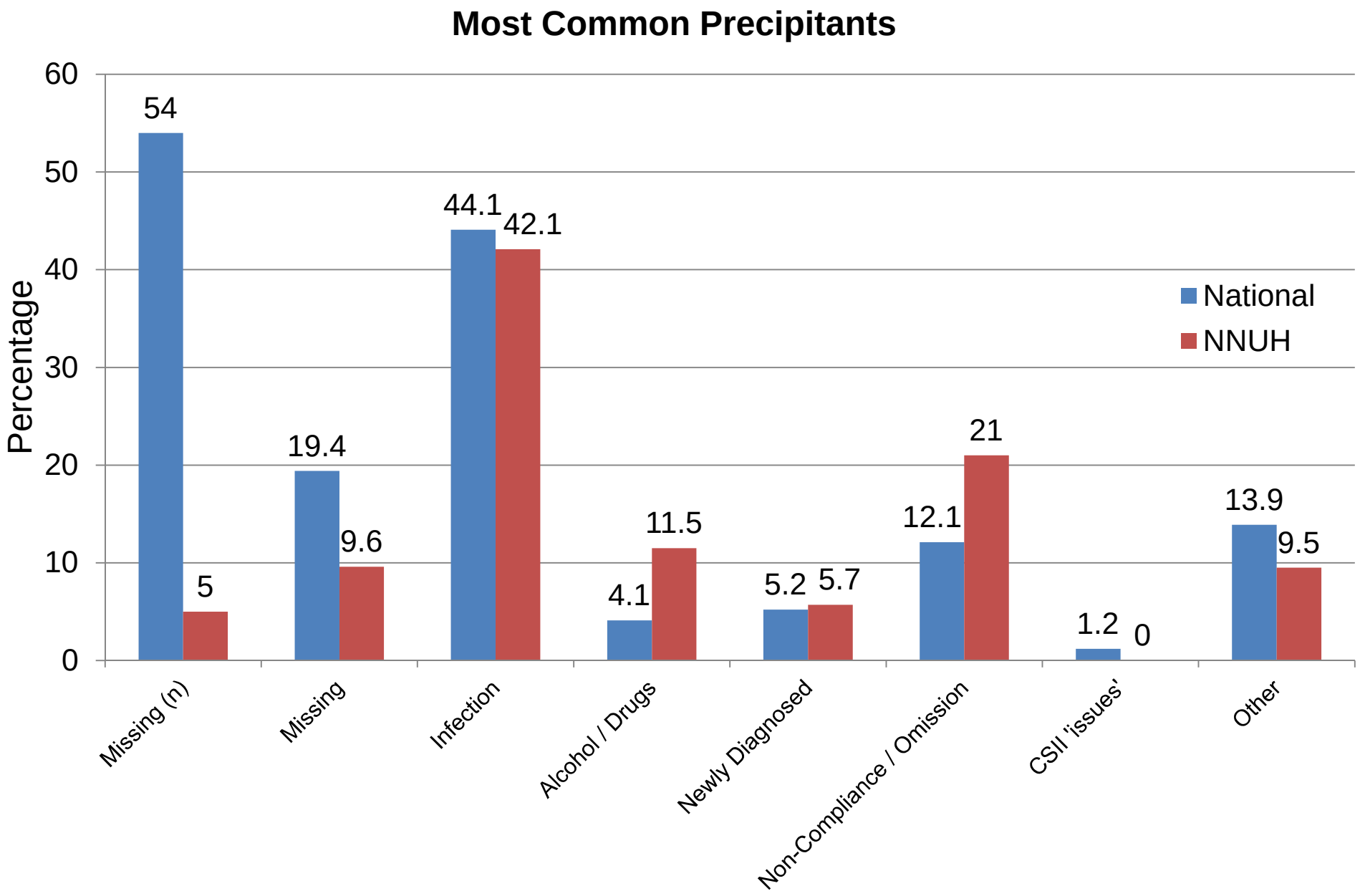


Which Is Similar to Other Data

- In 40 consecutive cases in a single centre in Canada
  - 38% developed significant hypokalaemia (<3.3 mmol/L) during the first 48 hours
  - Most were preventable
    - Not stopping insulin during hypokalaemia
    - Inadequate potassium replacement

Wong B, *et al. Can J Diabetes* 2016; in press; DOI: http://dx.doi.org/10.1016/j.jcjd.2015.10.002.


