T2DM IN TRANSITION-

AN ADULT DIABETES PERSPECTIVE

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MY COI DECLARATIONS

- I have not received any speaker fees or homoraria for this meeting
- In the past I/my team have received consultation and /or lecture fees or unrestricted travel or educational grants from:

- Novo Nordisk
- Eli Lilly
- Boehringer Ingelheim
- Astra Zeneca
- Abbott Diabetes
- NAPP
- Janssen
- Takeda
- Medtronic
- Sanofi

OUTLINE OF TALK

- Background to local service
- Local challenges
- Case histories to illustrate
- Key take away related to pharmacotherapeutics
- Diabesity meds
- Diabetes Remission
- Summary

OVERVIEW OF SERVICE AT WOLVERHAMPTON

Frequency: Once a month Transition clinic with agreement for 2-4 adhoc extra clinics a year based on demand & BPT standards. Supported by Admin from both sides. Not dedicated for Type of DM

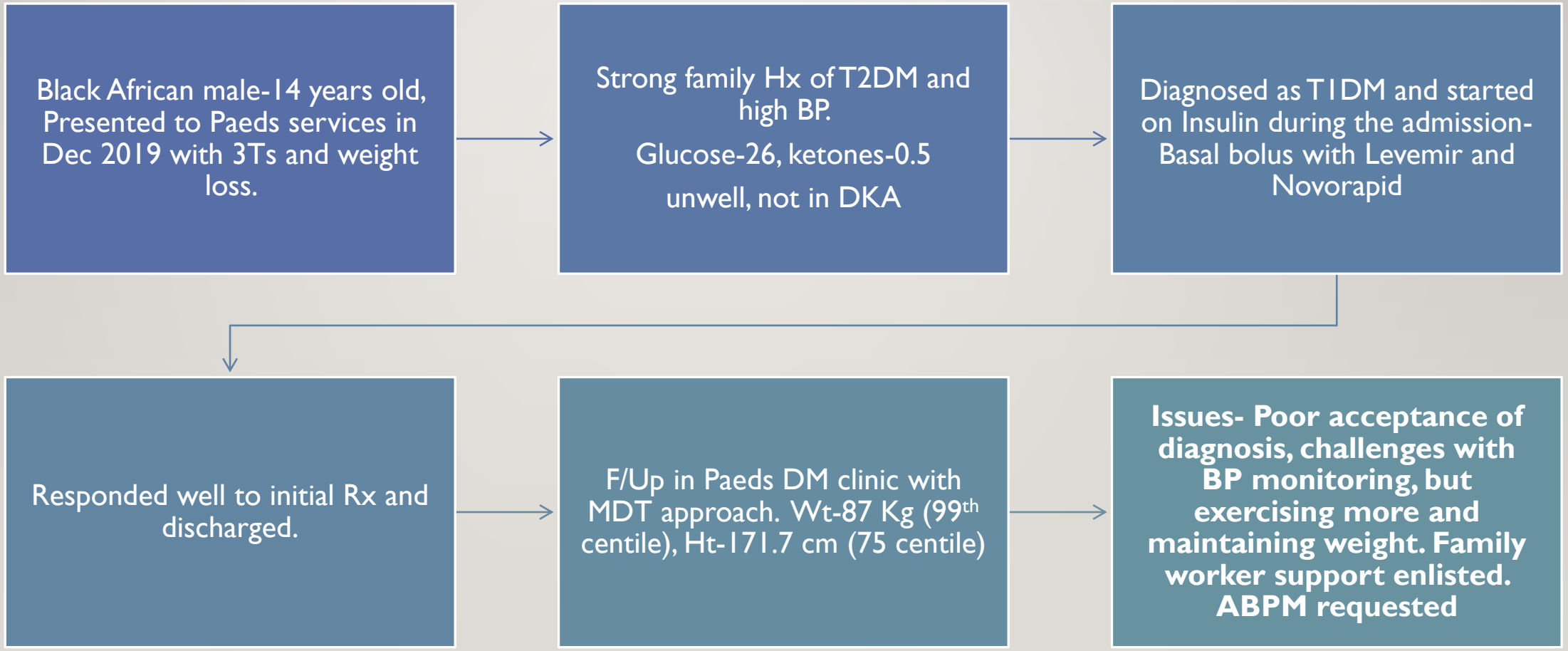
- **Staff:**
  - Paeds DM consultant + Paeds DSN (1 or 2 depending on availability) + Psychologist + Paeds Dietitian
  - Adult DM consultant + Adult DSN + Adult senior trainee
  - Others- Family Support worker- still not as consistent
- **Location:** Adult Diabetes Endocrine Centre – dedicated facility, other clinics limited to provide a contained waiting area for CYP and families to interact and to speak to staff in the service
- **Modus Operandi:** Patients prepped for clinic by Clinical nursing team with height, Wt, BMI, BP, Urinalysis, POCT HbA1c (whilst supplies available!).
- All patients discussed before and after clinic by MDT. Targeted support shared between Paeds/Adults
- "Carousel" approach with Joint review only for new patients and PRN use of allied specialities

