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Use of dry blood spot (DBS) HbA1c to facilitate the virtual paediatric diabetes clinics in UHL

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Outline

Paediatric diabetes service in ULHG

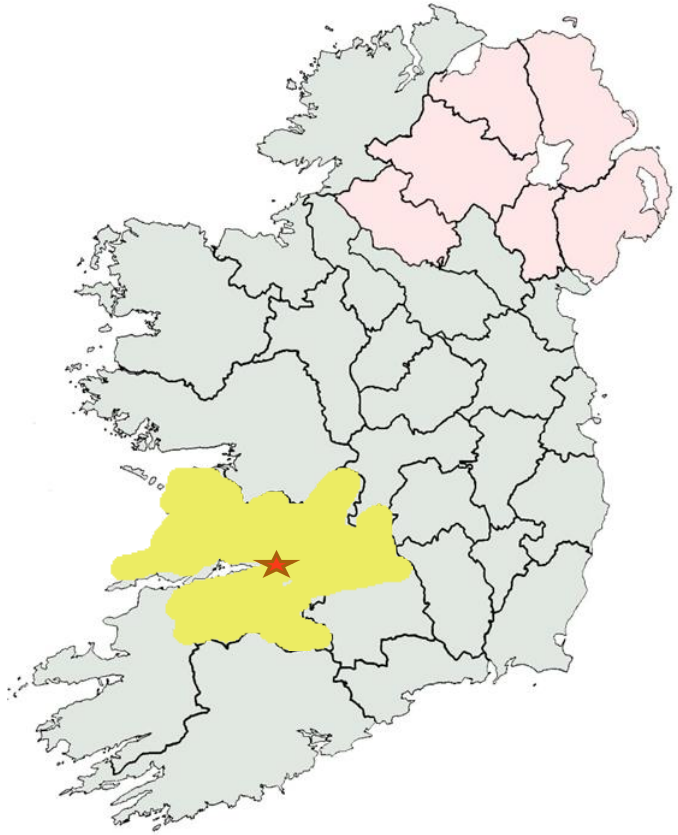
Impact of covid 19 lockdown

Virtual clinics & role of HbA1c analysis

DBS as sample type for HbA1c

DBS HbA1c assay performance

University Hospital Limerick Service



MW -100,000 children

229 patient service

- 207 T1DM
  - 35% CSII
  - 64% MDI; 1% BD injection
  - 90% CGM/FGM
  - 7.2% Coeliac (n=15)

- 22 – CFRD/T2DM or MODY/steroid induced

2018 Pilot Project Virtual Clinic

ISPAD recommendation of 3 monthly regular review appointments for all children with T1D [1]

30% of Centres in Ireland not achieving this target[2]

Recent statement Royal College of Physicians London "'One size fits all' outpatient care no longer fit for purpose"[3]

"A new approach to outpatient care is needed if it is going to meet growing demand and reduce disruption to patients' lives.."[3]

[1] ISPAD guidelines 2018 DiMeglio et al [2] IMJ Hawkes et al 2014
[3] "Outpatients: The Future – Adding Value through sustainability" Hillman et al Nov 2018

Methods

Patients using CSII/CGM recruited sequentially from OPD by the treating Endocrinologist

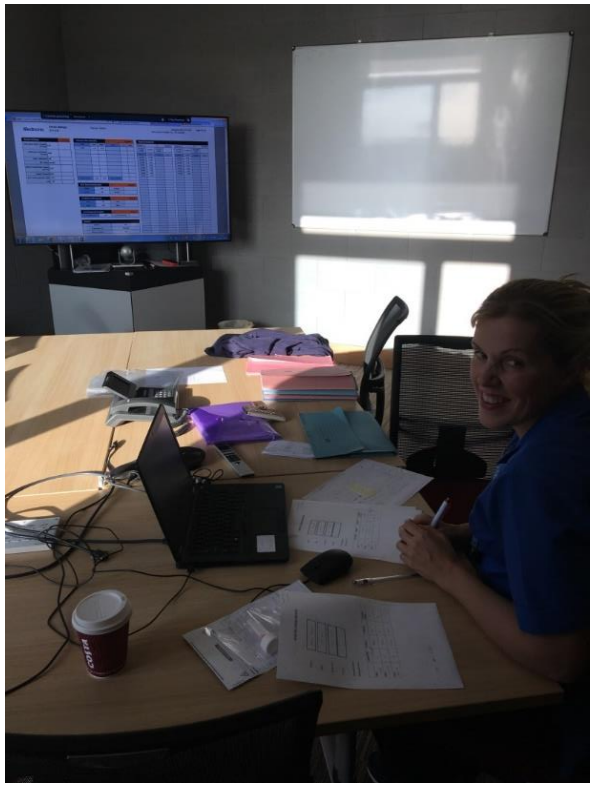
Offered 3 ‘virtual clinic’ sessions at 10-14 day intervals using ‘Skype for Business’

- Required 2 Mbps minimum internet speed
- Personal computer, webcam, microphone
- Aim of clinic similar to traditional, with focus on download & insulin setting adjustment

Clinics were organised with each clinic having a unique weblink

- Sent to participants via e-mail, with individual dial in times at half-hourly intervals
- Support instructions sent to participants
- Virtual ‘waiting room’ part of application – could be ‘admitted’ to the clinic by team once ready
- 30 mins allocated for each appointment

Clinic Setup – HbA1c: the prism through which a consultation is viewed…



Results

16 participants sequentially approached

- 10 consented to participate
  - 6 declined (3-exams, no time; 3-no computer/broadband)
- 2 later withdrew
  - 1-Terminated home internet subscription; 1-Computer broke down

