5th Niru Goenka Memorial Lecture
Legacy of the 2012 National Insulin Pump Audit

Dr Emma Wilmot
Consultant Diabetologist
Chair, ABCD Insulin Diabetes Technology Network UK

Niru's support

- Very supportive of the YDEF
  - Involved in YDEF taster evenings to attract trainees to the speciality
  - Co-authors on SCE column for Practical Diabetes International
- Both members of ABCD committee
  - ABCD Type 1 diabetes campaign
  - Commissioning specialist diabetes services for adult with diabetes: Diabetes UK Task and Finish Group
- YDEF dinner March 2012

"obvious passion for his patients and the diabetes community"
"selfless, happy to share his ideas with anyone"
"a very funny and intelligent man"
" a mischievous smile and great sense of humour"
"outstanding colleague and committed doctor"

Overview

Derby Teaching Hospitals NHS
NHS Foundation Trust

- 2012 National Insulin Pump Audit
- His influence on Derby service development
- The IPN-UK/DTN-UK story
- Reflections

DIABETIC Medicine

DiABETES UK
KNOW DIABETES. FIGHT DIABETES.

DIABETICMedicine

DOI: 10.1111/dme.12325

Research: Treatment

The UK service level audit of insulin pump therapy in adults

H. D. White[1], N. Goenka[2], N. J. Furlong[3], S. Saunders[4], G. Morrison[5], P. Langridge[2], P. Paul[6], A. Ghatak[6] and P. J. Weston[5]

[1]Aintree University Hospital NHS Trust, Liverpool, [2]Countess of Chester NHS Trust, Chester, [3]St Helens and Knowsley NHS Trust, St Helens, [4]Warrington and Halton Hospitals NHS Trust, Warrington, [5]The Royal Liverpool and Broadgreen University Hospitals NHS Trust and [6]Alder Hey Children's NHS Trust, Liverpool, UK

Accepted 19 September 2013

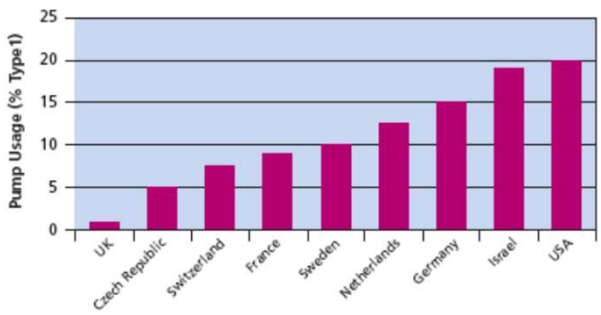
Abstract

Aims The National Institute for Health and Clinical Excellence (NICE) published guidelines for the use of continuous subcutaneous insulin infusion in 2008 (technology appraisal 151). The first UK-wide insulin pump audit took place in 2012 with the aim of determining adherence to the guidance issued in NICE technology appraisal 151. The results of the adult service level audit are reported here.

White HD, **Goenka N**, et al. Diabet Med. 2014 Apr;31(4):412-8.

Background

- Benefits of insulin pump therapy include
  - Improved glycaemic control
  - Reduced hypoglycaemia and
  - Improved quality of life (QOL)



Estimated pump use in different countries 2007-9 (Pickup)

Pickup JC. NEJM 2012; 366(17): 1616-24

Background: 2012

- Limited UK data available on the uptake of insulin pump therapy following NICE TA151 2008
- Recommended in those with Type 1 diabetes where:
  - attempts to achieve target HbA1c levels with MDI results in the person experiencing **disabling hypoglycaemia**

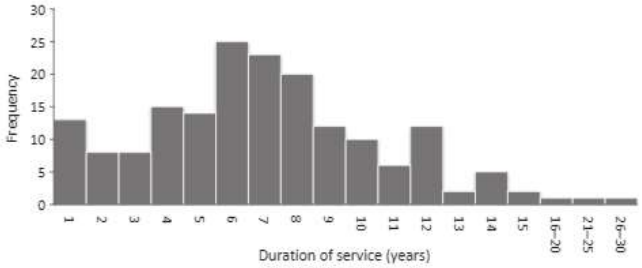
    or
  - **HbA1c** levels have remained high (**8.5% (69mmol/mol)** or above) on MDI therapy despite a high level of care
- First national service level audit to determine adherence with NICE TA 151
  - All UK centres invited to participate

2012 UK audit: insulin pump therapy

- 97% (178/183) of centres participated
- **Estimated 6% of those with T1DM using CSII**
- Well below the 15-20% anticipated by NICE

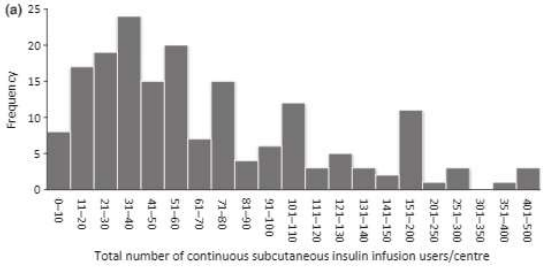
White HD, **Goenka N**, et al. Diabet Med. 2014 Apr;31(4):412-8.

Duration of insulin pump services

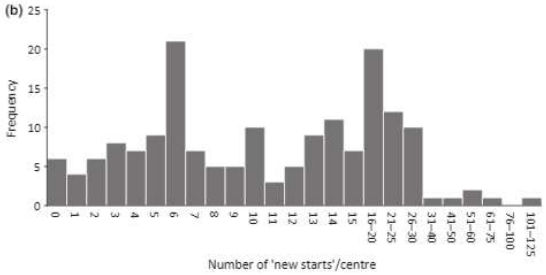


White HD, **Goenka N**, et al. Diabet Med. 2014 Apr;31(4):412-8.

Total users and new starts



75/ centre on average



14 in past 12 months

White HD, **Goenka N**, et al. Diabet Med. 2014 Apr;31(4):412-8.

Barriers to insulin pump uptake

- Funding was NOT a barrier for those who fulfilled NICE

- **Staffing was a key barrier**
  - 46% of centres had only 1 consultant involved in pump therapy services; 3% had no consultant input
  - 3/167 centres had no formally trained staff delivering services
  - HCP time drastically underfunded

White HD, **Goenka N**, et al. Diabet Med. 2014 Apr;31(4):412-8.

What's new?

- This is the first UK-wide service level audit of insulin pump therapy.
- The audit metrics were aligned to National Institute for Health and Clinical Excellence (NICE) technology appraisal 151.
- Of all UK insulin pump centres, 97.3% participated in the audit.
- The audit results provide up-to-date information regarding the number of people using insulin pump therapy and the prevalence of use amongst people with Type 1 diabetes in the UK.
- The audit outcomes identify a significant shortfall in the funding of healthcare professionals required to deliver pump services and explores the barriers to provision of insulin pump therapy in the UK.

White HD, **Goenka N**, et al. Diabet Med. 2014 Apr;31(4):412-8.

Derby

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NHS Foundation Trust

- Joined as a consultant, August 2014
- Lead of insulin pump service
  - ~230 patients on CSII
  - 1 day a week of DSN (0.2WTE), with no dedicated cover for the rest of the week
  - ½ a day a week (0.1 WTE) dietitian time

Challenges

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NHS Foundation Trust

- New consultant
- No idea how well the patients were/ were not doing
- No capacity to see them frequently
- Where to start?

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New to market pump

- Pump of choice in successive patients, large number had started in short space of time
- No formal process for review/limited capacity
- Further investigation with support from the company revealed performance issues which needed addressing
- One serious incident, leading to recall

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NHS Foundation Trust

Lessons learned

- New insulin pumps are not subjected to the same rigorous randomised controlled trials as drugs

- When introducing a new pump to your service
  - Review how many other centres have used it
  - What, if any, data is available?
  - When starting, chose experienced, existing pump users who will feedback any issues
  - Have infrastructure for regular review of outcomes

Issues

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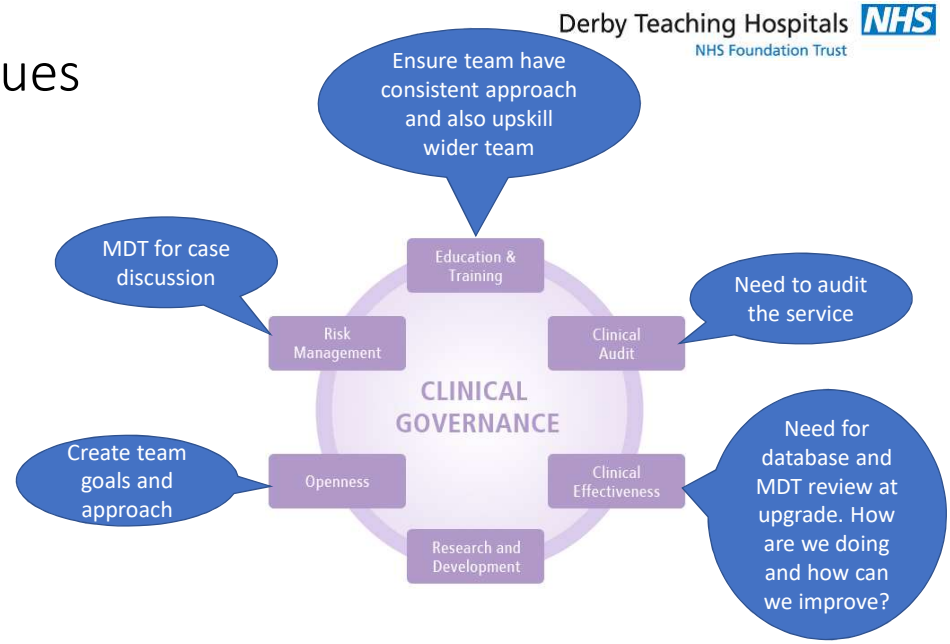

Taking pride in caring

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DIABETICMedicine

DOI: 10.1111/dme.13367

Short Report: Care Delivery

Continuous subcutaneous insulin infusion (CSII) therapy at Derby Teaching Hospitals: sustained benefits in glucose control

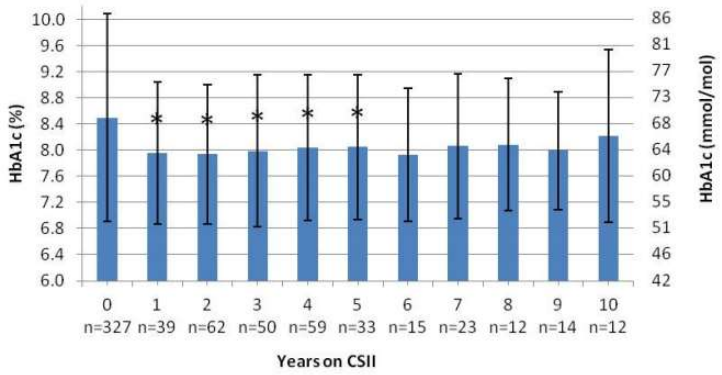
U. Anyanwagu[1], H. Olaoye[1], P. Jennings[2], S. Ashton-Cleary[2], S. Sugunendran[2], D. Hughes[2], I. Idris[1,2] and E. G. Wilmot[2]

[1]Division of Medical Sciences & Graduate Entry Medicine, School of Medicine, University of Nottingham, Nottingham and [2]Diabetes Unit, Royal Derby Hospital, Derby, UK

Anyanwagu U, Wilmot EG. Diabet Med. 2017 Aug;34(8):1154-1157.

King's College London

Derby Teaching Hospitals NHS
NHS Foundation Trust



Beato-Víbora P et al. Diabet Med. 2015 Nov;32(11):1453-9.

Aim

Derby Teaching Hospitals NHS
NHS Foundation Trust

- To assess the impact of insulin pump therapy on:
  - Glycaemic control
  - Hypoglycaemia
  - Quality of life
- Explore patient confidence to self manage pump therapy

Methods

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Data

- Hospital records for insulin pump users 1997-2014
  - Demographics
  - HbA_{1c}
  - Indication for CSII
- Questionnaire sent to all users. Likert scale to assess
  - Hypoglycaemia
  - Quality of life
  - Confidence to self manage

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Results

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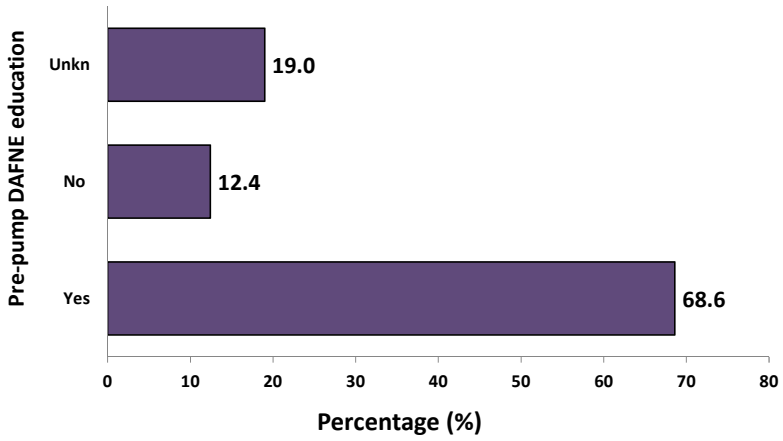
Baseline Characteristics

N = 258	Mean (SD) *IQR
Mean age (yrs)	43.9 (13.4)
Female (n, %)	155 (60.1)
Type 1 diabetes (n, %)	258 (100)
Baseline HbA1c mmol/mol	78 (2)
%	9.3 (2.0)
Diabetes Duration (yrs)	24.4 (12.4)
Duration on CSII (yrs)	4.4 (2.7-7.2)*
Indication for CSII n (%)	
Hypoglycaemia	95 (36.8)
Poor glucose control	75 (29.1)
Hypo + poor glucose control	87 (33.7)