CHALLENGES WE FACE & POSITIVES

- Staffing issues – Sickness, capacity etc
- Space becoming a constraint recently
- During the pandemic – increase in DNA/WNB rates and institution of hybrid clinics
- High deprivation and high rates of DM in local community
- No specific provision for CYP T2DM in transition

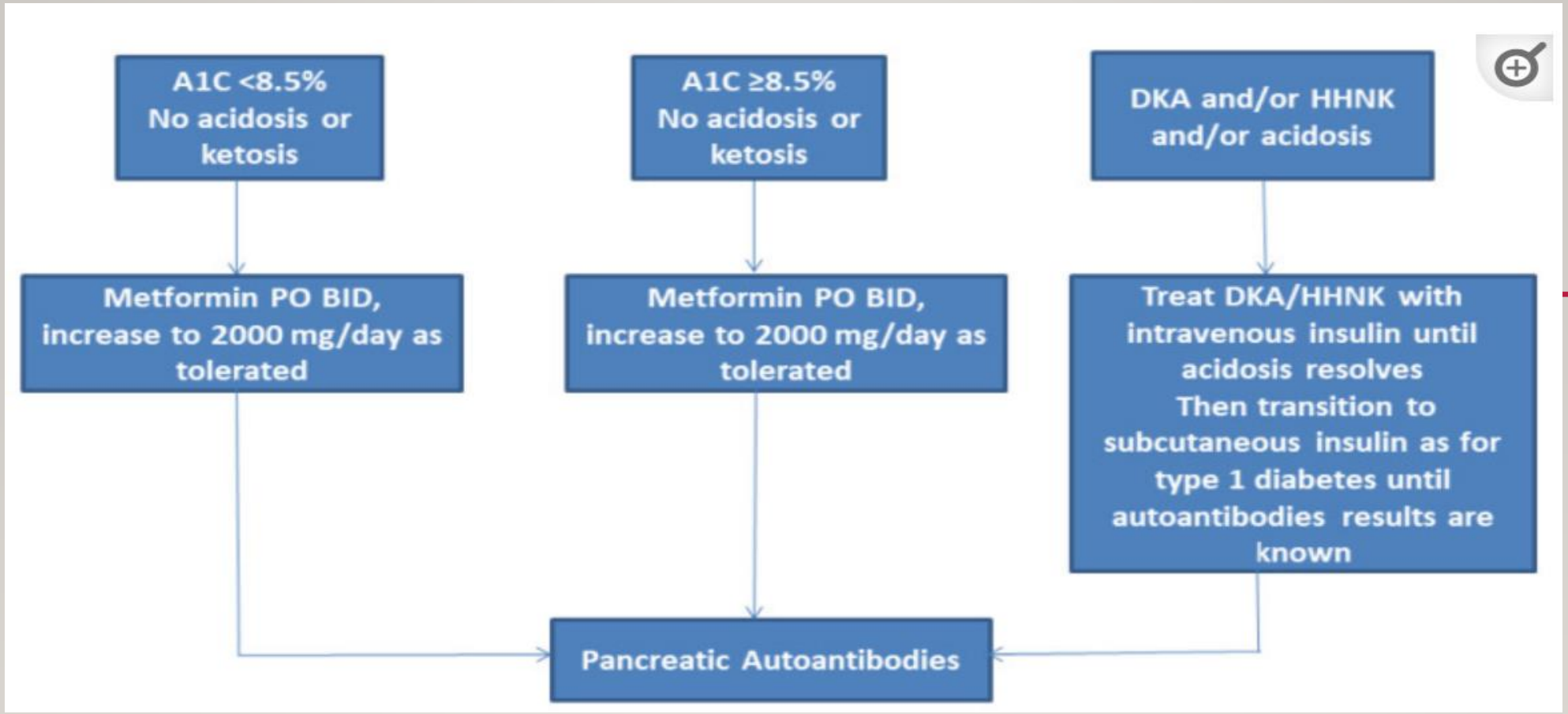
- Experienced staff
- Generally good team work and communication between clinics with an "MDT" Approach
- Recent business case approval to get a transition co-ordinator
- Tier-3 and Tier-4 Obesity services locally