Final number of 8 participants

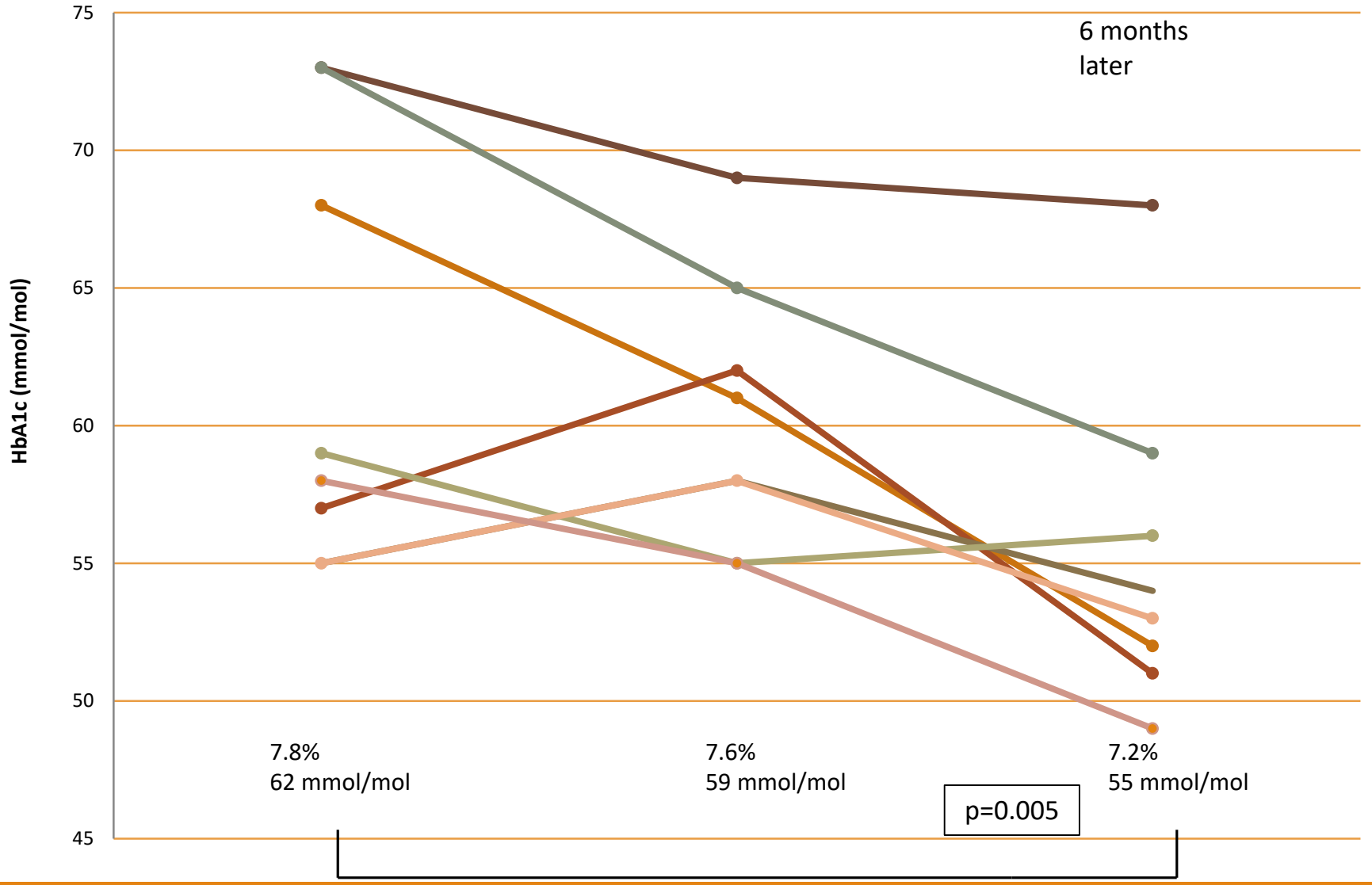
- (30% - IT issues precluding)

Total of 24 virtual clinic encounters

21 ‘successful’ clinics (88%)

- 2 : no connection (same family)
- 1 : Broadband ‘down’ previous night – couldn’t download

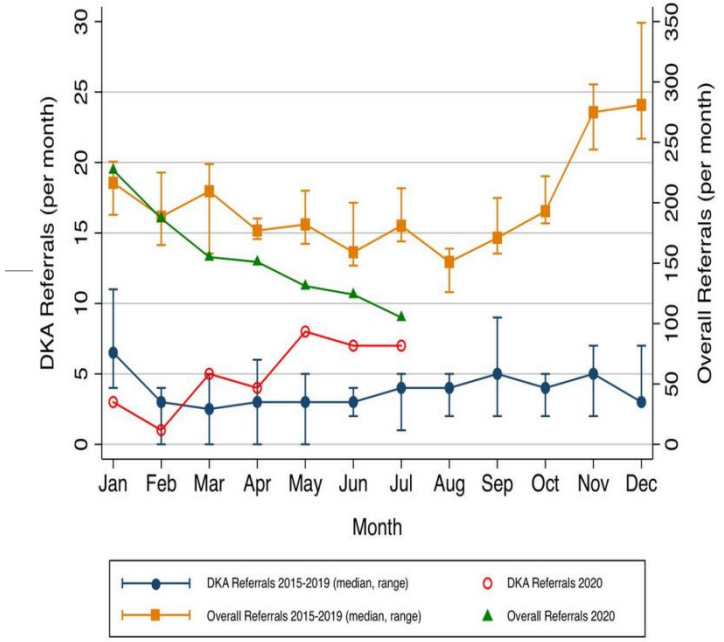
HbA1c decrement over time



ISPAD WILEY

COVID-19 outbreak and pediatric diabetes: Perceptions of health care professionals worldwide

Nancy Samir Elbarbary[1] | Tiago Jeronimo dos Santos[2] | Carine de Beaufort[3] | Juliana Chizo Agwu[4] | Luis Eduardo Calliari[5] | Andrea Enzo Scaramuzza[6]