22

Results

Proportion that attended pre-pump DAFNE education



Taking pride in caring

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Results

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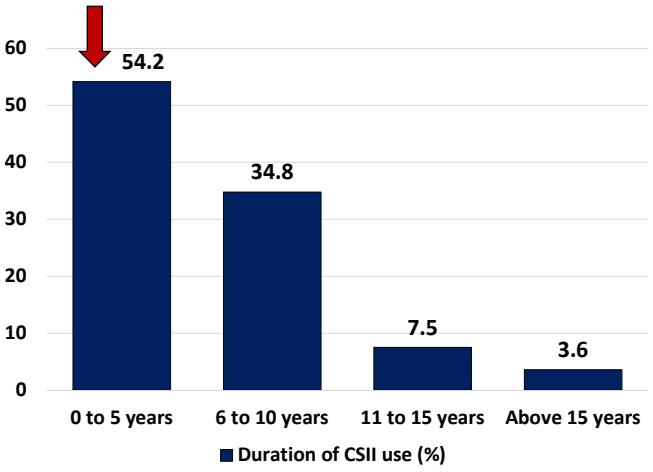
Proportion of CSII duration (%)



Results

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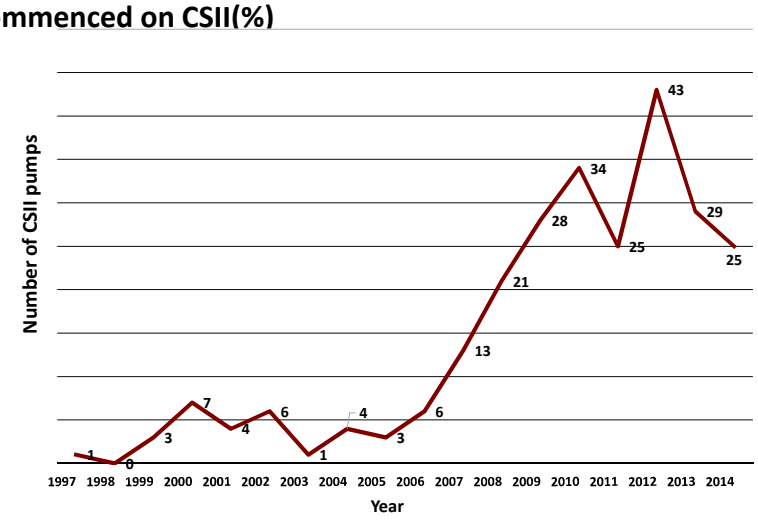
Year commenced on CSII(%)



Results

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Yearly mean HbA1c in all patients

HbA1c levels	Baseline (239)	6 months (121)	1 year (136)	2 years (158)	3 years (129)	4 years (109)	5 years (89)	6years (61)
All patient-population								
Mean HbA1c (%)	9.3	8.5	8.7	8.4	8.6	8.4	8.5	8.2
Mean diff from baseline (%)	-	-0.64	-0.68	-0.91	-0.83	-1.00	-1.08	-1.07
(95% Confidence Interval)	-	(-0.91 to -0.37)	(-0.94 to -0.41)	(-1.15 to -0.66)	(-1.08 to -0.58)	(-1.28 to -0.73)	(-1.42 to -0.75)	(-1.45 to -0.69)
P-value	-	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Anyanwagu U, Wilmot EG. Diabet Med. 2017 Aug;34(8):1154-1157.

Results

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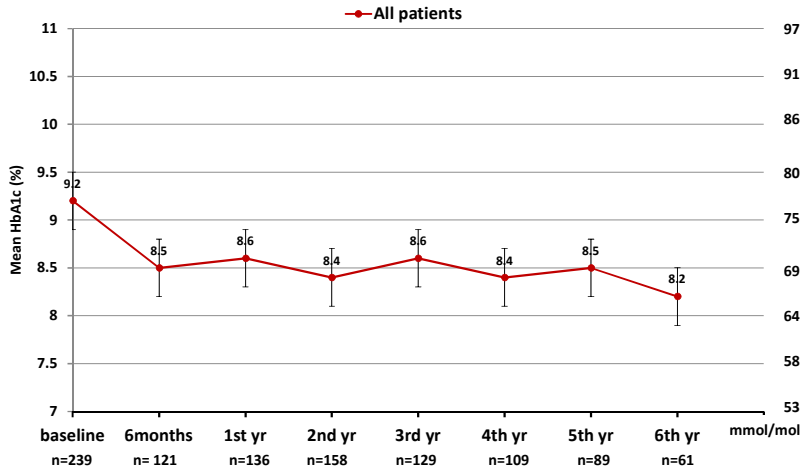
Yearly mean HbA1c in all patients



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Results

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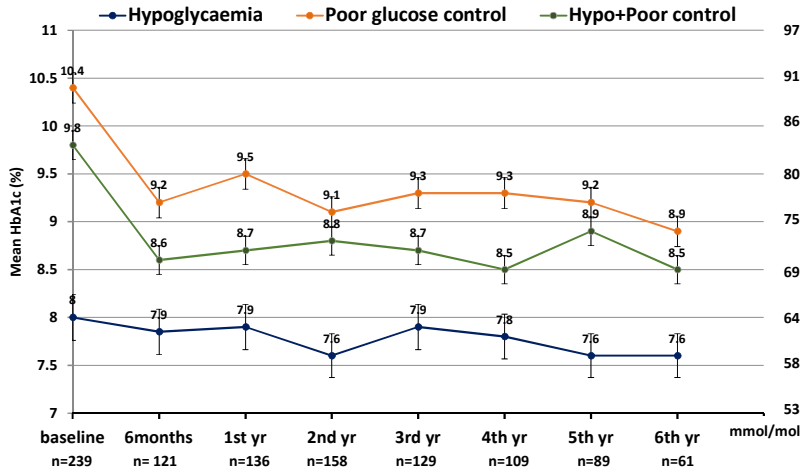
HbA1c by indication



Anyanwagu U, Wilmot EG. Diabet Med. 2017 Aug;34(8):1154-1157.

Results

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Questionnaire

- Response rate 46% (n=121)
- Agree or strongly agree insulin pump therapy
  - improved quality of life 94% (n=114)
  - reduced hypoglycaemia 80% (n=95)
- Satisfied with the quality of care 86% (n=104)

Anyanwagu U, Wilmot EG. Diabet Med. 2017 Aug;34(8):1154-1157.

Results

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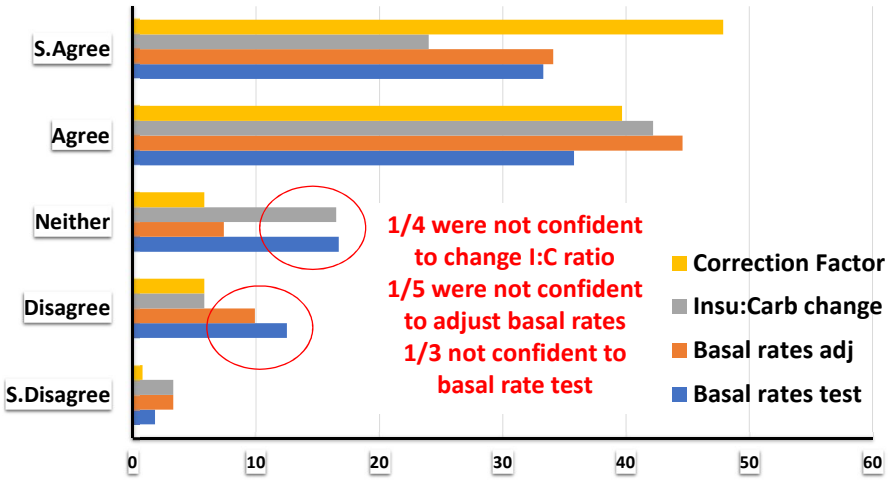
NHS Foundation Trust

Confidence in insulin adjustment



Anyanwagu U, Wilmot EG. Diabet Med. 2017 Aug;34(8):1154-1157.

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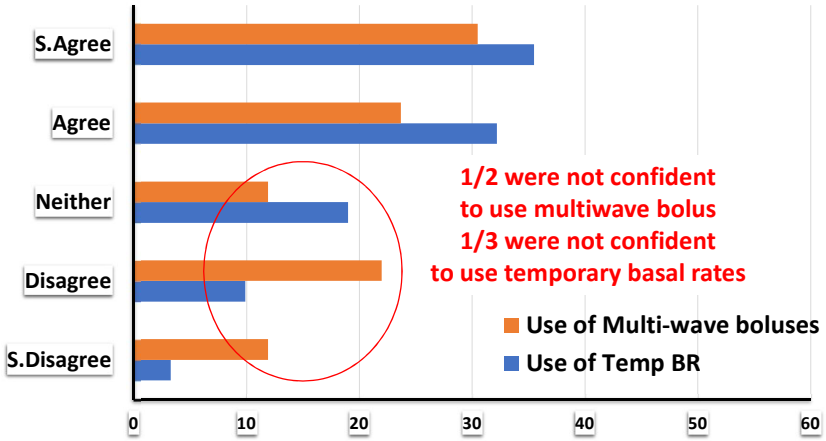
NHS Foundation Trust

Results

Confidence in the use of advanced features



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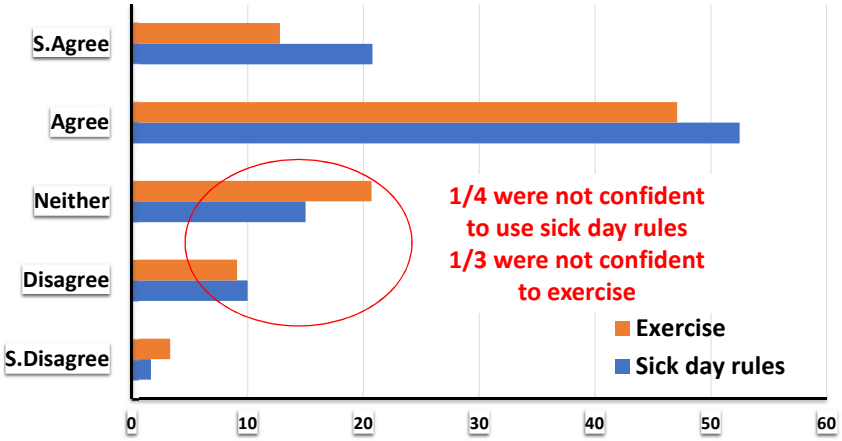
NHS Foundation Trust

Results

Confidence in ability to exercise, use of sick day rules



Summary

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- Significant, sustained benefit in glycaemic control
  - 0.7% HbA1c reduction by year 1
- Majority confident in their use of CSII

Discussion

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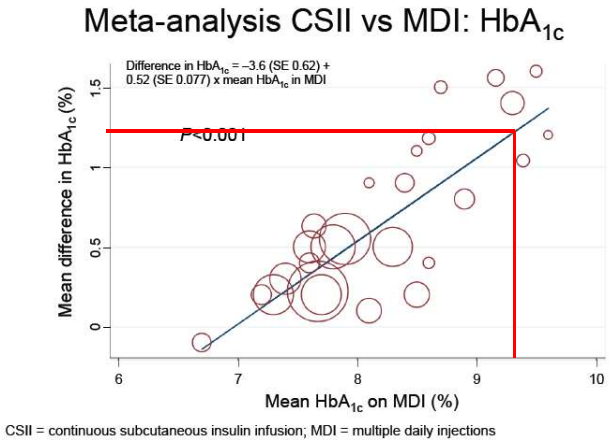

CSII = continuous subcutaneous insulin infusion; MDI = multiple daily injections

Pickup JC. Diabetic Medicine 2008 Jul;25(7):765-74.

Conclusion

Derby Teaching Hospitals NHS
NHS Foundation Trust

- Despite limited HCP support, CSII users experienced a significant, sustained improvement in glucose control
- Self reported improvements in hypoglycaemia and quality of life
- Further education and support required for
  - Basal rate testing and insulin adjustment
  - Use of advanced features
  - Sick day rules
- Perhaps we could do better?

Initial improvements

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Capacity and team education

- Team pump away day to upskill inpatient team
- Review admin processes (DSN time dependent)
- Embed pump in clinical pathway & define referral pathways
- Some additional staff time given but ultimately we needed more staff to safely run the service

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Initial improvements

Safety

- New insulin pump starts suspended
- Fortnightly MDT review of patients
  - Are there safety concerns?
  - Do they met criteria for ongoing pump therapy?
- Pump clinic proforma to ensure key safety aspects covered
  - Sick day rules, back up pens
  - Use of advanced pump features

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Business case for additional staff

- Serious concerns about staffing levels
  - new starts suspended
- For 300 pump patients:
  - 1.7 PA consultant time
  - 2.5 days a week DSN time
  - 1 day a week dietitian time

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Growth in CSII users

Year	Number of patients on CSII
2000	11
2005	26
2010	112
2015	258
2016 (May)	303
2020 predicted	500

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Business case: Drivers for change

1. **Safety**
   - Insulin pump service on Trust Risk Register for >1 year
   - Current capacity allowed DSN review once every 2 years
   - Suboptimal support existing patients, increasing the risk of complications and admission to hospital
2. **Demand**
   - The number of patients on insulin pump therapy had substantially increased but staffing had remained static
3. **Non-compliance with NICE**
   - Suspended new pump starts due to safety concerns

2012 audit data

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NHS Foundation Trust

	National audit data 2012 (mean)	Derby 2016 staffing	Predicted RDH need based on pt numbers
Service size (n)	74	303	303
Consultant (PA)	1.1	1.7	4.5
DSN (WTE)	0.69	0.5	2.8
Dietician (WTE)	0.37	0.2	1.5

	Detail
7 day DSN service	Deliver 7 day DSN service, facilitating discharge and reduce length of stay.
Increase trust income from paediatric BPT	Extend BPT from 18 to 19 years which at ~£3K per patient per year will support additional staff. 25 x £3k = £75K income.
Increased income from DKA & hypo BPT	7 day DSN service to increase our income from the DKA and Hypo BPT.
Reduction in admissions with DKA via increased access to DAFNE	RDH experiences above expected admissions for patients with diabetic ketoacidosis (DKA) (157 vs 129 in 2012/13). Improving patient access to DAFNE reduces admissions with DKA by up to 58% (10 events avoided per yr/100 Type 1 diabetes pts. Reduce DKA admissions to as expected =28 x £1176.53= potential cost savings of £32,942.84 per annum.
Reduce long term frequency of clinic visits	The DSNs could facilitate the delivery of intensive education for patients in the first year of pump therapy which would equip them with lifelong skills, improve clinical outcomes and reduce the frequency of follow up in clinic thereafter.