CASE STUDY-1- CHALLENGES IN DIAGNOSIS/MGMT



AUDIENCE POLL

- If you had a case like this now, would you anything different?
  (Tick all that apply)
  1. Provide a CGM device and training
  2. Check antibodies
  3. Check C-peptide
  4. Start Metformin as well
  5. Would not do anything else until next review



- Initial management of new onset diabetes in youth with overweight or obesity. DKA, diabetic ketoacidosis; HHNK, hyperosmolar hyperglycemic nonketotic syndrome. Adapted from American Diabetes, A., 13. Children and Adolescents: Standards of Medical Care in Diabetes-2020. *Diabetes Care* **2020**, *43* (Suppl. 1), S163–S182.

CASE STUDY-1 CONTD

4 week f/up Jan 2020- Anti GAD and islet negative,

Doing OK, weight stable, some hypos, lots of questions around diagnosis and management

Seen by self with parental consent.

Taken through rationale for insulin Rx and need for monitoring etc

Plan to see regularly and transitional care at age 16 broached.

Further support from Family support worker offered.

CASE STUDY-1 CONTD MARCH 2020!

Attended clinic with mother (social worker)- not been on Insulin since Feb 2020
POCT A1c- 49 mmol/mol (6.7%) >>> Wt-87.1 Kg, BP-137/77 mmHg,
Drinking high energy drinks and having chocolate regularly as per mother
Patient himself- asymptomatic, good energy levels and feels well.
Further family Hx- Mother T2DM aged 40; Mat aunt in Oz-T2DM; Mat cousin- T1DM diagnosed aged 19 years Oz.
Patient's father also had T2DM diagnosed around 40 years age.
Counselled further re T2DM diagnosis and started on Metformin MR 500mg OD and then BD after 1 week

CASE STUDY-1 1ST TRANSITION RVW SEPT 2021

T2DM on Metformin M/R 500mg od nearly 2 years since diagnosis- unclear concordance. Reticent but talked a bit. Had declined Libre and psychology support in Paeds clinic. Last A1c -56 mmol/mol but some time ago

Wt down from 92kg to 84kg with multiple diet and lifestyle changes as per patient and mother. A1c last recorded at 56 mmol/mol 4 months prior. BP-143/85 mmHg. Features of Acanthosis.