86 paediatric patients with diabetes reported with COVID-19 infection

5 patients ICU – 3 had T2DM, of which 2 needed ventilation

No deaths reported

Delayed diagnosis and increased Diabetic ketoacidosis presentation

March 2020 – F2F out-patients precluded

27th Feb 2020 – 1st Case NI

29th Feb 2020 – 1st Case RoI

12th March 2020 – schools closed, no OPD

Switched to virtual appts:

- Skype/Pexip/Zoom/Webex

HbA1c - postal capillary sample

Capillary tube

- LiHep used – decided to switch to EDTA
- Sarstedt Microvettes
- TOSOH automated Glycohaemoglobin analyser HLC-723G8(HPLC)

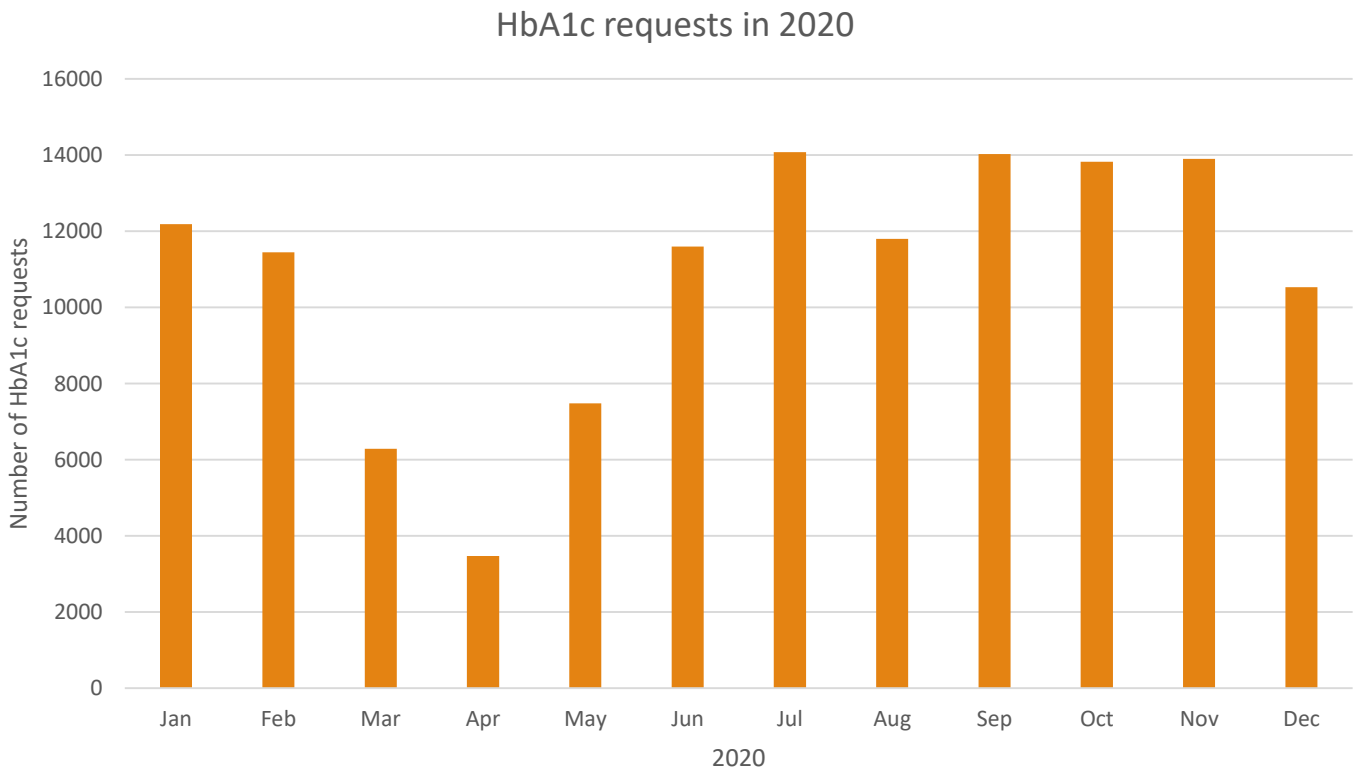
Clinical Impact

- In a national survey of UK paediatricians, 32% of clinicians reported having witnessed delayed presentations to emergency care over a 2- week period in April 2020. (1)
- Reduction in HbA1c requests from primary and secondary care
- Hospital phlebotomy appointments were cancelled
- F2F consultations were replaced by either virtual or telephone consults
- It was reported that in the UK between March & December 2020 there were approx 60,000 missed or delayed diagnoses of type 2 diabetes (2)

To ensure that patients with diabetes are receiving the necessary care, alternative solutions to increase accessibility to testing are required

1. Basatemur et al Arch Dis Child April 2021 Vol 106 No 4
2. https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00116-9/fulltext