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Business case developed

- Successfully negotiated additional
  - 2 PA consultant time
  - 1 WTE band 7 DSN
  - 0.5 WTE band 7 dietitian
  - Admin time

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The team has grown!

- Now have 336 patients on pumps
- Staffing
  - 3 consultants
  - 5 trained pump competent DSNs
  - 3 pump dietitians
  - Dedicated admin time
- Clinical governance
  - MDT, functioning database, process for signing off consumables/ organising and approving upgrades, troubleshooting, DNA processes etc
  - Consistency in team messages

Where does DTN-UK fit in?

- Arrived in Derby in 2014
- No training in CSII as SpR apart from YDEF pump course
- No experience of using downloads in clinics as trainee

Lots to learn

- Who are the best candidates for insulin pumps?
- Who should be considered for pump withdrawal, if any?
- Basal rate testing, is it worth it?
- 500/100 rule, seems news to many, should it be?
- Best approach to downloads?

Clear from Niru's 2012 audit that availability of skilled HCPs were a key barrier to the uptake of insulin pumps and….
…..there are experts across the UK who know the answers to the questions many smaller centres must have…. we could work together to support growing services and upskill HCPs…..
So I discussed the idea with Rob Gregory who was supportive…as were the device companies…and
ABCD IPN-UK was established

IPN UK
collaborate · evolve · support

DTN-UK

DTN UK

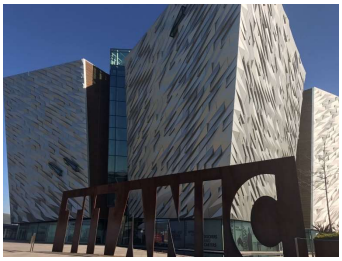
- Developed committee of UK experts
- Designed logo
- Set up website
- Developed event programme
- Launch April 2016

Launch 2016

- First event a great day…170 applied for 100 places
- Feedback excellent
- Hunger for education on diabetes tech

Belfast 2017

- May 2017, >100 delegates iconic Titanic building



DTN-UK 2018

- >520 members
- 8 national educational events to date
  - 3x Annual day 100 places, 5x team days 60 places
- Representation at ABCD, DUK, NDA

Best Practice Guides www.DTN-UK.care

Thank you!

CSII clinical guide
Leads:
Dr Emma Wilmot,Derby
Dr Peter Hammond, Harrogate

Working group:
Dr Pratik Choudhary, London
Dr Rob Gregory, Leicester
Geraldine Gallen, London
Chris Headland, Wales
Dr Sufyan Hussain, London
Dr Peter Jennings, Derby
Dr Lala Leelarathna, Manchester
Dr Alistair Lumb, Oxford
Dr Dinesh Nagi, Yorkshire
Prof Nick Oliver, London
Dr Vernon Parfitt, Bristol
Dr Neil Walker, Devon
Contributions from
Dr Una Graham, Belfast
Dr Brian Kennon, Glasgow
Dr Helen Partridge, Bournemouth
Dr Julia Platts, Wales
Dr Andrew Solomon, Hertfordshire

CSII in hospitalised patients
Leads:
Parth Narendran, Birmingham (Chair)
Ali Karamat, Birmingham (co-Chair)

Working group:
Kate Evans, Plymouth
Emma Green
Barbara Hudson, Birmingham
Martha Stewart, Birmingham
Mark Evans, Cambridge
Rob Gregory, Leicester
Emma Wilmot, Derby

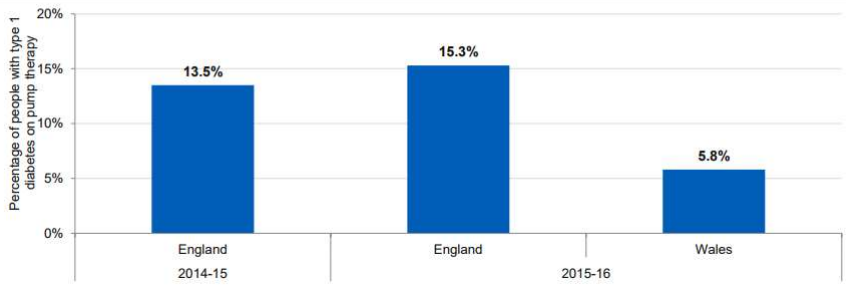
CSII service guide
Leads:
Dr Sufyan Hussain, London
Dr Vernon Parfitt, Bristol
Dr Emma Wilmot,Derby

Working group
Dr Pratik Choudhary, Senior Lecturer, London
Dr Rob Gregory, Leicester
Geraldine Gallen, London
Chris Headland, Wales
Dr Peter Hammond, Harrogate
Dr Peter Jennings, Derby
Dr Lala Leelarathna, Manchester
Prof Nick Oliver, London
Dr Neil Walker, Devon

National Pump Audit

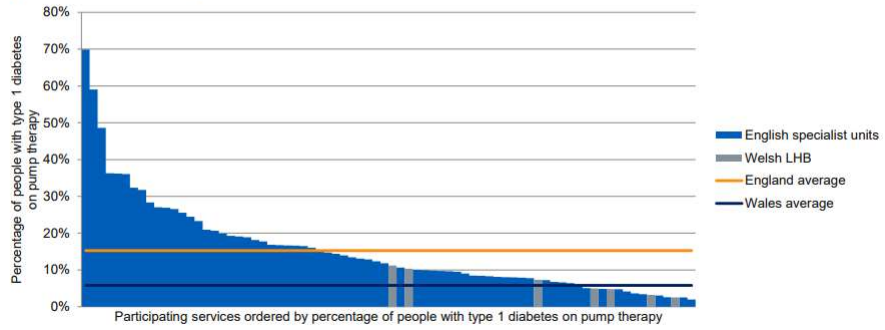
- Expert advisory group for NDA pump audit
- Promote participation
- Year on year increase in uptake, 6% in 2012

Figure 2: Percentage of people with Type 1 diabetes on an insulin pump, by audit year, 2014-2016



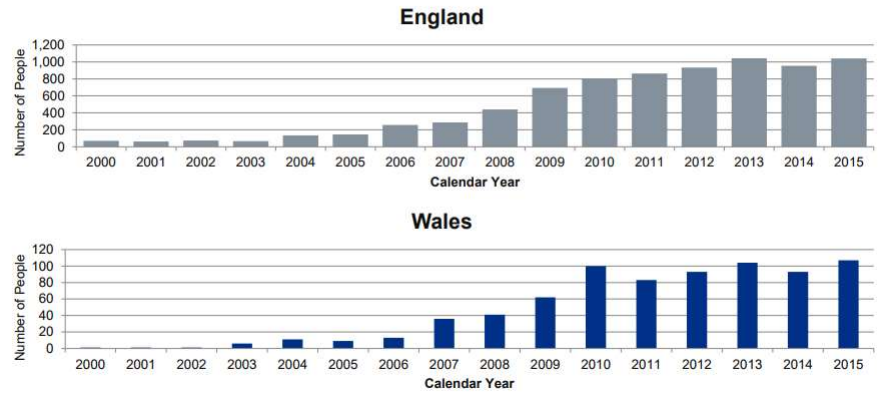
Variation

Figure 1: Percentage of people with Type 1 diabetes on pump therapy by participating specialist service[1], 2015-2016



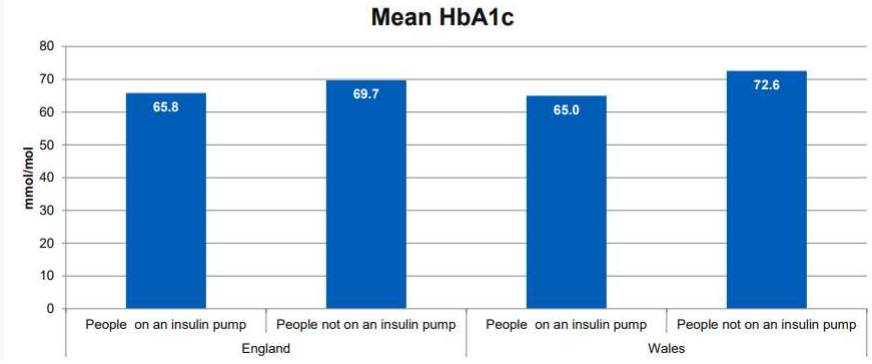
Pump starts

Figure 3: Number of people with Type 1 diabetes by year started on pump, by country, 2015-16.



HbA1c

Figure 10: Mean HbA1c (mmol/mol) for those with Type 1 diabetes on an insulin pump compared to those not on a pump, 2015-2016



Overall

- Access to CSII has improved
- Pump starts have plateaued which could indicate reduced demand or staffing issues
- CSII associated with lower HbA1c

- We need a further service level audit to identify current barriers to uptake

Access to CGM

- Roche commissioned FOI to determine whether CGGs in England have policies for the reimbursement of CGM
- Responses 99% (205/207) CCGs
- 45% (92/205) had policy on funding of CGM
- **Only 21% (43/205) commission CGM in-line with NICE guidance**

Perera R, Oliver N, Wilmot EG, Marriott C. Submitted 2018.

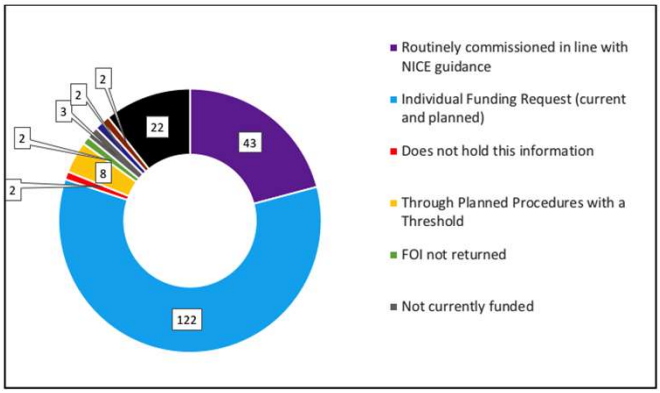
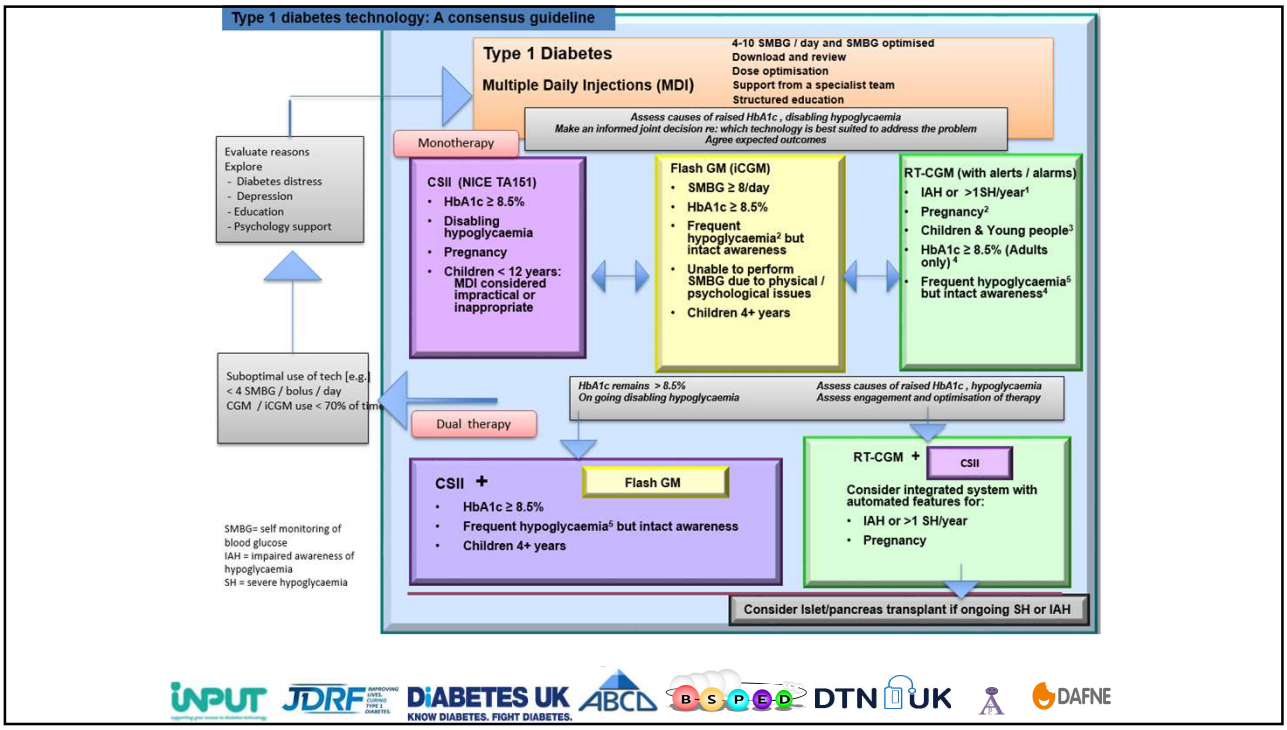


Figure 1: Current routes to funding for continuous glucose monitoring (CGM)
Response to the question "How is CGM currently funded within your CCG?"