Not had eye screening since diagnosis in Dec 2019

Studying engineering at college. Interested in Gym and football (5-a-side)

Cut down ETOH and non-smoker

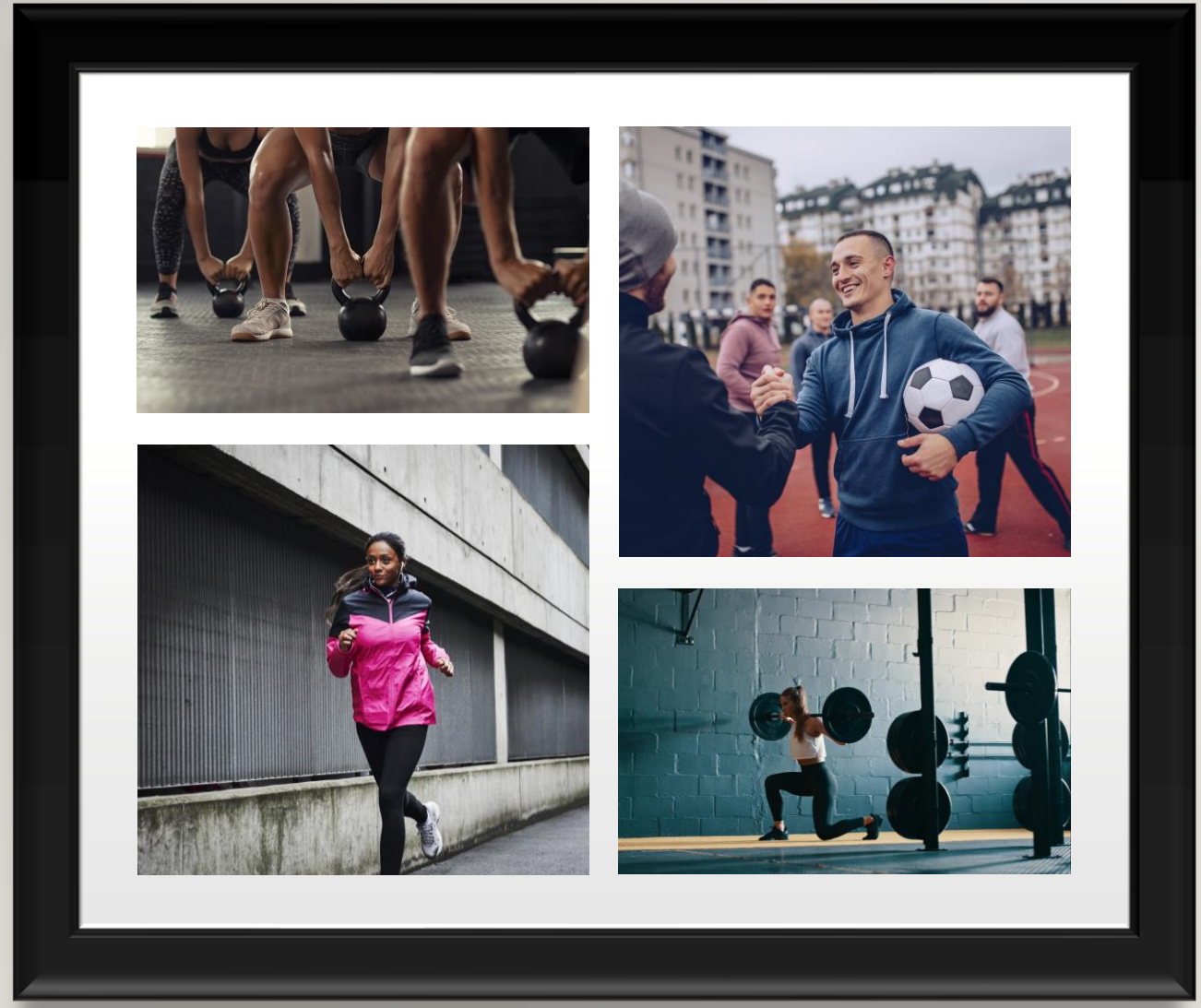
Supportive advice and positive reinforcement on what was going well and gently nudged re Metformin use. Bloods taken (HbA1c POCT not available)