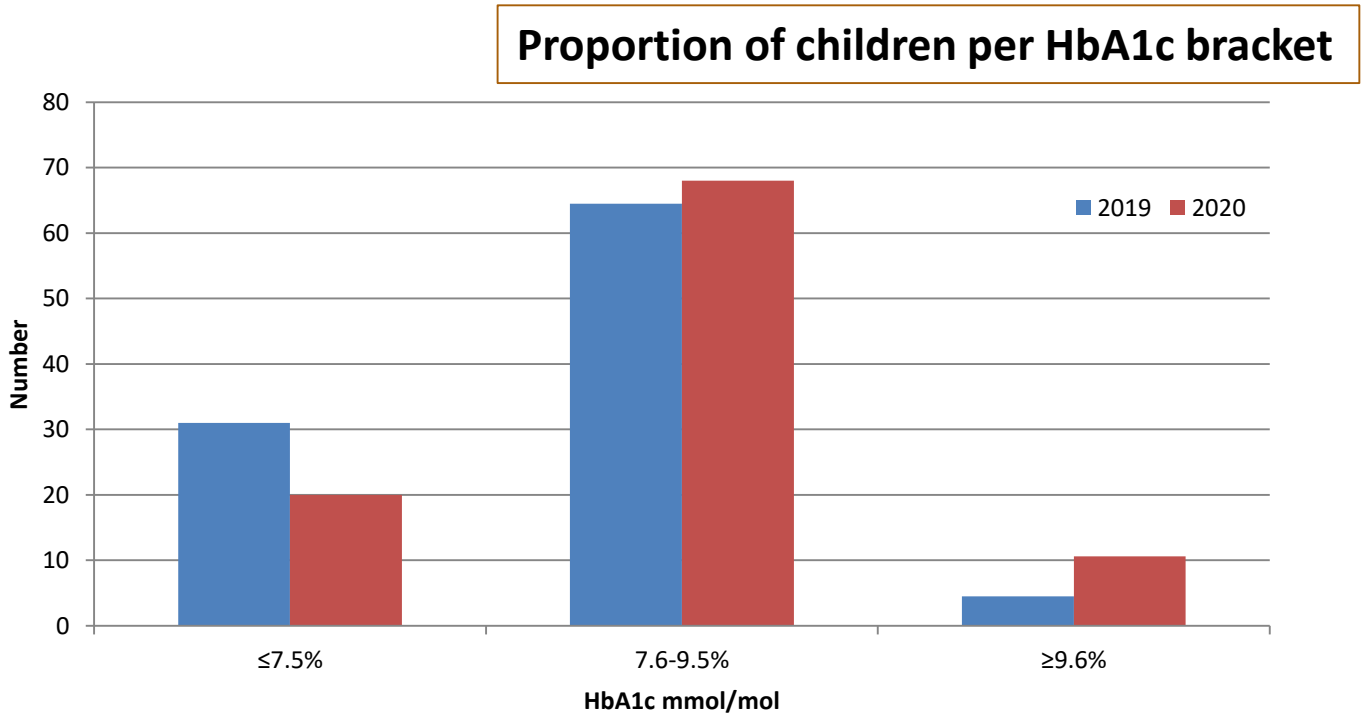
HbA1c workload in 2020 – Biochemistry UHL



COVID collateral damage

Rate of DKA increased X 8, increased severity

Mean HbA1c of clinic population : 68 mmol/mol (8.4%) in 2020; 63 mmol/mol (7.9%) in 2019



Data c/o Therese Dunne, Senior Diabetes Dietician

Other impacts

Group education halted

- Structured carbohydrate counting
- CGM starts
  - Went virtual
- New insulin pump starts
  - More recently moved off-site
- School education sessions – teachers, SNAs
  - Zoom sessions

Clinic non-attenders/High HbA1c

- HARP program
- Weekly MDT meeting

Results

Cycle 1 : 70% successful samples

Failures: clotted sample; failure to cap and leakage; insufficient

21 (30%) failures over 6 weeks

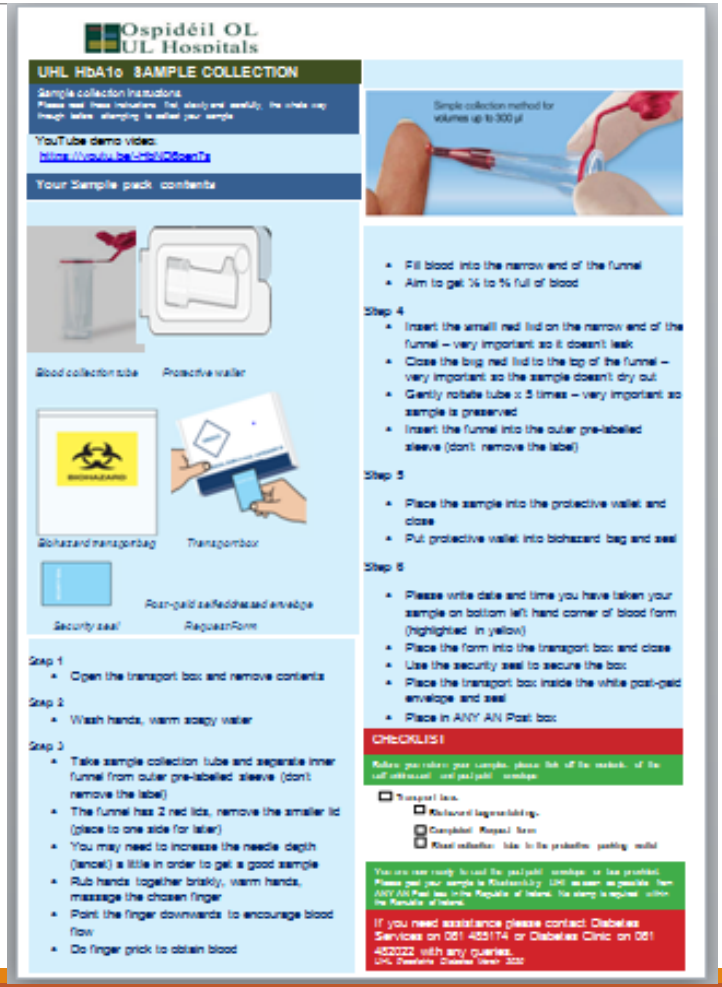
Cycle 2:

Collection box

Revised instructions

YouTube video [Carolyn Holt]