Main route to reimbursing CGM: Individual Funding Requests (IFRs) 60% (122/205).

Perera R, Oliver N, Wilmot EG, Marriott C. Submitted 2018.



Plans for the future

- DTN-UK
  - National Service Level Audit
  - Continue to run educational events
  - Launch more Best Practice Guides
    - CGM
    - Pregnancy
  - Promote access to insulin pumps and technology
  - National FreeStyle Libre Education programme

Date for your diary

- 16th May 2019
- Annual pump day, Loughborough

- Join DTN-UK

  https://abcd.care/dtn/join

Thank you Niru!

- **Provided much needed data which formed the basis of my successful business case in Derby**
- **Identified the key barrier to insulin pump uptake, inspiring development of ABCD DTN-UK**

"We think of Niru a lot in Liverpool as you can imagine and we always remember his stories and good humour. He was a great friend and we all miss him hugely especially around this time of year the anniversary of his death. Behind the humour though was a man who was passionate about diabetes and about improving diabetes services both locally, around his hospital in Chester, but also on the national level.

He had a rare vision for seeing how services could be developed and had the communication skills to bring everyone along with his vision. Our deep sadness at his loss locally is in part because we recognize the loss to diabetes across the nation."

Phillip Weston, Liverpool

"There will be a palpable gap within ABCD. Niru possessed a rare combination of compassion and altruism mixed with intelligence and a fabulous sense of humour. I miss him both as a colleague and more importantly as a friend."

Dr Susannah Rowles

Derby Teaching Hospitals NHS
NHS Foundation Trust

DTN UK

Thank you

@wilmotemma
Emma.Wilmot2@nhs.net

ABCD
Association of British Clinical Diabetologists

AUTUMN MEETING
BMA House, London
8th & 9th November 2018

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The sponsoring pharmaceutical companies have not had any editorial input into the agenda or material being presented, with the exception of the sponsored symposium

Physician perception and clinical practice regarding use of SGLT2 inhibitors in patients with foot ulcer disease

Dr John Bassett CMT 1 Diabetes & Endocrinology

Countess of Chester

SGLT-2 inhibitors

- Novel agents that utilise the sodium-glucose cotransporter 2 to prevent glucose reuptake in proximal tubule of the nephron.
- SGLT-2 is responsible for 90% of glucose reuptake, where as SGLT-1 is only 10% so is a natural drug target.

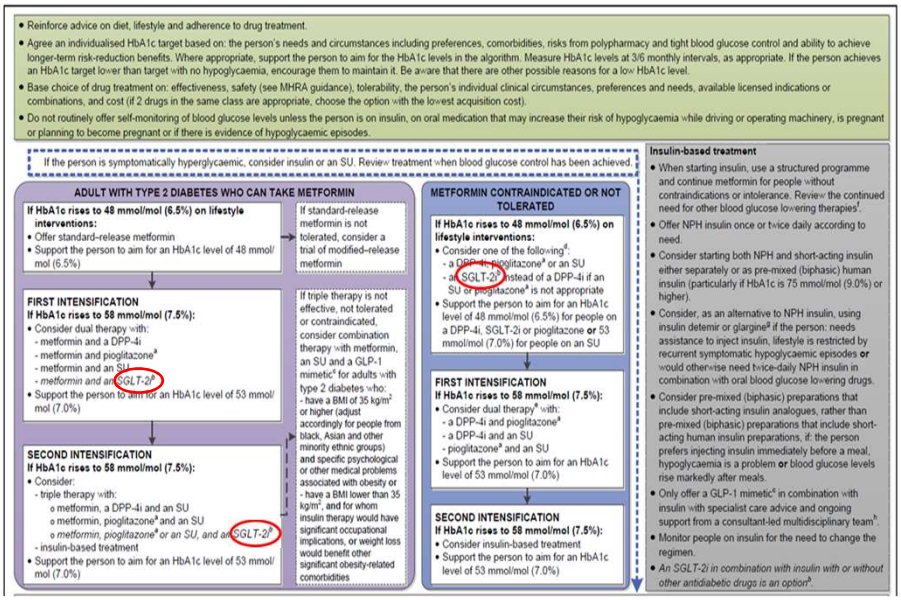
Introduced in the UK

- Dapagliflozin – June 2013
- Empagliflozin – May 2014
- Canagliflozin – June 2014

- Recent NICE recommendations – greater use of SGLT-2 inhibitors.
- More data becoming available associating SGLT-2 inhibitor use with favourable cardiovascular outcomes

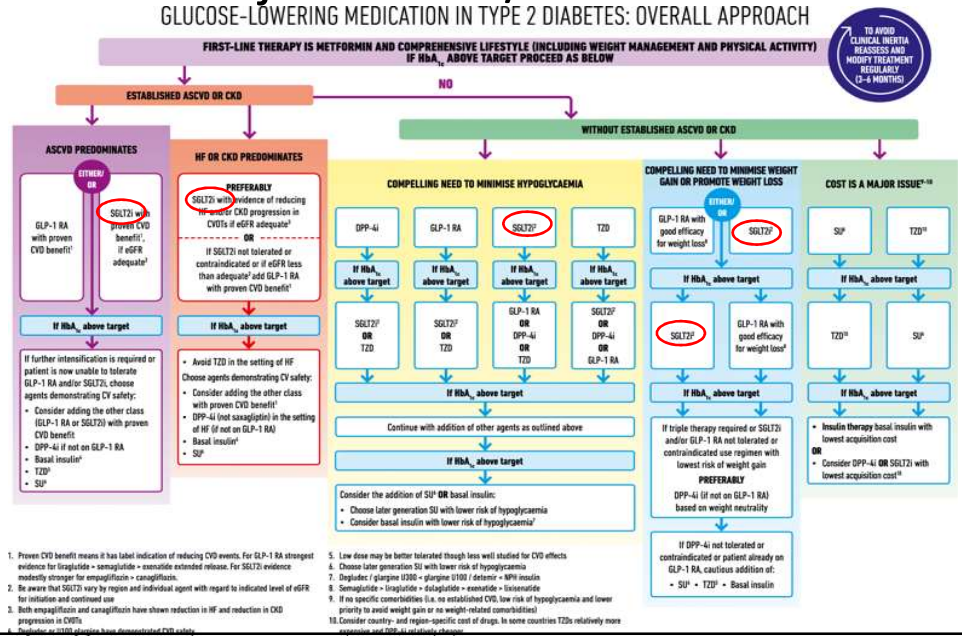
NICE National Institute for Health and Care Excellence

Algorithm for blood glucose lowering therapy in adults with type 2 diabetes



Recent joint EASD/ADA statement

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U300 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycaemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

	Canagliflozin	Dapaglifozin	Empagliflozin
Study	CANVAS-R	DECLARE-TIMI	EMPA-REG
Participants (n)	10,102	17,000	7,020
OUTCOMES			
Heart Failure	NR 0.67	Fewer patients hospitalised	0.65 (p=0.002)
non-fatal myocardial infarction	HR 0.85		HR 0.87 (p=0.22)
non-fatal stroke	HR 0.90		HR 1.24 (p=0.16)
Composite of death from cardiovascular causes, non-fatal stroke and non-fatal MI	HR 0.86 P=<0.001 for inferiority/0.02 for superiority	Reduced	HR 0.86 (p=0.04 for superiority)
All cause mortality	HR 0.87		HR 0.68 (p=<0.001)
Amputations	HR 1.97 (P=<0.001)		HR 1.00

Controversies – barriers affecting SGLT2 prescription

	Canagliflozin	Empagliflozin	Dapagliflozin
DKA	Event rate 0.6 vs 0.3 in placebo (p=0.14)	4 in EMPA-REG (0.1)	Incidence 0.03%
Lower limb amputation	Nearly 2-fold risk compared to placebo * $p < 0.001$	HR 1.00	IRR 1.04 (Scheen)

*CANVAS trial - cohort relatively high risk with individuals having PAD and a history of amputations. Possible increased likelihood of amputations in this cohort.

Foot risk in dapagliflozin/empagliflozin

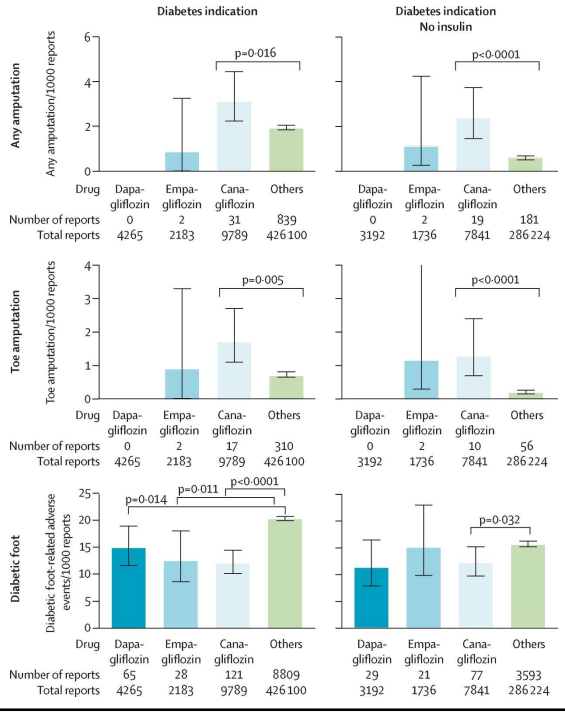
- EMPA-REG trial - event rate of lower limb amputations was equal in the treatment and control group (HR=1.00)
- Meta-analysis of 30 trials - incidence of lower limb amputation with dapagliflozin was 0.1% (0.2% in controls)

Real World Data on foot risk and SGLT2 inhibitor use

- Truven MarketScan database- 119,567 patients with T2DM – decreased incidence rate of below knee leg extremity amputation for SGLT-2 inhibitors compared to other glucose lower agents (1.22/1000 vs 1.87/1000).

SGLT2 inhibitors and amputations in the US FDA Adverse Event Reporting System

- 9,217,555 adverse event reports up to 31/03/2107, 66 were SGLT2 inhibitor-associated amputations.
- (57 [86%] of 66) listed canagliflozin as a suspect or concomitant drug.
- Frequency of amputations with non-SGLT2 inhibitor drugs- 3 times higher



Hypothesis to explain increased amputation risk with canagliflozin

- Roussel et al.- Canagliflozin may cause an increased risk in amputation like diuretics do via hypovolemia.
- Roussel observed doubling of risk for amputation with diuretic use.
- Patients with heart failure have ↑ risk of amputation- not included is a cofounder.
- 12.7% of the diuretic users versus 7.2% of nonusers (P = 0.001).

Discussion

- Osmotic diuresis was observed more often with canagliflozin than placebo (34.5 vs 13.3, $p < 0.001$)
- More severe volume depletion with canagliflozin than empagliflozin (HR 1.44 vs 0.99)
- Canagliflozin has shown increased glucose excretion after 4 hours compared to other SGLT-2 inhibitors.
- Canagliflozin also has more affinity for SGLT-1 than other SGLT-2 inhibitors.
- Is the increased risk of amputation seen in canagliflozin related to its greater hypovolaemic effect compared to other SGLT-2 inhibitors?

Our study

Physician perception and clinical practice regarding use of SGLT2 inhibitors in patients with foot ulcer disease

Methods

- A questionnaire was sent to 70 consultants/SpRs in diabetes and endocrinology with the following questions:
- A) Would you start anyone with a history of but currently inactive foot ulcer disease on dapagliflozin or empagliflozin?
  - a) I would not start at all
  - b) I will start regardless of aetiology of previous ulcer
  - c) I will only start if previous ulcer was purely neuropathic in origin
- B) Would you stop dapagliflozin or empagliflozin in anyone with incident foot ulceration?
- C) If you do stop at incident ulceration, would you re-consider dapagliflozin or empagliflozin, if the ulcer was confirmed to be neuropathic in origin?
- D) If you do not stop at incident ulceration, would you stop dapagliflozin or empagliflozin, if the ulcer was confirmed to be neuro-ischaemic or ischaemic in origin?

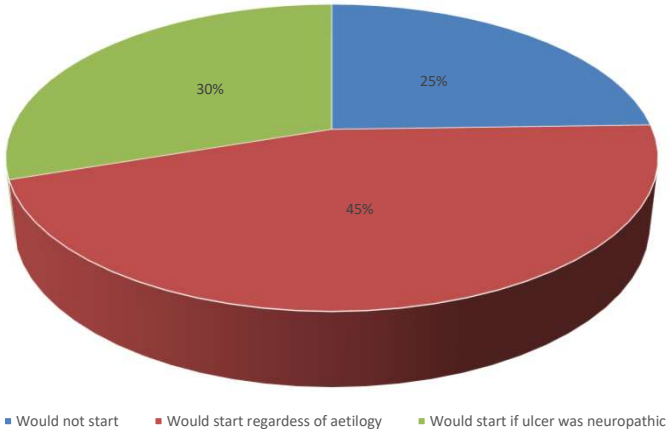
Methods

- Sent to several Diabetes consultants and specialist trainees as individual emails- known contacts, emails obtained through Deanery distribution lists in NW
- 61 responded
- 53 clear “yes/no” answers

Results

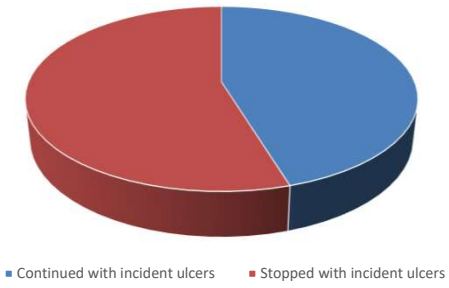
- 25% consultant/SpR would not start dapagliflozin/empagliflozin under any circumstances.
- 45% would consider dapagliflozin/empagliflozin regardless of aetiology of previous foot ulcers.
- 30% would start if ulcers were of neuropathic origin.