3 month f/up planned

DIET & LIFESTYLE MEASURES

- Increase fresh veg and greens and fruits
- Reduce/avoid consumption of energy dense food and high calorie drinks
- Portion control & cut down snacking
- Could try meal replacement (<800 kcal) but need support & guidance
- Caution with low carb diets if on Insulin and with linear growth

Children (Basel). 2021 Jan; 8(1): 37, NICE NG18, ACDC guidance



- Culturally appropriate
- Regimen that can fit current social situation
- Increase activity and break sedentary time
- Aerobic & Resistance training combination at least 3 times per week
- Aim for 5-10% weight loss
- Non-academic screen time < 2 hrs/day
- Involving the wider family important

CASE STUDY 1 – TRANSITION CONTD

Bloods back- HbA1c- 118 mmol/mol…!!

Patient recalled to clinic -1/12 as not engaging on phone

DNA next clinic and letter sent about bloods and concerns and need for insulin initiation

Next attended Nov 2021-

- Sullen! Non-conversant, Mother stated not accepting diagnosis and not keen to follow any advice. Eating and drinking high calorie and high carb food and drink
- Appetite dropped, wt down to 79.9 Kg,
- Discussed risks & rationale for insulin but said taking Metformin again and will continue this instead.
- Agreed on Dose increase and safety netted with close followup

CASE STUDY 1 TRANSITION JAN 2022

Further wt loss but less pronounced at 76 kg

Attending GYM 5days/wk, diet good and feels well.

Random glucose in afternoon clinic 14 mmol/L, HbA1c-116 mmol/mol

Discussed once again re insulin and Libre-2 monitoring but declined.

More willing to discuss re diagnosis and implications

MODY testing considered given family history etc. Bloods sent for C-peptide

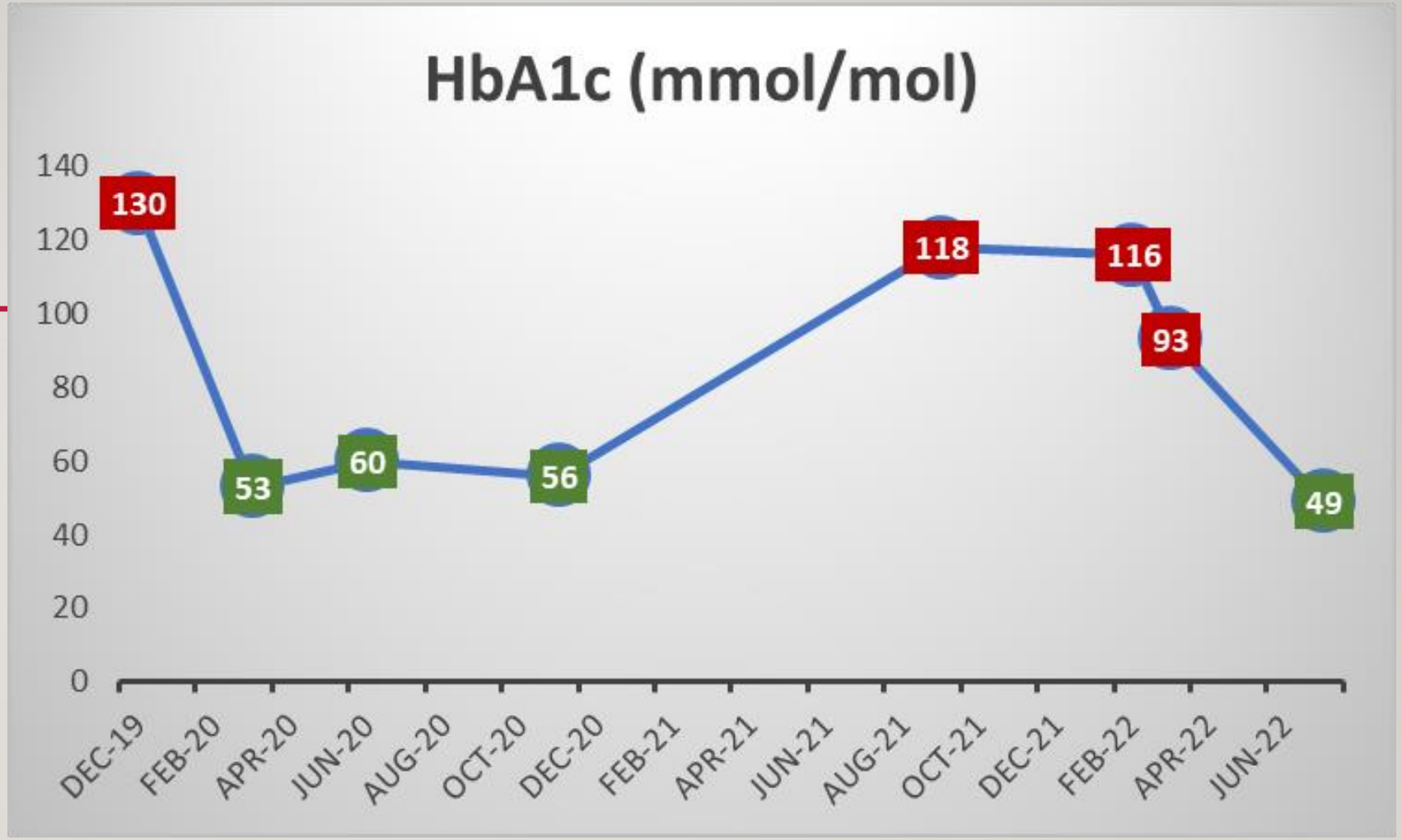
Gliclazide M/R trial and Metformin promoted again as reduced concordance.