https://youtu.be/-HbND6oen7s



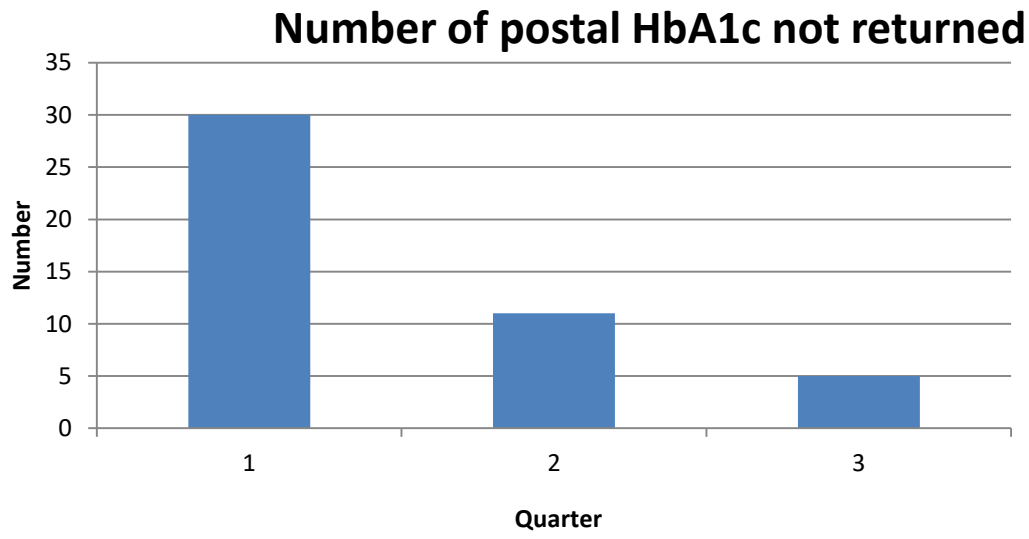
March to end of 2020

Total 335 HbA1c requested

- 75 requests had no HbA1c available = 22% sample rejection rate

24 virtual clinic appts – 46 (13%) HbA1c requests not sent by post

- Numbers decreased when youTube instructions were provided



Q1: April – June
Q2: July – Sept
Q3: Oct - Dec

Data c/o Therese Dunne, Senior Diabetes Dietician

Was it worth it?

March to end of August all clinics delivered virtually

Improved clinic attendance rate compared to same period 2019

	OPD appointments	DNA (%)
2019	364	40 (11%)
2020	270	20 (7.5%)

The Future…

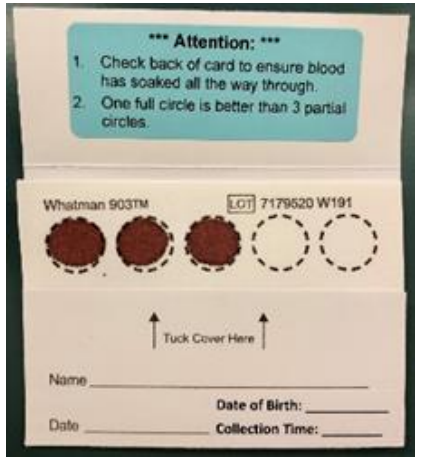
Likely will need to incorporate virtual element to OPD

Limitations:

- Time
- Access to data downloaded from technologies
- HbA1c information available for consultation

Improved HbA1c transportability

- Filter paper/dried blood spot HbA1c



Study 2 - method

Assess performance DBS HbA1c vs venous EDTA blood HbA1c

- 100 participants recruited for comparison study
- Elution of blood from DBS punches reduced from overnight to 2 hours
- Verification of this sample type

Ensure stability within postal system

- 10 volunteer participants; 2x DBS samples collected - one sent to the Lab immediately and the other sent by post to Biochemistry.

POSTAL DRIED BLOOD SPOT HBA1C BLOOD TEST- INSTRUCTIONS

In the current Covid-19 situation, please **do not send** blood sample in **if anyone** in your household is ill to reduce the risk to lab staff of contracting COVID 19.

- Open your postal pack and read instructions carefully
- Wash hands, rub hands together briskly
- Make sure the hands are *warm* before doing finger prick(as it will increase blood flow in the fingers)
- Do finger prick to obtain blood
- You may need to increase the needle depth a little in order to get a good sample
- Fill blood into the circles on the filter paper
- Start filling circles on the paper side where instructions are written
- Fill all circles one by one making sure that each circle is fully soaked with blood and you can see blood on the other side of paper
- Aim to get at least 3 circles completely filled, if possible. One v full circle is better than 3 patchy ones!
- Once done leave the paper out to dry for at least 1 hour.
- Label the filter paper correctly at the Bottom of paper including name of your child and date of collection
- Insert filter paper (in biohazard bag) into clear pocket at back of blood form
- Try to avoid folding of the filter paper
- Post back to lab in enclosed addressed envelope (no need for stamp) ideally the Mon-Wed before your virtual clinic appointment

Watch our new YouTube video!

- Either use this link: https://youtu.be/eF91ro7ElFU
- or scan the QR code below on your phone for quicker access