Percentage of clinicians who would start empagliflozin or dapagliflozin in patients with a history of foot ulcers



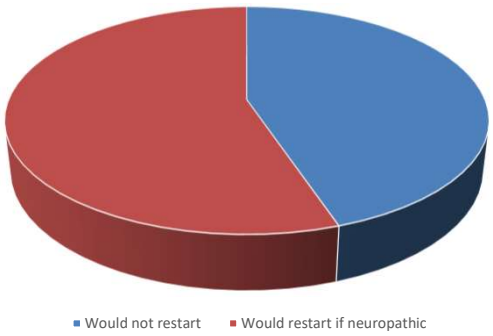
Would you stop dapagliflozin or empagliflozin in anyone with incident foot ulceration?

- 55% would stop with an incident foot ulcer
- 45% would not stop with an incident foot ulcer



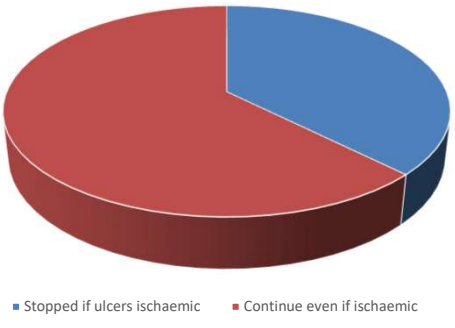
If you do stop at incident ulceration, would you re-consider dapagliflozin or empagliflozin, if the ulcer was confirmed to be neuropathic in origin?

- 55% would restart if ulcer is neuropathic
- 45% would not restart even if ulcer is neuropathic



If you do not stop at incident ulceration, would you stop dapagliflozin or empagliflozin, if the ulcer was confirmed to be neuro-ischaemic or ischaemic in origin?

- 37.5% would stop if ulcers ischaemic
- 62.5% would not stop even if ulcers are ischaemic



Respor	a	b	c	d	e	f
A1	No	NA	NA	Yes	No	NA
A2	No	NA	NA	Yes	No	NA
A3	No	NA	NA	Yes	No	NA
A4	No	NA	NA	Yes	No	NA
A5	No	NA	NA	Yes	No	NA
A6	No	NA	NA	Yes	No	NA
A7	No	NA	NA	Yes	No	NA
A8	No	NA	NA	Yes	No	NA
A9	No	NA	NA	Yes	No	NA
A10	No	NA	NA	Yes	No	NA
A11	No	NA	NA	Yes	No	NA
A12	No	NA	NA	Yes	No	NA
A13	No	NA	NA	Yes	No	NA
A14	Yes	Yes	NA	No	NA	No
A15	Yes	Yes	NA	No	NA	No
A16	Yes	Yes	NA	No	NA	No
A17	Yes	Yes	NA	No	NA	No
A18	Yes	Yes	NA	No	NA	No
A19	Yes	Yes	NA	No	NA	No
A20	Yes	Yes	NA	No	NA	No
A21	Yes	Yes	NA	No	NA	No
A22	Yes	Yes	NA	No	NA	No
A23	Yes	Yes	NA	No	NA	No
A24	Yes	Yes	NA	No	NA	No
A25	Yes	Yes	NA	No	NA	No
A26	Yes	No	NA	No	NA	No
A27	Yes	Yes	NA	No	NA	No
A28	Yes	Yes	NA	No	NA	No
A29	Yes	Yes	NA	No	NA	Yes
A30	Yes	Yes	NA	No	NA	Yes
A31	Yes	Yes	NA	No	NA	Yes
A32	Yes	Yes	NA	No	NA	Yes
A33	Yes	Yes	NA	No	NA	Yes
A34	Yes	Yes	NA	No	NA	Yes
A35	Yes	Yes	NA	No	NA	Yes
A36	Yes	Yes	NA	No	NA	Yes
A37	Yes	Yes	NA	No	NA	Yes
A38	Yes	No	Yes	Yes	Yes	NA
A39	Yes	No	Yes	Yes	Yes	NA
A40	Yes	No	Yes	Yes	Yes	NA
A41	Yes	No	Yes	Yes	Yes	NA
A42	Yes	No	Yes	Yes	Yes	NA
A43	Yes	No	Yes	Yes	Yes	NA
A44	Yes	No	Yes	Yes	Yes	NA
A45	Yes	No	Yes	Yes	Yes	NA
A46	Yes	No	Yes	Yes	Yes	NA
A47	Yes	No	Yes	Yes	Yes	NA
A48	Yes	No	Yes	Yes	Yes	NA
A49	Yes	No	Yes	Yes	Yes	NA
A50	Yes	No	Yes	Yes	Yes	NA
A51	Yes	No	Yes	Yes	Yes	NA
A52	Yes	No	Yes	Yes	Yes	NA
A53	Yes	No	Yes	Yes	Yes	NA

Results

- From the results 4 groups emerge:

Group 1) Those who would not start empagliflozin/dapagliflozin under any circumstances (24.5%)

Group 2) Those who would start in a patient with ulcers of neuropathic origin but would stop if there were incident foot ulcers until confirmed to be neuropathic (30.1%)

Group 3) Those would start empagliflozin/dapagliflozin regardless of aetiology but would stop if the foot ulcer was confirmed to be of ischaemic origin (16.9%)

Group 4) Those who would start empagliflozin/dapagliflozin regardless of foot ulcer aetiology and would not stop it regardless of incident foot ulcer. (28.3%)

Results

	Registrars	Consultants
Group 1	6	7
Group 2	10	6
Group 3	5	4
Group 4	7	8
Total	28	25

Conclusion

- Currently limited evidence of foot risk with empagliflozin and dapagliflozin.
- Unclear if increased foot amputations seen in canagliflozin is a class effect.
- This survey indicates there are a group who do not think that this is class effect

Message

- Are we being too conservative with our use of SGLT-2 inhibitors for the undoubtedly large cardiovascular benefits they confer?

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Mitochondrial diabetes- don't ignore clinical clues!

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DR R RAVINDRAN
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YSBYTY YSTRAD FAWR HOSPITAL, CAERPHILLY
U.K.

ABCD MEETING
09.11.18

Case presentation

- An 18 year old female with increased BMI (30kg/m^2) was referred to Diabetic Clinic following recent DM2 diagnosis
- She had fasting glucose of **7.2**mmol/L and at 2 hours following OGTT-**13.4**mmol/l
- Asymptomatic at presentation (no osmotic symptoms, no weight loss, ketone-free, no tiredness)
- PMHx: fibromyalgia (seen previously by pain team and rheumatology), HTN (on perindopril, no secondary cause identified); headaches (seen by Neurology- normal CT Head, ?myalgic encephalitis)
- Positive family hx: **mother, maternal grandmother and grandfather and maternal great grandmother**

Diagnosis:
?DM1
?DM2
?other

Presentation:

1. Family history of diabetes- maternal side
2. Lack of DM1 symptoms- no osmotic symptoms, no weight loss, not ketotic
3. Phenotype not in keeping with DM2- non-obese; Caucasian

Referred to clinical genetics

NEGATIVE MODY SCREEN: NO HNF OR GLUCOKINASE MUTATIONS

M.3243A>G MUTATION FOUND = MITOCHONDRIAL DIABETES

Test methodology

1. Analysis of all the coding regions and exon/intron boundaries of the monogenic diabetes genes *GCK, HNF1A, HNF4A, HNF1B, NEUROD1, INS, INSR, KCNJ11, ABCC8, PDX1, GATA6, LMNA, PPARG* and the m.3243A>G MIDD mutation by targeted next generation sequencing (Agilent custom capture v5/Illumina HiSeq). This assay can also detect partial/whole gene deletions and duplications (Ellard *et al* 2013 Diabetologia 56, 1958-1963 open access available at http://dx.doi.org/10.1007/s00125-013-2962-5).
2. Confirmation of the mitochondrial DNA mutation A>G at nucleotide 3243 (NC_012920.1: m.3243A>G) by TaqMan genotyping assay.

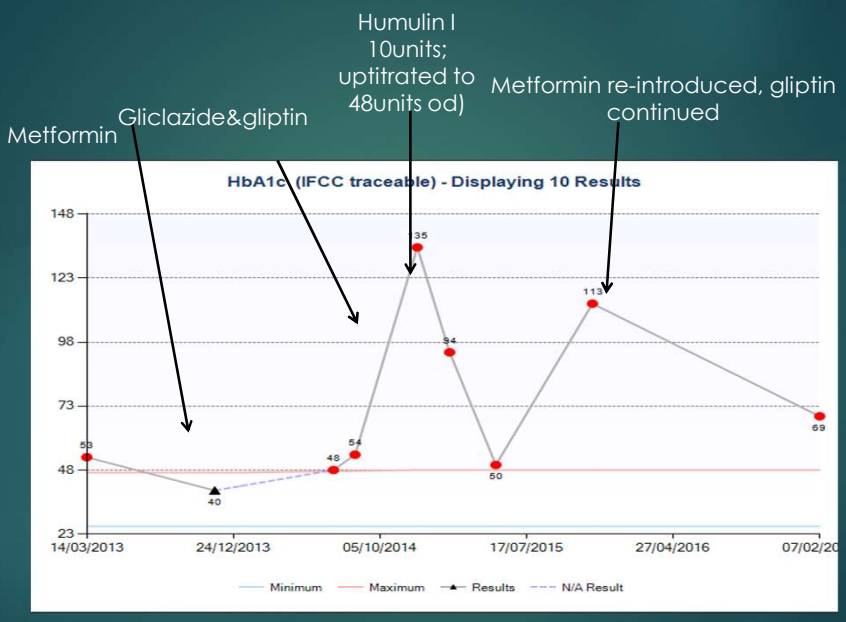
Result:	m.3243A>G mutation detected

Interpretation

The mitochondrial DNA mutation m.3243A>G was detected in [redacted] leukocyte DNA sample. This result confirms that the m.3243A>G mutation is the cause of [redacted] clinical phenotype (diabetes). The m.3243A>G mitochondrial mutation is associated with MIDD (maternally inherited diabetes and deafness) and MELAS (mitochondrial encephalopathy, lactic acidosis and stroke-like episodes). However, it is not possible to predict the likely clinical course associated with this mutation due to the variation in phenotype which may depend in part on the level of heteroplasmy in specific target tissues (Nesbitt *et al* 2013 J Neurol Neurosurg Psychiatry 84, 936-938). Testing is now possible for [redacted] maternal relatives (by referral to the local Clinical Genetics service). Since this mutation is transmitted though the maternal line, [redacted] offspring are likely to inherit this mutation.

Management

- Initially: metformin 500mg bd (HbA1c improved from 63 to 48mmol/mol)
- Metformin stopped once mitochondrial diabetes diagnosis made due to risk of lactic acidosis
- Sitagliptin & gliclazide introduced
- Insulin- Humulin I
- Metformin re-introduced



Follow up

FAMILY SCREENING BEING UNDERTAKEN

CARDIOLOGY REFERRAL- NORMAL ECG AND ECHO

Mitochondrial diabetes

- Incidence of ~1%
- Maternally inherited due to mutations in mitochondrial DNA (mtDNA)
- Average age at presentation 38years (11-68)
- Leads to gradual beta cell failure and progressive impaired insulin secretion due to defects in ATP synthesis
- 75% of patients have bilateral hearing impairment (reduced perception of high frequency noises; usually present before diabetes is clinically overt)
- Associated with: myopathies and MELAS or MERF, Kearns-Sayre syndrome, Pearson syndrome

Initial diagnostic tools/clues for mitochondriopathy in patients with diabetes

Lactate levels	Elevated in blood fasting and after exercise; elevated in CSF; elevated lactae/pyruvate ratio
Muscle status	Proximal muscle weakness; elevated CK
Neurologic exam	Ataxia, dystonia
Neuroimaging	T2-hyperintense lesions in cortex and basal ganglia; strokes in MELAS
Endocrinological disorders	GH deficiency, hypogonadism, hyperparathyroidism
Opthalmoscopy	Macular dystrophy, pigmented retinal lesions, optic atrophy, external opthalmoplegia
Audiometry	Bilateral sensorineural hearing loss
ECG, ECHO	Cardiomyopathy, cardiac arrythmia, conduction blocks
Renal	Proteinuria (F>M); most commonly: focal segmental glomerulosclerosis, can lead to ESRF;
EEG	Slow activity, slow waves, seizures
Others	Short stature

mtDNA A3243G mutation

- Penetrance almost 100% (in a Dutch series nearly all carriers developed IGT or DM before the age of 70)
- The A3243G mutation is present in heteroplastic form (mixture of wild type mtDNA and mtDNA carrying the mutation)
- High heteroplasmy levels predispose to an earlier onset of diabetes
- Heteroplasmy levels may be low in leukocytes and decline upon aging (~0.7%per year)
- Urine epithelial cells and mouth mucosa cells are tissue of choice for detection (average 1.7 higher heteroplasmy values)
- Heteroplasmy levels tend to be high in tissues with low mitogenic activity

How to test- Exeter Clinical Laboratory

- Urine epithelial cells contain the highest levels of m.3243A>G mutation –preferred sample to test
- 20mLs of early morning urine into sterile universal container; needs to be sent on the day of collection
- Blood: at least 10-20mls samples in EDTA tubes transported at ambient temperature- samples can be stored at 4°C but not to be frozen; need to arrive within 5 days of venesection
- DNA: minimum 5 micrograms (sent at room temperature)
- Saliva: Oragene sample collection kit
- Cost: £75.00

Pathophysiological mechanisms leading to diabetes:

- Altered glucose metabolism of muscle
- Deregulated hepatic glucose production (as mitochondrial dysfunction in the muscle leads to higher lactate flux to the liver, fueling gluconeogenesis)
- Impaired pancreatic insulin secretion in response to glucose stimulation
- High heteroplasmy levels lead to attenuated oxygen consumption and functional impairment of respiratory chain
- The disturbed ATP/ADP ratio affects K-ATP channels involved in insulin secretion
- Other signalling molecules also likely affected: Ca, glutamate, cytochrome C, lactate, radicals
- Progressive loss of beta cells with age enhanced by increased ROS production
- Deregulation of the complex interaction between mitochondrial function and nuclear gene expression

Prognosis

- Most patients require insulin therapy within few years of diagnosis due to progressive beta cells dysfunction
- Nephropathy/proteinuria may develop early- U&E to be done annually; early introduction of ACE-I advised
- ??Macular pattern dystrophy protects against diabetic retinopathy through reduction in retinal metabolism and decrease in oxygen consumption
- ? Differences between Western and Asian populations in mtDNA haplogroups result in different presentations
- Genetic counselling and family case detection should be undertaken
- ?CoenzymeQ supplementation can be beneficial to slow down beta cell failure progression- data inconclusive

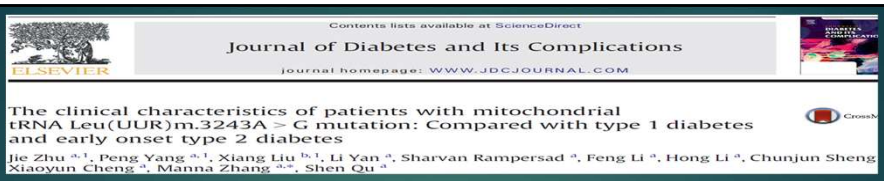
Eur J Pediatr (2016) 175:613–622
DOI 10.1007/s00431-015-2675-5

ORIGINAL ARTICLE

Low prevalence of patients with mitochondrial disease in the German/Austrian DPV diabetes registry

Christina Reinauer[1] · Thomas Meissner[1,2] · Michael Roden[2,3,4] · Angelika Thon[5] · Paul-Martin Holterhus[6] · Holger Haberland[7] · Elisabeth Binder[8] · Wolfgang Marg[9] · Esther Bollow[10] · Reinhard Holl[10]

- Only 13 patients (0.02%) were identified with mitochondrial diabetes (KSS-5, Pearson-3, MELAS 2)
- Age of onset 14.2 (IQR 7.1-16 years)- later than DM1 but earlier than DM2
- Mild elevation of glucose concentration at presentation without ketoacidosis
- Lower BMI (-1.39(0.28)kg/m2) compared to peers with DM1 or DM2
- Higher triglycerides than in DM1 and high rate of dyslipidaemia (86%)
- All patients treated with insulin: insulin requirements (0.58, IQR 0.39-0.9 U/kg/d) – between requirements of DM1 and DM2 peers; stable over the 5 year follow up period
- HbA1c (7.4(0.52))%- comparable to age-matched DM2 peers and stable over 5 year follow up


Contents lists available at ScienceDirect
Journal of Diabetes and Its Complications
journal homepage: WWW.JDCJOURNAL.COM

The clinical characteristics of patients with mitochondrial tRNA Leu(UUR)m.3243A > G mutation: Compared with type 1 diabetes and early onset type 2 diabetes

Jie Zhu [a,1], Peng Yang [a,1], Xiang Liu [b,1], Li Yan [a], Sharvan Rampersad [a], Feng Li [a], Hong Li [a], Chunjun Sheng [a], Xiaoyun Cheng [a], Manna Zhang [a,*], Shen Qu [a,*]

- 9 patients identified from 5 unrelated families
- Age of onset 31.2 (7.2) years
- 2 patients required insulin at presentation; 6 progressed to insulin requirement after mean of 7.2 years
- Beta cell function (assessed by fasting and postprandial C-peptide) was intermediate between levels found in DM1 and early onset DM2 patients
- 4/9 had retinopathy and 5/9 nephropathy
- 6 patients had hx of ketoacidosis and 3 presented with acute pancreatitis at the time of DKA
- 8 patients were diagnosed with mitochondrial diabetes after they had been initially diagnosed with DM2 for 11 years on average (3-18 years)
- 7 patients had abnormal ECG: ventricular pre-excitation, pulmonary P wave, ST depression, T wave inversion)

Clinical clues- in retrospect

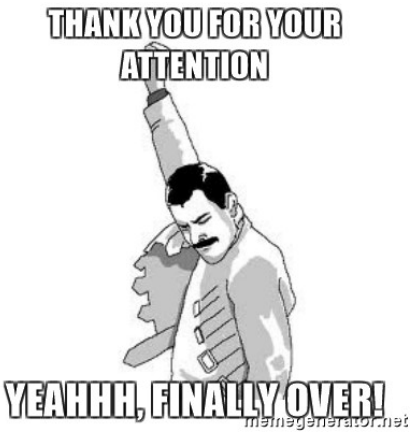
Strong family (maternal history)

Symptoms of myopathy rather than presumed fibromyalgia

Relatively early onset for DM2 without significant BMI elevation; no phenotypical or clinical features of DM1

Learning points

- An atypical diabetes presentation coupled with strong family history should alert the physicians re the possibility of mitochondrial mutation
- Only women transmit the disease to their offspring
- Early introduction of insulin therapy is usually required
- Genetic counselling and family case detection should be undertaken



Any questions?

References

- Maasen JA et al. Mitochondrial Diabetes. Molecular mechanisms and clinical presentation. Diabetes, vol 53, supplemet 1, Feb 2004
- Zhu J e al. The clinical charecteristics ofnpatients with mitochondrial tRNA Leu(UUR)m.3243A.G mutation: Compared with type 1 diabetes and early onset type 2 diabetes. Journal of Diabetes and Its Complications 31(2017) 1354-1359
- Reinauer C. Low prevalence of patients with mitochondrial disease in the German/Austrian DPV registry. Eur J Pediatr (2016) 175:613-622

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Leading the way in Children's Health

National Children and Young People's Diabetes Quality Programme

Children and Young People's National Diabetes Network

The Paediatric Diabetes QI Collaborative: A National Pilot of 10 Paediatric Diabetes Units in England

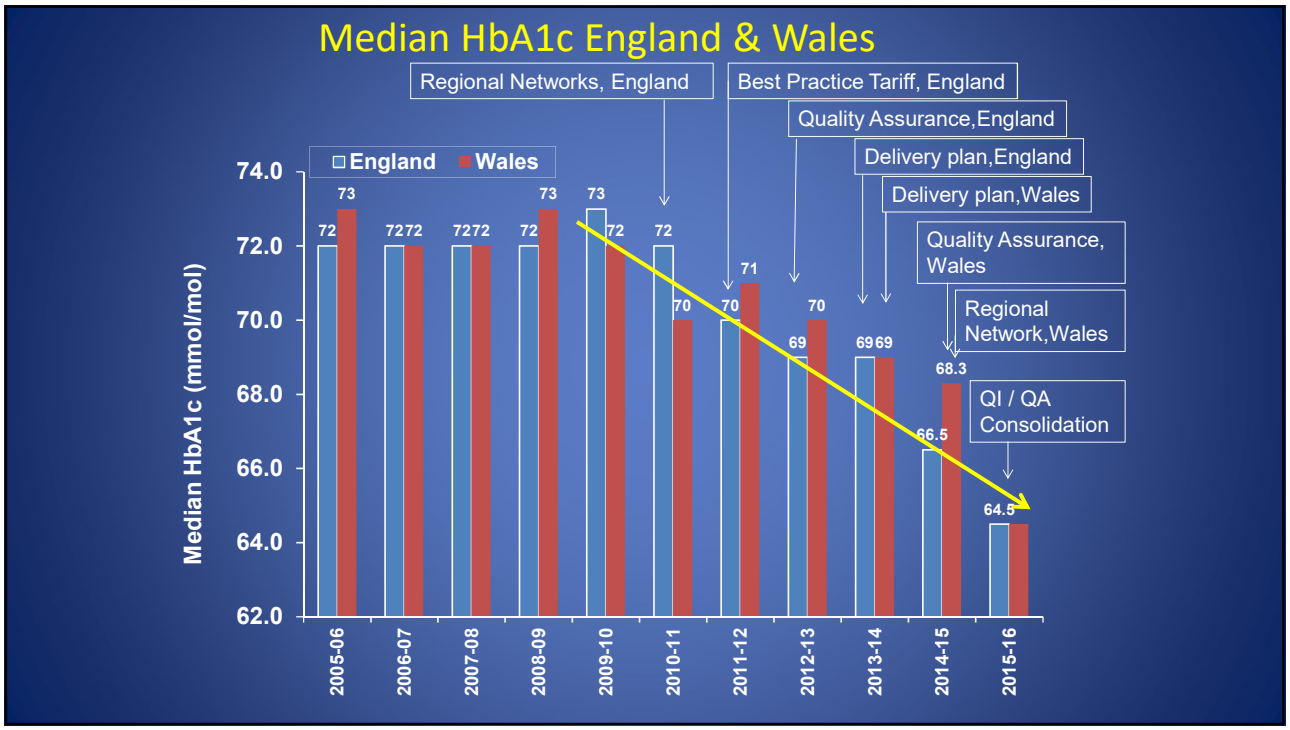
National CYP Diabetes Quality Programme

ABCD Autumn Meeting November 9th 2018

Dr Megan Peng

Objectives

- Timeline of Quality Improvement initiatives so far
- Overview of Swedish QI Collaborative (QIC) initiative
- Overview of the UK pilot QIC initiative 2017-2018
- Snapshot of the achievements of the 10 pilot QIC teams
- Outcomes and Feedback from 10 pilot QIC teams
- Post-pilot QIC plans beyond 2018


Median HbA1c England & Wales
Regional Networks, England
Best Practice Tariff, England
Quality Assurance,England
Delivery plan,England
Delivery plan,Wales
Quality Assurance, Wales
Regional Network,Wales
QI / QA Consolidation
England
Wales
Median HbA1c (mmol/mol)
74.0
72.0
70.0
68.0
66.0
64.0
62.0
2005-06
2006-07
2007-08
2008-09
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2010-11
2011-12
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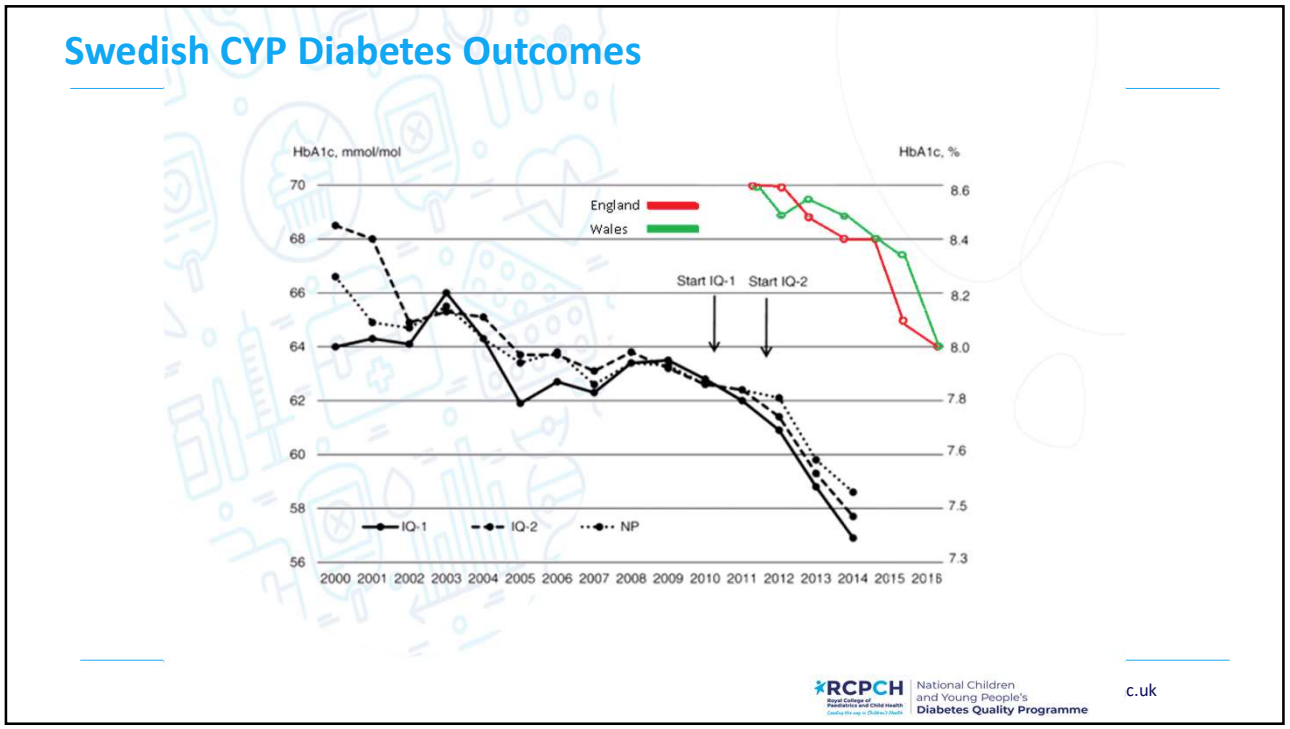
2013-14
2014-15
2015-16


Swedish CYP Diabetes Outcomes
HbA1c, mmol/mol
HbA1c, %
England
Wales
Start IQ-1
Start IQ-2
IQ-1
IQ-2
NP
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
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National Children and Young People's Diabetes Quality Programme
c.uk

What Worked in Sweden?