Audience Poll

Would you think of MODY and check C-peptide ? ---- Yes/No/Not sure
What would you estimate the calculator to say? ----- High /Intermediate/Low probability

Follow-up	Case review	Actions/plans
Feb 2022	A1c down to 93 mmol/mol. Feeling fine and weight up. (C-peptide-786 with glucose 16 mmol/L) Taking Gliclazide daily and less often MF Brick-laying course	Genetic tests sent off to Exeter with questionnaire Dietetic support provided in clinic
May 2022	DNA/WNB – rebooked for 1/12	Tel contact by PDSN attempted and informed that things well and BGs better
June 2022	Tel rvw at patient request. Dropped out of college and working as a labourer several days a week. On and off with Metformin use and stopped Gliclazide! Says he is better and smoking Cannabis once daily.!	Metformin use reinforced and to re-consider Gliclazide. Blood form sent to get up to date A1c July 2022- A1c-**49** mmol/mol
Sept 2022	Tel review again as message to say cant attend. Hit and miss with tablets. Still undertaking heavy manual work and attends GYM.	Encouraged to take meds and continue diet and lifestyle. Congratulated on positives
Dec 2022	Tel contact- family bereavement. Mother away	Advised to continue and to get repeat bloods or attend in person for POCT
Feb 2023	Tel contact- cant come in person. Both MF+Gliclazide being taken 4/7 days	No bloods yet but remains well. Encouraged to attend for complications screening etc