HbA1c assay performance

Inter-individual CV 7.1%

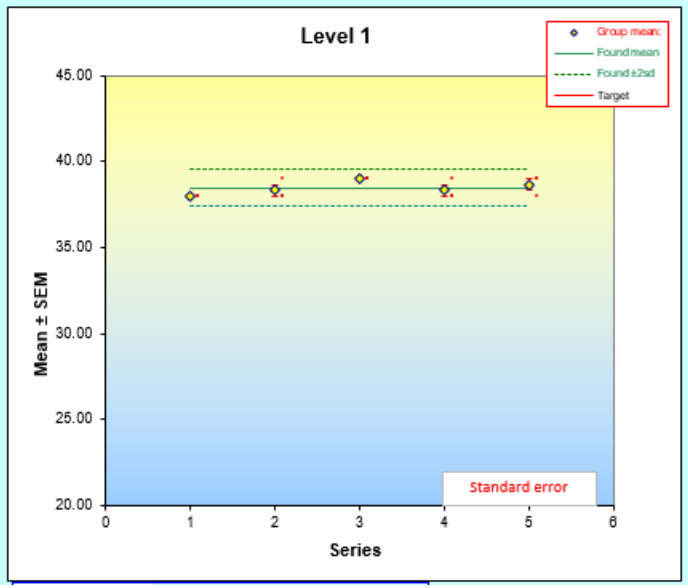
Intra-individual CV 2.5%

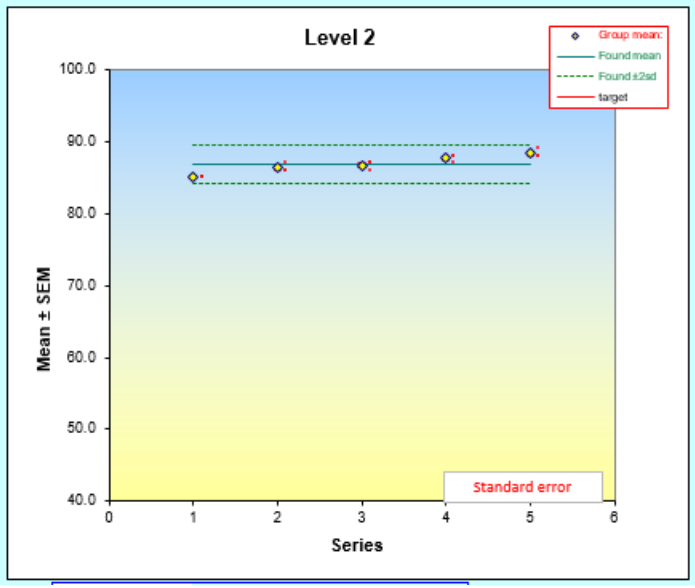
Index of individuality 0.35

CV of method : There are few published data as to the analytical performance required for HbA1c methods used for diagnosis, but as a minimum the within-laboratory imprecision should be <3% CV and between-laboratory agreement must be <5% CV based on SI units (mmol/mol) (Weykamp *et al*). Certain methods, in particular point of care devices, may not achieve minimum requirements for diagnosis.

Critical difference 9.5%

ACB template -Imprecision: Randox IQC





Level 1:
Mean = 38.47 mmol/mol
CV% Intralab Imprecision = 1.4

Level 2:
Mean = 86.80 mmol/mol
CV% Intralab Imprecision = 1.6

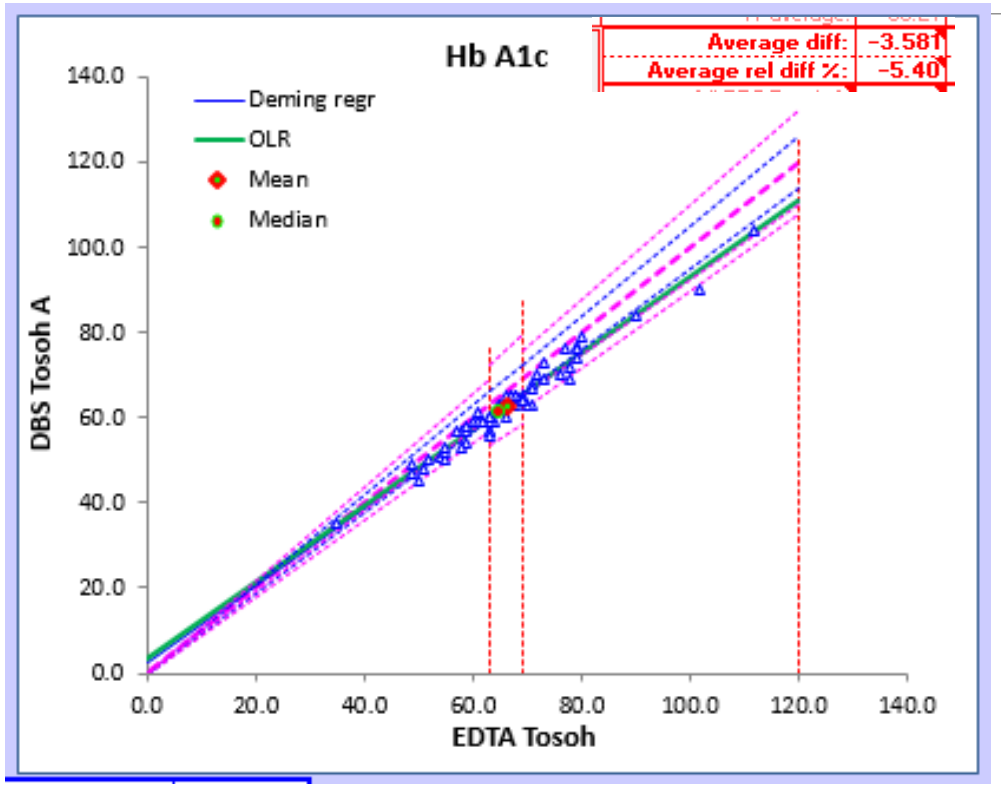
UKNEQAS performance:

	EQA mmol/mol Distribution 455									
	Tosoh A					Tosoh B				
	ALTM Target	EQA	DBS	% Diff DBS to EQA	% Diff DBS to ALTM	ALTM Target	EQA	DBS	% Diff DBS to EQA	% Diff DBS to ALTM
EQA1	56.9	57	55	-3.5	-3.3	56.9	58	54	-6.9	-5.1
EQA2	54.8	55	53	-3.6	-3.3	54.8	55	56	1.8	2.2
EQA3	43.7	44	44	0.0	0.7	43.7	45	42	-6.7	-3.9
Bias%				-2.4	-2.0				-3.9	-2.3