Comparison of Bicarbonate Values of Patients Presenting with DKA - National vs Local
Bicarbonate (mmol/L)
30
25
20
15
10
5
0
Admission (n=144/52)
1 hour (n=0/50)
2 hours (n=136/35)
4 hours (n=142/33)
6 hours (n=140/33)
12 hours (n=127/22)
18 hours (n=78/13)
24 hours (n=71/6)
National (Mean +/- SD)
NNUH (Mean +/- SD)


Most Common Precipitants
Percentage
60
50
40
30
20
10
0
National
NNUH
54
5
19.4
9.6
44.1
42.1
4.1
11.5
5.2
5.7
12.1
21
1.2
0
13.9
9.5
Missing (n)
Missing
Infection
Alcohol / Drugs
Newly Diagnosed
Non-Compliance / Omission
CSII 'issues'
Other

Causes of DKA Across the World

Precipitating cause, %	Australia	Brazil	China	Indonesia	Korea	Nigeria	Spain	Syria	Taiwan	USA	UK
New diagnosis of diabetes mellitus	5.7	12.2	NR	3.3	NR	NR	12.8	NR	18.2	17.2–23.8	6.1
Infection	28.6	25.0	39.2	58.3	25.3	32.5	33.2	47.8	31.7	14.0–16.0	44.4
Poor adherence	40	39	24	13.3	32.7	27.5	30.7	23.5	27.7	41.0–59.6	19.7
Other	25.7	15	10.9	17.1	11.2	4.8	23.3	7.8	6.2	9.7–18	10.8
Unknown	NA	8.8	25.9	8	30.8	34.6	NA	20.9	16.2	3.0–4.2	19.0

NA, not available; NR, not reported.

Umpierrez G, *et al. Nat Rev Endocrinol* 2016;12:222–232; Dhatariya KK, *et al. Diabet Med* 2016;33:252–260.