HBA1C TREND GRAPH FOR CASE STUDY-1



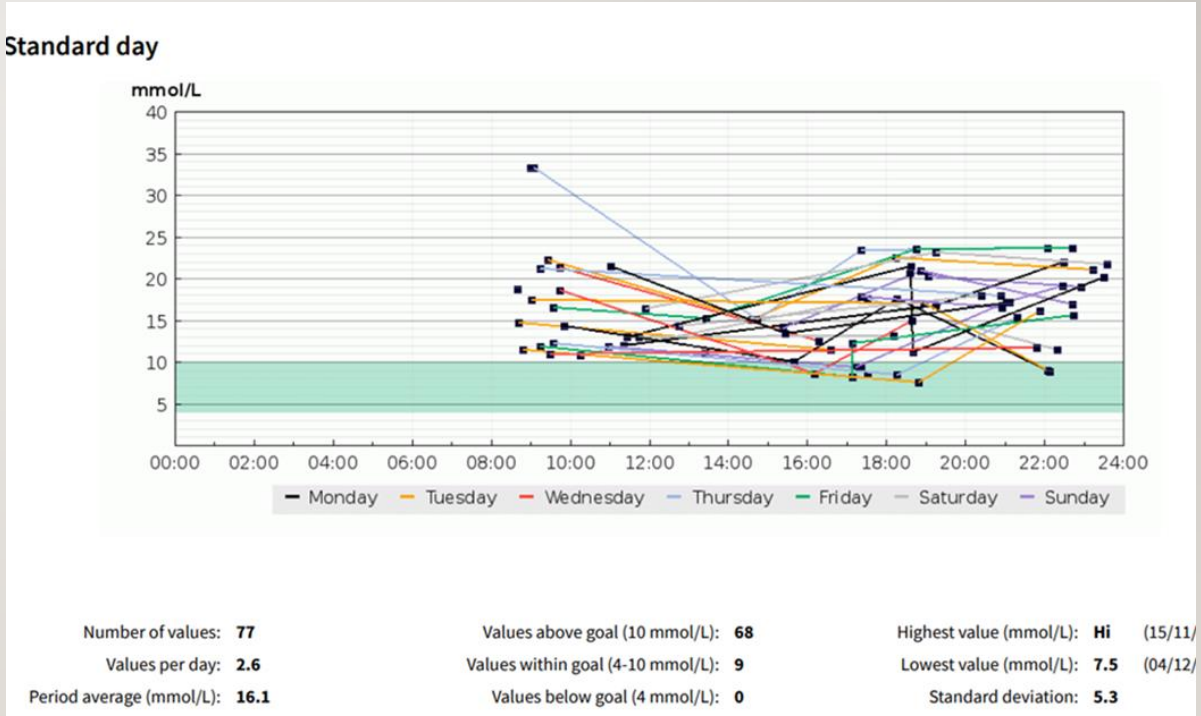
- 18 years old, working in a warehouse, recognises impact of high glucose on day to day life, restarted Gliclazide and wanted more info re MF. Convinced to have Dexcom One sensor and next step would be Insulin or SGLT-2i depending on current response to Rx.

CASE STUDY-2: DIABESITY IN CYP

- Afro-Caribbean background - Referral at age 18 years to Transition as recently diagnosed T2DM with A1c of 12.7% foll glucose 17 in clinic. Asymptomatic
- Previously under Paeds Endo-Diab and CAMHS with
  - Obesity (Wt-99th centile, Ht-25th Centile) + Acanthosis Nigricans – Refd to Genetics of Obesity study
  - Autism spectrum disorder
  - ADHD and low mood
  - Fatty Liver – Aripiprazole stopped and diet and lifestyle support provided
- Some concerns re delayed puberty but resolved over followup period and developing fine.
- Recalled immediately and as declined insulin started on Metformin with diet and lifestyle advice and glucose and ketone monitoring

CASE STUDY-2
TRANSITION 3 MONTHS POST DIAGNOSIS

- **History- Very fussy eater and prefers high calorie food**
- **Wt-106 Kg (99th centile) ; Ht-174 cms (25th centile)**
- **BMI- 35**
- **HbA1c- 101 mmol/mol**
- **Current Rx- MF 2g/day, Levemir 14 units OD**
- **Proposed Rx- Started on Dulaglutide 750mcg OW**
- **Regular PDSN support ongoing**
- **Diabetes remission with weight loss discussed**