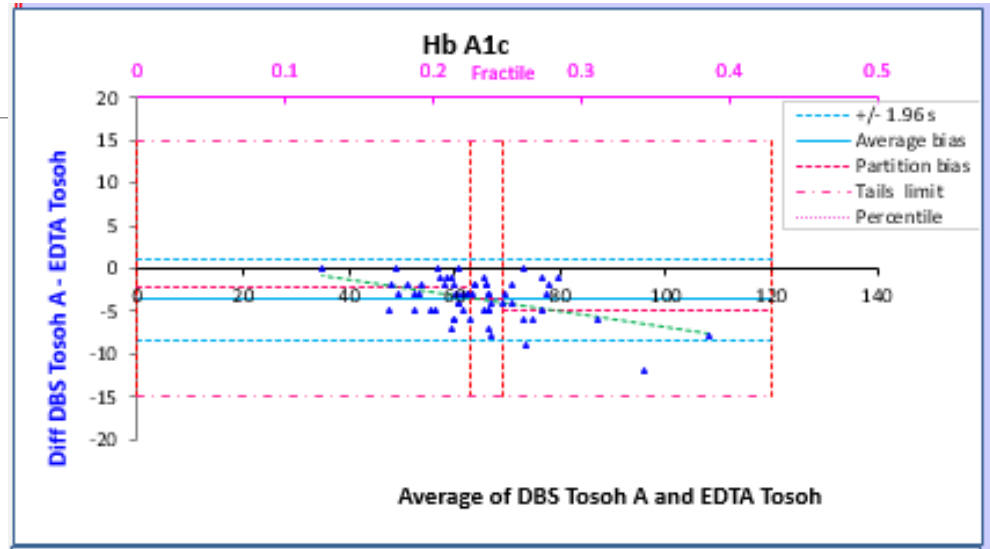
Results - demographics

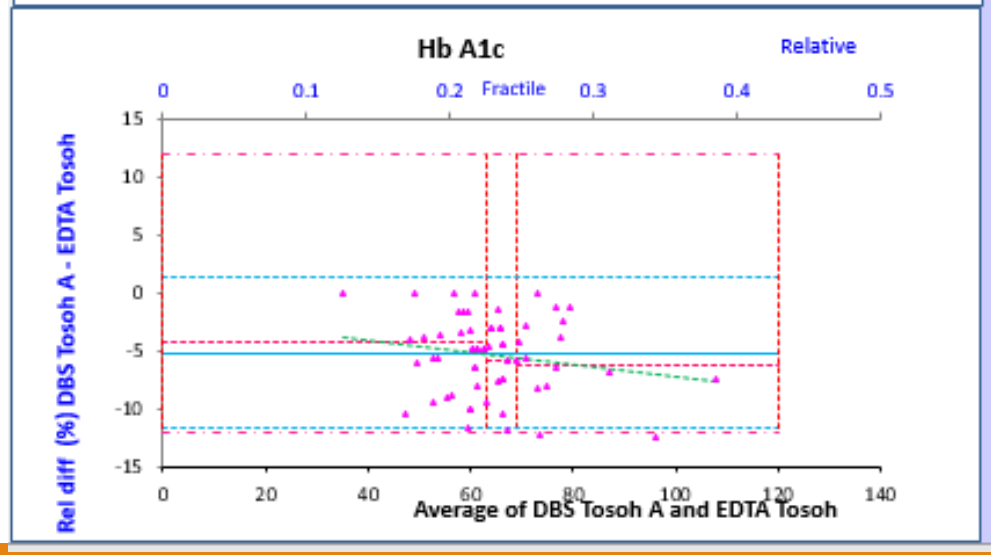
N=63	95% T1DM
M:F (%)	47:53
Age (yrs;mean±SD)	13.3±3.5
CSII (%)	28 (44%)
Mean HbA1c (mmol/mol)	66.9 ± 12.7
Range (mmol/mol)	38 - 112

Comparison between venous and DBS HbA1c



Partitioning of EDTA Tosoh results				Number:	Average bias	Bias %
Low:	0.0	to	63.00	21	-2.29	-4.2
Mid:	63	to	69.00	20	-3.65	-5.9
High:	69	to	120.00	21	-4.81	-6.3