- Clear and consistent messages from every member of the Multi Disciplinary Team
- Every staff member felt involved and valued
- Positive 'can-do' attitude from the team
- Perception of a well-functioning team
- Reduced targets for HbA1c
- Robust national audit and identifiable unit comparisons
- Supportive regional networks prepared to share good practice with a view to improving outcomes and reducing regional variation

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First Steps – Phase 1 Pilot Outline

16 teams applied
10 units selected (100 healthcare professionals)

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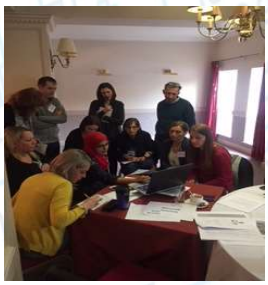
Training Event 1: November 2017

- Microsystems at work and improving outcomes in complex systems
- A focus on team dynamics – the values and behaviours of high performing teams
- Improvement methods in healthcare
- Process mapping and fishbone analysis
- The PDSA cycle



Training Event 2: February 2018

- Team sharing – The World Café
- Human Factors in clinical practice
- The 'Six Thinking Hats' principle
- Time ordered data and outcome measures




Training Event 3: April 2018

- Shared the Swedish experience with Dr Lena Hanberger, Linkoping University
- Team presentations about their QI journey
- 'Making improvement our core business'
- 'How to sustain and spread improvement'

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Training Event 4: July 2018

- Team feed back on progress and achievements using poster presentations
- How to disseminate learning and share within regional networks and beyond
- Learning about the habits of a continuous improver
- The engagement of children and young people with the RCPCH &Us Team

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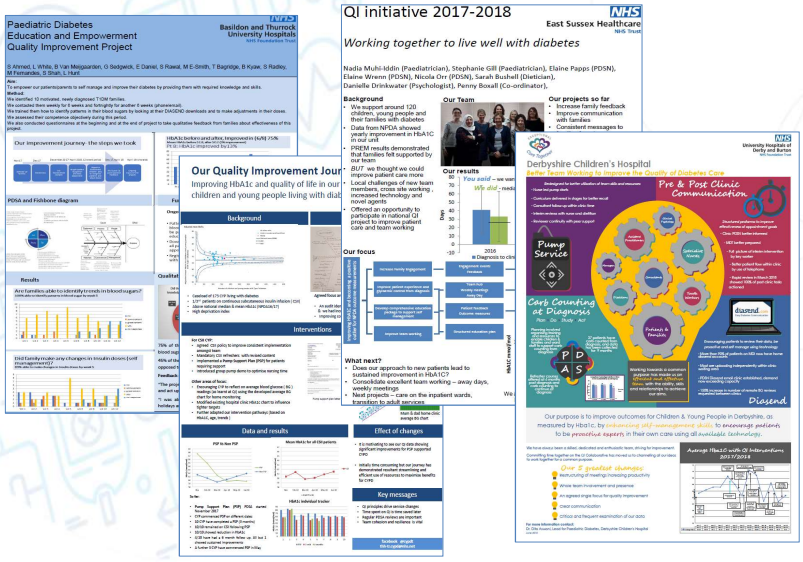
Team Posters



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What Were Pilot Teams Working On?

Basildon – Clear targets for self-management, Diasend introduction from diagnosis.

Bolton – Carb counting at diagnosis, shared purpose, pre and post clinic MDT huddle.

East Sussex – Structured education package, maintaining reduced HbA1c at 6 and 12 months post-diagnosis, increased family engagement events.

West Sussex – Improved MDT working by video linked meetings, high HbA1c policy, introduction of 'Diasend Master Classes'.

Derby – Improved use of Diasend, a nurse-led pump process, remote Diasend email clinic, new MDT structure.

Gloucester - Reinventing the clinic experience.

QI Team Focus and Initiatives

Bedford – 'Self-Management', increased clinic appointments to 40 minutes, topics choice for consultation, Novo Goals for all contacts.

Hillingdon – Reducing pump patients HbA1c by 10mmols using pump refreshers/ contracts/policy. Use of an HbA1c map.

Sheffield – Officer of Fun in MDT, innovative newly-diagnosed pathway, trust management awareness.

South Tees – A patient education booklet and newly diagnosed quiz to assess knowledge prior to discharge, encouraging patients to download own meters in clinic, 'Takeover Saturday' CYP engagement event with families.

Intervention Example – Outpatient Clinic

To empower our children and young people to become confident and competent adults, with good mental and physical health, through improved clinic experience

Clinic Experience

- Clinic Goals Sheet
- Diasend in Clinic
- Clinic Timings
- Clinic Layout

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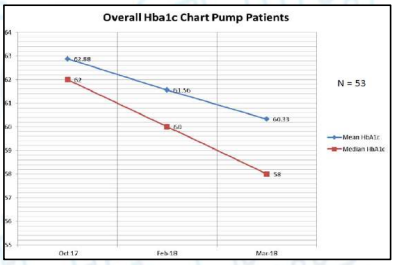
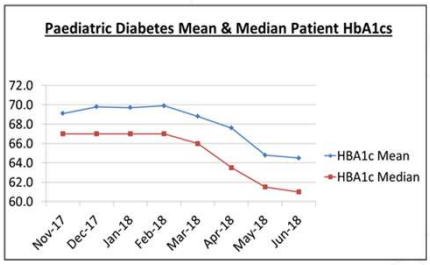
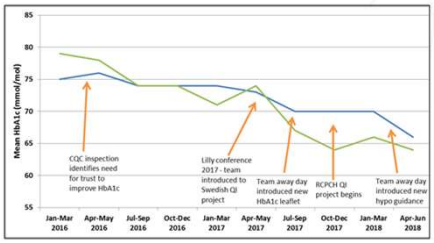
Team Outcome Measures





HbA1c in mmol/mol	3 months after diagnosis	6 months after diagnosis
Pre QI		
Mean	53.3	55
Median	49	51
Post QI		
Mean	47.6	47.8
Median	46	45



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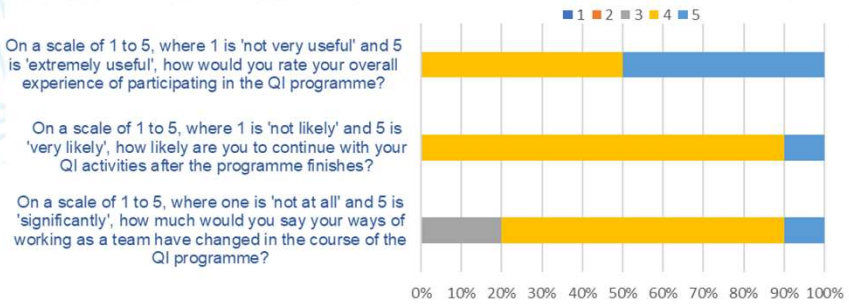
Team Feedback

"We were able to understand the basic problems when we did the mapping exercise. We are more focused, learned a common skill set, increased team motivation, improved team cohesion and now have a common language and goals."

"We have a stronger focus now and clearer shared goals. We are giving more consistent advice to patients and families. By doing the QI we have spent more time analysing our HbA1c and tracking our progress in a more formal way, which has provided motivation and direction."



Quality Improvement Collaborative

2018 - 2021

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Post-pilot plans - Overview

- **All units enrolled in the National CYPD Quality Programme are entitled to apply for a place in the QI Collaborative**
- **Application process**: statement of purpose, declaration of commitment from all of the team and support from their Trust Medical Director to take part
- **Two options for participation**: national and regional

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QI Collaborative – Waves 2 and 3

- **Modelled on the pilot QIC** (110 healthcare professionals) **with the same master trainer** who developed and delivered the pilot with support from RCPCH QI staff
- **2 National Waves** starting in October 2018 involving 14 new teams (180 healthcare professionals) across all 11 CYP Diabetes Regional Networks in England & Wales
- **1 residential weekend, 3 one-day events**

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Regional QI Collaboratives – Waves 4 to 12

- **2019 – 2021 up to 10 waves** starting in March 2019
- **3 waves per year of 4 one-day events**
- **Expert trainer** delivering the core content with support from the RCPCH QI staff
- **Regional cohorts from diabetes networks:**
  - South West and Wessex
  - East of England and Thames Valley
  - London and South East
  - North East and Cumbria, North West
  - Yorkshire and Humber
  - East and West Midlands
  - Wales

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THANK YOU

Dr Fiona Campbell
Dr Tricia Woodhead
Dr Justin Warner
Dr Neil Hopper
Dr Lena Hanberger
Kasia Muszynska
Sue Eardley

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QUESTIONS?

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What is the NCYPD Quality Programme?

The last piece in the jigsaw to drive and monitor improvement in paediatric diabetes outcomes

A three-year integrated programme transforming teams to improve outcomes and deliver best practice care efficiently

National Programme benefits, supported by clinical teams, managed centrally with proven methods

Peer Review
- three year cycle

External Verification
- annually

Self Assessment
- annually

Quality Improvement Collaborative

ABCD audits update

Dr Bob Ryder

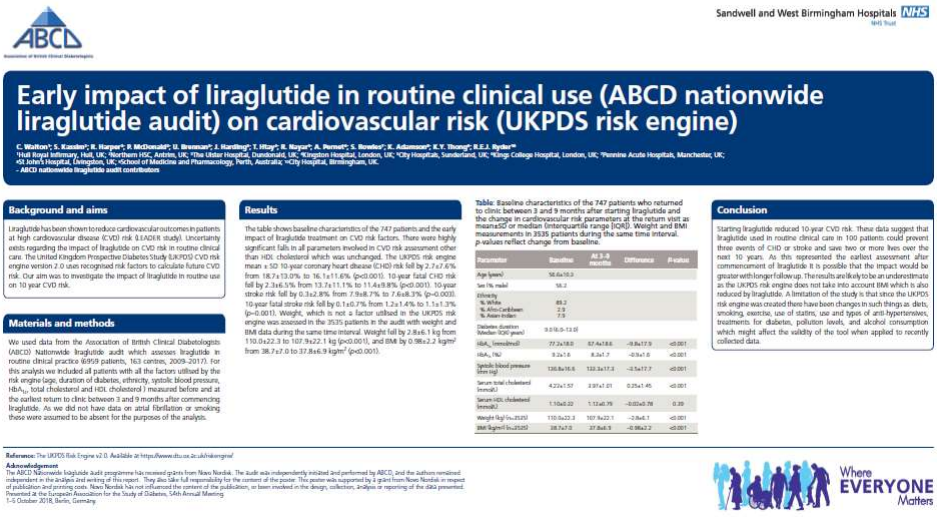
ABCD Autumn Meeting, London

November 9, 2018

ABCD Spring Meeting Presentation

- 52 slides packed into 15 minutes attempting to cover all our audits since 2009, what we did and what we found, and where we are going now
- Please see that presentation for all that
- This presentation:
  - What has happened since May 2018
  - Where are we now and what is important now

Poster from the liraglutide audit presented at EASD



Sandwell and West Birmingham Hospitals NHS

Early impact of liraglutide in routine clinical use (ABCD nationwide liraglutide audit) on cardiovascular risk (UKPDS risk engine)

C. Walton[1], S. Kassler[2], R. Harper[3], R McDonald[4], U. Brennan[5], J. Harding[6], T. Hlleg[7], R. Nayar[8], A. Pernet[9], S. Bowden[10], K. Adamson[11], K.Y. Thong[12], R.E.J. Ryder[13]
[1]Hull Royal Infirmary, Hull, UK; [2]Northern HSC, Antrim, UK; [3]The Ulster Hospital, Dundonald, UK; [4]Kingston Hospital, London, UK; [5]City Hospitals, Sunderland, UK; [6]Kings College Hospital, London, UK; [7]Pennine Acute Hospitals, Manchester, UK; [8]St John's Hospital, Livingston, UK; [9]School of Medicine and Pharmacology, Perth, Australia; [10]City Hospital, Birmingham, UK.
- ABCD nationwide liraglutide audit contributors

Background and aims

Liraglutide has been shown to reduce cardiovascular outcomes in patients at high cardiovascular disease (CVD) risk (LEADER study). Uncertainty exists regarding the impact of liraglutide on CVD risk in routine clinical care. The United Kingdom Prospective Diabetes Study (UKPDS) CVD risk engine version 2.0 uses recognised risk factors to calculate future CVD risk. Our aim was to investigate the impact of liraglutide in routine use on 10 year CVD risk.

Materials and methods

We used data from the Association of British Clinical Diabetologists (ABCD) Nationwide liraglutide audit which assesses liraglutide in routine clinical practice (6959 patients, 163 centres, 2009–2017). For this analysis we included all patients with all the factors utilised by the risk engine (age, duration of diabetes, ethnicity, systolic blood pressure, HbA_{1c}, total cholesterol and HDL cholesterol) measured before and at the earliest return to clinic between 3 and 9 months after commencing liraglutide. As we did not have data on atrial fibrillation or smoking these were assumed to be absent for the purposes of the analysis.

Results

The table shows baseline characteristics of the 747 patients and the early impact of liraglutide treatment on CVD risk factors. There were highly significant falls in all parameters involved in CVD risk assessment other than HDL cholesterol which was unchanged. The UKPDS risk engine mean ± SD 10-year coronary heart disease (CHD) risk fell by 2.7±7.6% from 18.7±13.0% to 16.1±11.6%, (p<0.001). 10-year fatal CHD risk fell by 2.3±6.5% from 13.7±11.1% to 11.4±9.8%, (p<0.001). 10-year stroke risk fell by 0.3±2.8% from 7.9±8.7% to 7.6±8.3%, (p=0.0033). 10-year fatal stroke risk fell by 0.1±0.7% from 1.2±1.4% to 1.1±1.3% (p=0.001). Weight, which is not a factor utilised in the UKPDS risk engine was assessed in the 3535 patients in the audit with weight and BMI data during the same time interval. Weight fell by 2.8±6.1 kg from 110.0±22.3 to 107.9±22.1 kg (p<0.001), and BMI by 0.98±2.2 kg/m² from 38.7±7.0 to 37.8±6.9 kg/m² (p<0.001).

Table: Baseline characteristics of the 747 patients who returned to clinic between 3 and 9 months after starting liraglutide and the change in cardiovascular risk parameters at the return visit as means±SD or median (interquartile range [IQR]). Weight and BMI measurements in 3535 patients during the same time interval. *p*-values reflect change from baseline.