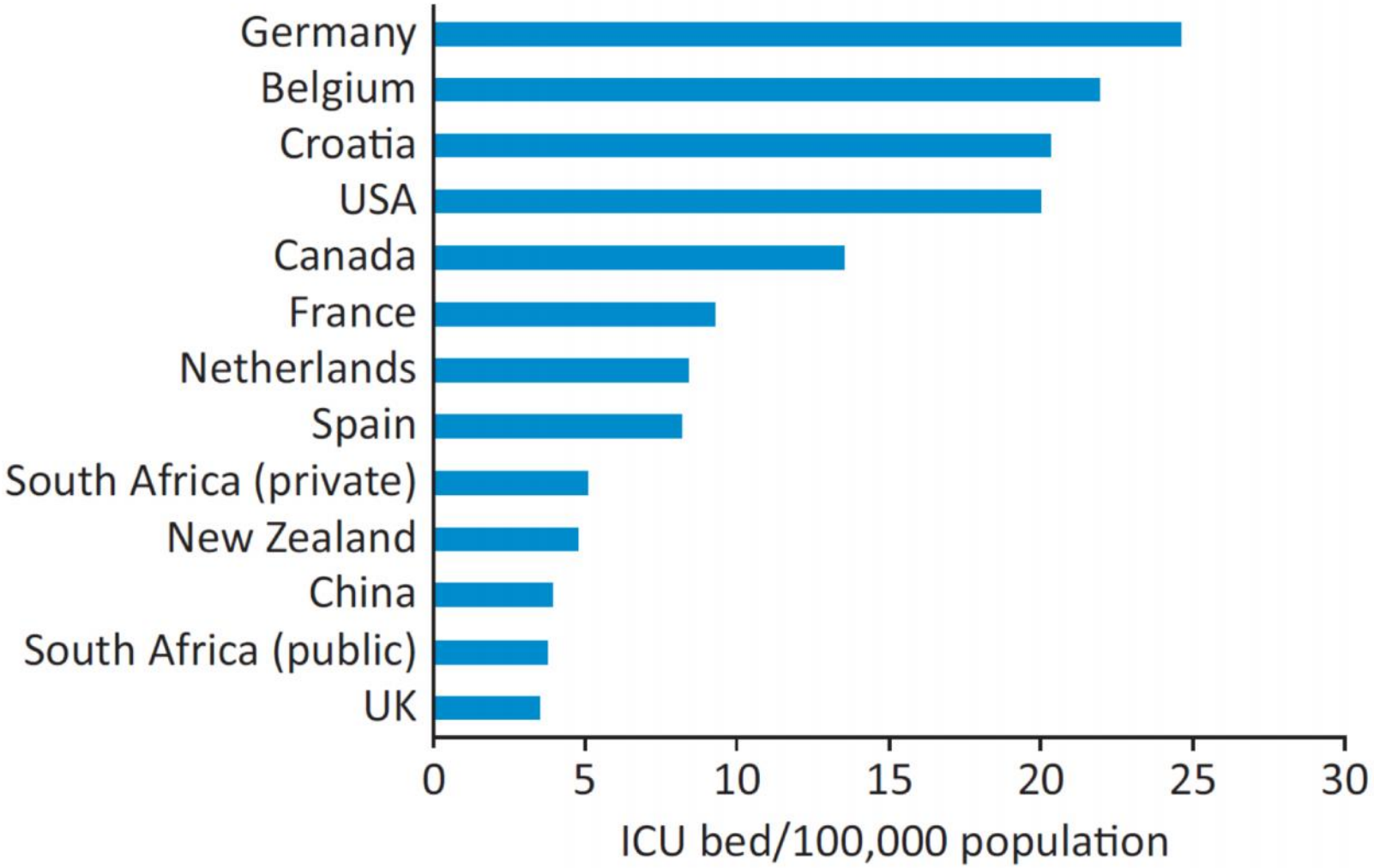
Current Work

- An economic analysis of the costs of DKA – using the national survey data
- An identical survey of adolescents and young adults (with an equivalent economic analysis)
- A survey of outcomes of 188 children

Questions for Discussion – in No Particular Order

- The ‘processes’ at the front door were done well – but later were done less well
  - What can be done to ensure consistent good practice?
- In 67% of patients, potassium dropped to less than 4.0mmol/L at 24h. No harm came to them, but was this luck or judgement?
  - Should the rate of potassium infusion be increased, even if this incurs more resource – e.g. central lines, transfer to HDU, more intensive monitoring?