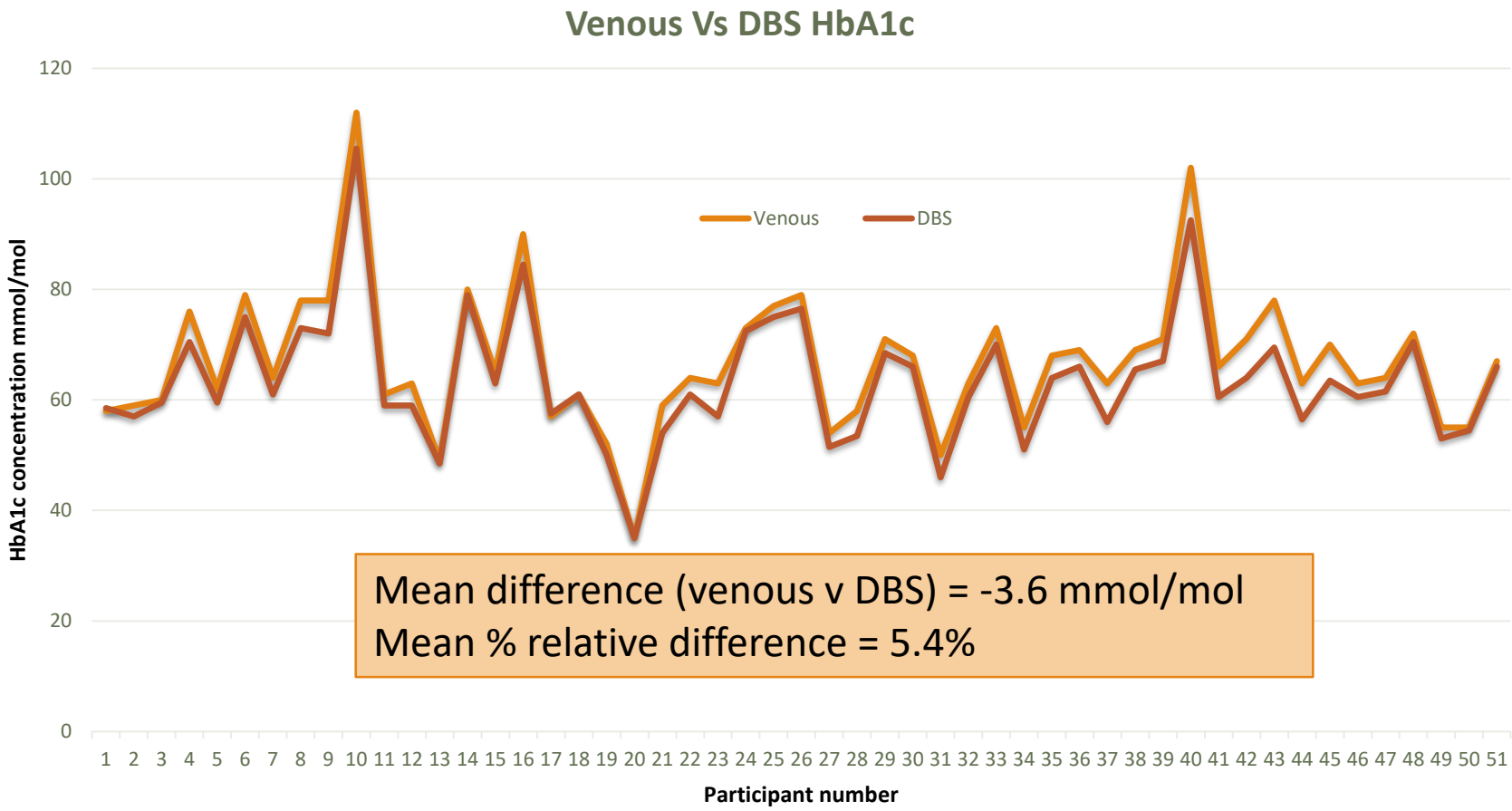




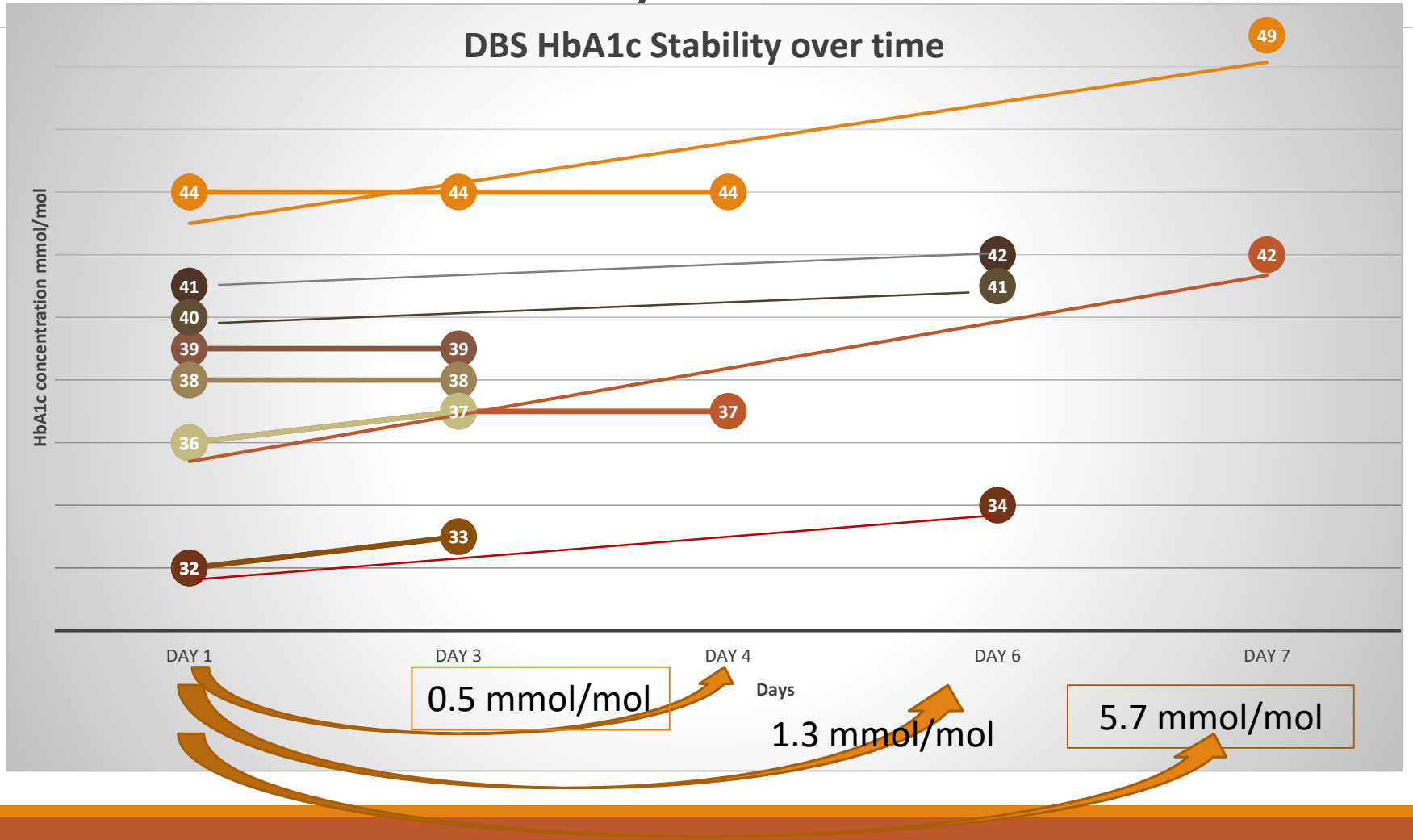
OLR slope = 0.89 and intercept = 3.43

Deming R slope = 0.91 and intercept= 2.29

Comparison between venous and DBS HbA1c



DBS HbA1c Stability data



Conclusion

Paediatric population relatively spared direct effects of COVID-19, but significant indirect effects on mental and physical health

Virtual appointments likely to be incorporated into outpatient clinic structure in the future

DBS HbA1c suitable sample type for Paediatric Diabetes service

- Enables sample collection at remote locations – school, home etc ; patient centric
- No requirement for phlebotomy
- Capillary blood - low volume
- Stable during typical postal time period
- Our data shows good correlation to those of venous blood samples

Many thanks to all involved

All the Biochemistry staff

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Dr Orla Neylon

Prof Clodagh O'Gorman

Dr Zia and Dr Hameed

Therese Dunne, Senior Dietician

Dr Niall Dalton

Ms Sarah Nash, Sophie Corbett, diabetes admin staff

AND our patients for their patience….