DIABETES REMISSION IN CYP WITH T2DM

- Remission is defined as A1c<6.5% or 48 mmol/mol with fasting glucose less than 7 mmol/L maintained without any drugs for at least 6 months
- In Adults weight loss linked to remission and good success rates within 5-8 years of diagnosis (Lean et al, DIRECT study 2018)
- Little direct evidence available in CYP- but weight loss considered a key and beneficial therapeutic focus with indirect measures to support. TODAY study less promising (NEJM, 2012) but more work needed
- A small study showing that remission does occur in adolescents with T2DM
  - 20 CYP aged 14-15 years- VLCD ketogenic diet for min 6/52 led to weight loss, improved glucose levels and A1c reduction of ~1.4% and sustained (up to 2 years) remission from medication use in 19/20 patients (SM Willi et al Diabetes Care 2004 Feb;27(2):348-53)
- Watch out for the LEGENDary study from Dr.Sachdev studying remission in T2 Youth and supported by DUK

CASE STUDY 2 – FOLLOW-UP

Tel review following month

Some confusion re dose titration of Dulaglutide and after the start up dose being given 750mcg/1500mcg alt week by mother!

Well tolerated and some improvement in BG. Wt-105 kg

Attended clinic 3 months later- Anxiety++ at clinic attendance

A1c-69 mmol/mol; glucose readings down and Dulaglutide 1.5mg OW+Levemir 14 units and Metformin M/R 2gm/day.

Further dietetic support and advised re importance of diet and exercise along with meds

Offered FGM at subsequent visit as not monitoring

T2DM THERAPEUTICS FROM AN ADULT PERSPECTIVE

- High levels of familiarity with all T2 drugs
- GLP-1 use for over a decade. Experience in Diabesity and obesity management
- Recent impetus with Liraglutide, Dulaglutide and Empgaliflozin for over 10 years via NICE NG 18 but still "off-label" use
- More comfortable with off-label prescribing of these meds
- Oral Semaglutide available now (Rybelsus 3mg OD to 14mg daily = 0.5mg weekly injectable)
- Caution as well in terms of SGLT-2 inhibitors and euglycaemic DKA and need for good education around glucose and ketone monitoring
- Good history around background and familial risk – esp gallstone disease, pancreatitis, thyroid cancer (theoretical risk)

THE OBESITY ANGLE

High dose GLP-1 for obesity management in 18 and older (Nice TA 664 for Saxenda and NICE TA875 for Wegovy March 2023)
Recent FDA approval (Dec 2022) for Wegovy (high dose Semaglutide) to cover CYP aged 12 and over for Obesity
Dulaglutide can also be used in 3mg and 4.5 mg dosing for obesity management
Availability of OW GLP-1s have been very patchy in the last 18 months
Global supply chain issues and risk of Rx interruptions
However, caveats and unclear re long term implications and sustainability esp GLP-1 therapy

POSITIVES AND PITFALLS IN T2DM TRANSITION CARE

Pros	Cons
Adult diabetes teams- Vast experience with medications in T2DM	Important to recognize key differences in presentation and progression
Choice of therapeutics Comfort with off-label use	Risk of "normalizing" Getting lost in the "sea" of T2 diabetes amongst adults
Understanding the transition to autonomy and choice with personal care and health	Risk of losing "control" over the situation and care "drifting"
Experience with obesity management (some)	Challenges in focused care delivery without a specific service
Experience with complications management	Not recognizing the time window/differing thresholds for interventions
Opportunity to share good practice between Paeds and Adults and esp good for trainees	Building expertise with smaller numbers in each area can be challenging

SUMMARY

- T2DM in CYP is a growing problem
- Ethnic minorities disproportionately affected
- Stigma greater in some respects – important to get teens away from stigma/guilt
- Burden of long-term health consequences high
- Risk of co-morbidities such as obesity, NAFLD, Htn, CVD, OSA and increased mortality
- Need for MDT approach and perhaps early intervention whilst avoiding alienating young people from healthcare
- Adult diabetes physicians and DSN can help with earlier interventions in this population
- Keep reviewing Rx options and approaches constantly as things can change quickly
- Should we push for earlier transition? Pros and Cons?
- Role of remission strategies, obesity management including bariatric surgery is likely to become more relevant

QUESTIONS/ COMMENTS