But the Beds Aren’t Available

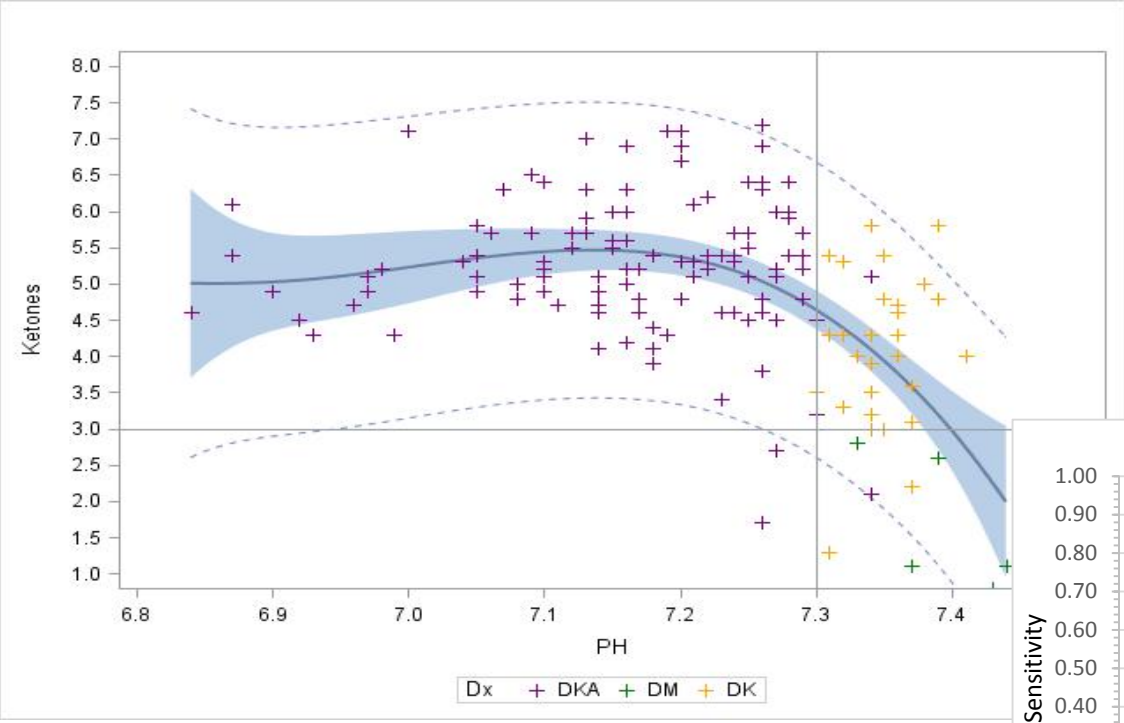


Fletcher S Future Hosp J 2016;3(1):55-57

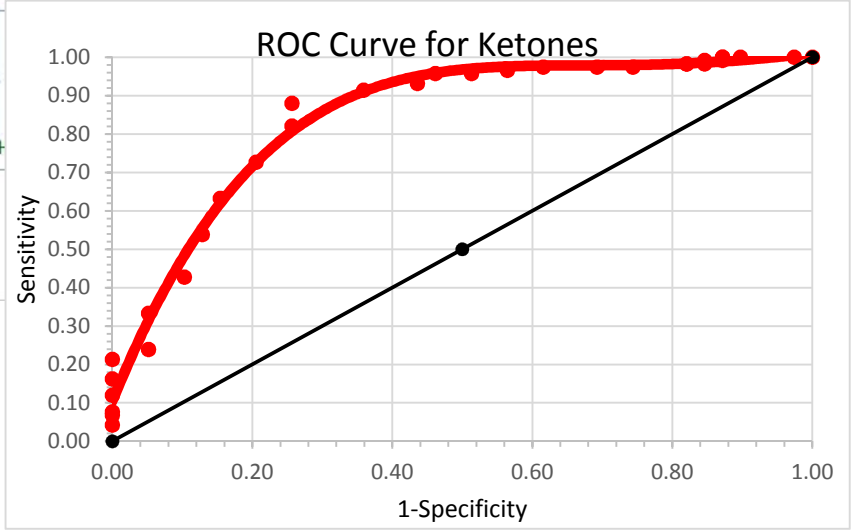
Hypoglycaemia

- 27.6% of patients had glucose levels <4.0mmol/L during their treatment
  - Should anything be done about that?
- In the patients in whom the long acting insulin was not continued, 30% patients became hypoglycaemic, in those in whom it was continued, 36.6% developed hypoglycaemia
  - Does this matter?
- One suggestion is to change to a VRIII when the ketone levels drop to <3mmol/L regardless of the glucose

Where Did a Ketone Concentration of 3.0mmol/l Come From?



188 children admitted with an hyperglycaemic emergency between 2009 and 2014 with DKA, DK or DM



A cut-off point of 3mmol/l has a sensitivity of 97.4% and a specificity of only 30.8%
A cut-off point of 4.4mmol/l has a sensitivity of 88% and a specificity of 74.4%

Clarke N et al Submitted for publication

Overview

- Why I think the ADA is wrong
- The pathogenesis of DKA
- A bit of history (where we have been)
- Where we are now
- What is going on
- Where do we want to be

Picture This: DKA – Current Management and Future Challenges

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Association of British Clinical Diabetologists

SPRING MEETING

Renaissance Manchester Hotel

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