Parameter	Baseline	At 3–9 months	Difference	*P*-value
Age (years)	58.6±10.3			
Sex (% male)	58.2			
Ethnicity % White % Afro-Caribbean % Asian-Indian	85.2 2.9 7.9			
Diabetes duration (median [IQR] years)	9.0 [6.0–13.0]			
HbA_{1c} (mmol/mol)	77.2±18.0	67.4±18.6	-9.8±17.9	<0.001
HbA_{1c} (%)	9.2±1.6	8.2±1.7	-0.9±1.6	<0.001
Systolic blood pressure (mm Hg)	136.8±16.6	133.3±17.3	-3.5±17.7	<0.001
Serum total cholesterol (mmol/L)	4.22±1.57	3.97±1.01	0.25±1.45	<0.001
Serum HDL cholesterol (mmol/L)	1.10±0.22	1.12±0.76	-0.02±0.78	0.39
Weight (kg) (n=2125)	110.0±22.3	107.9±22.1	-2.8±6.1	<0.001
BMI (kg/m²) (n=2125)	38.7±7.0	37.8±6.9	-0.98±2.2	<0.001

Conclusion

Starting liraglutide reduced 10-year CVD risk. These data suggest that liraglutide used in routine clinical care in 100 patients could prevent three events of CHD or stroke and save two or more lives over the next 10 years. As this represented the earliest assessment after commencement of liraglutide it is possible that the impact would be greater with longer follow up. The results are likely to be an underestimate as the UKPDS risk engine does not take into account BMI which is also reduced by liraglutide. A limitation of the study is that since the UKPDS risk engine was created there have been changes in such things as diets, smoking, exercise, use of statins, use and types of anti-hypertensives, treatments for diabetes, pollution levels, and alcohol consumption which might affect the validity of the tool when applied to recently collected data.

Reference: The UKPDS Risk Engine v2.0. Available at https://www.dtu.ox.ac.uk/riskengine/

Acknowledgement
The ABCD Nationwide liraglutide audit programme has received grants from Novo Nordisk. The audit was independently initiated and performed by ABCD, and the authors maintained independent in the analysis and writing of this report. They also take full responsibility for the content of the poster. This poster was supported by a grant from Novo Nordisk in respect of publication and printing costs. Novo Nordisk has not influenced the content of the publication, or been involved in the design, collection, analysis or reporting of the data presented.
Presented at the European Association for the Study of Diabetes, 54th Annual Meeting
1-5 October 2018, Berlin, Germany

Where EVERYONE Matters

Walton C. et al; Diabetologia (suppl); 2018

Poster from the liraglutide audit presented at EASD

Conclusion

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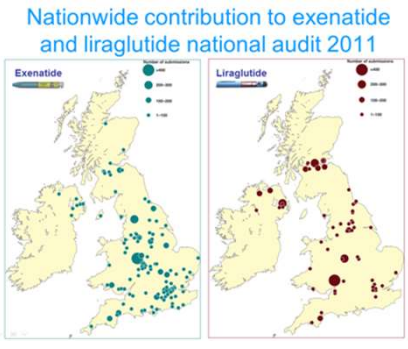
Walton C. et al; Diabetologia (suppl); 2018

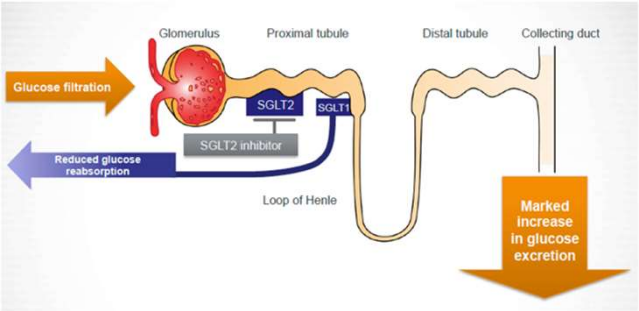
ABCD nationwide exenatide and liraglutide audits



- Real-life data
  - >13000 patients from
  - >150 centres
  - >500 contributors
- There had been (by 2018)
  - 12 published papers
  - 24 abstracts
  - 13 oral presentations

http://www.diabetologists-abcd.org.uk/GLP1_Audits/PresentationsPostersAbstractsExenatide.htm
http://www.diabetologists-abcd.org.uk/GLP1_Audits/PresentationsPostersAbstractsLiraglutide.htm

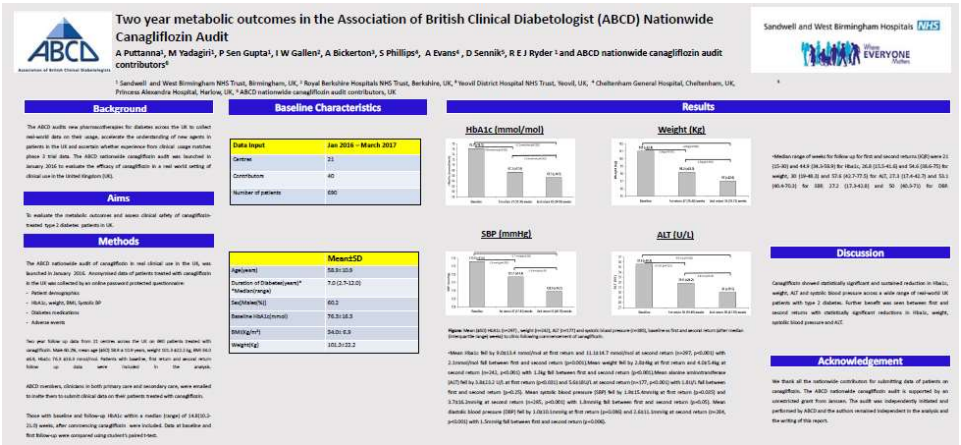
SGLT2 inhibitors – audit update



- Canagliflozin
- Dapagliflozin
- Empagliflozin

Bailey CJ (2011) *Trends Pharmacol Sci* **32**: 63–71

Poster from the canagliflozin audit presented at EASD



Two year metabolic outcomes in the Association of British Clinical Diabetologist (ABCD) Nationwide Canagliflozin Audit

A Puttanna[1], M Yadagiri[1], P Sen Gupta[1], I W Gallen[2], A Bickerton[3], S Phillips[4], A Evans[4], D Sennik[5], R E J Ryder[1] and ABCD nationwide canagliflozin audit contributors[6]

[1] Sandwell and West Birmingham NHS Trust, Birmingham, UK, [2] Royal Berkshire Hospitals NHS Trust, Berkshire, UK, [3] Yeovil District Hospital NHS Trust, Yeovil, UK, [4] Cheltenham General Hospital, Cheltenham, UK, Princess Alexandra Hospital, Harlow, UK, [5] ABCD nationwide canagliflozin audit contributors, UK

Sandwell and West Birmingham Hospitals NHS

Background

Aims

Methods

Baseline Characteristics

Data Input	Jan 2016 – March 2017
Centres	20
Contributors	40
Number of patients	690

	Mean±SD
Age(years)	58.8±10.9
Duration of Diabetes(years)* *Median(range)	7.0 (2.5-12.0)
Sex(Males)(%)	60.2
Baseline HbA1c(mmol)	76.3±18.3
BMI(Kg/m²)	34.0±6.9
Weight(kg)	101.3±22.2

Results

HbA1c (mmol/mol)

Weight (Kg)

SBP (mmHg)

ALT (U/L)

Discussion

Acknowledgement

We thank all the nationwide contributors for submitting data of patients on canagliflozin. The ABCD nationwide canagliflozin audit is supported by an unrestricted grant from Janssen. The audit was independently initiated and performed by ABCD and the authors remained independent to the analysis and the writing of this report.

Puttanna A. et al; Diabetologia (suppl); 2018

Canagliflozin audit – further improvement between first and second return

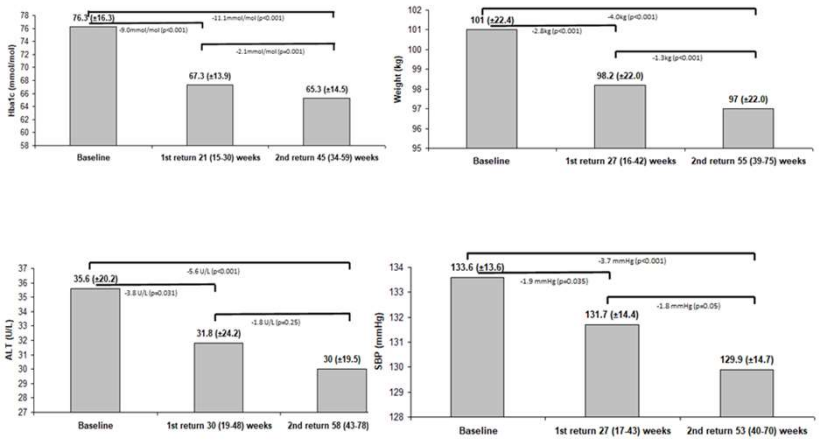


Figure: Mean (±SD) HbA1c (n=297) , weight (n=242), ALT (n=177) and systolic blood pressure (n=285), baseline vs first and second return (after median (interquartile range) weeks) to clinic following commencement of canagliflozin.

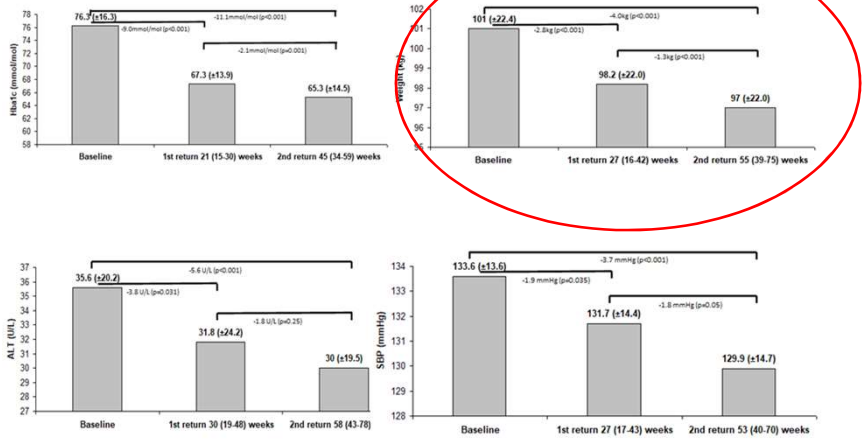
Puttanna A. et al; Diabetologia (suppl); 2018

Canagliflozin audit – further improvement between first and second return

Figure: Mean (±SD) HbA1c (n=297) , weight (n=242), ALT (n=177) and systolic blood pressure (n=285), baseline vs first and second return (after median (interquartile range) weeks) to clinic following commencement of canagliflozin.

Puttanna A. et al; Diabetologia (suppl); 2018

Canagliflozin audit – further improvement between first and second return



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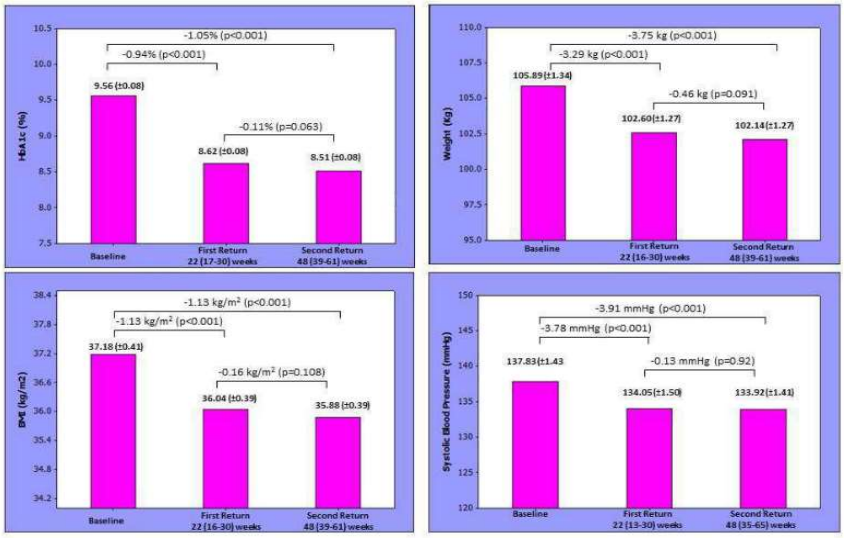
Puttanna A. et al; Diabetologia (suppl); 2018

Dapagliflozin – improvements sustained



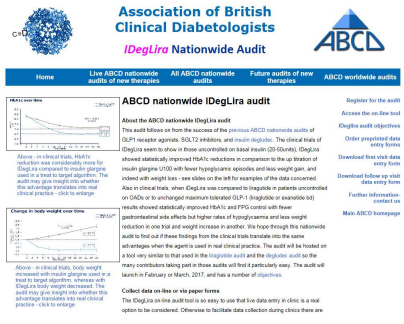
Data presented at ADA meeting, New Orleans, June 2016

ABCD nationwide degludec audit

- Definitive paper now being written
- All contributors will be acknowledged

http://www.diabetologists-abcd.org.uk/Degludec/Degludec_Audit.htm

ABCD nationwide IDegLira audit



- First abstract planned for ADA 2019 – please submit your data

http://www.diabetologists-abcd.org.uk/IDegLira/IDegLira_Audit.htm

Future audits – watch this space …

- ABCD nationwide testosterone in diabetes audit coming in 2019 …..

Two big audits of the moment

ABCD Nationwide FreeStyle Libre Audit

Now fully live and collecting data

ABCD Nationwide FreeStyle Libre Audit

- Abstract submitted to DUK – very small numbers but FSL associated with a significant fall in HbA1c
- Now looking for big numbers and first proper analysis for ADA 2019
  - abstract deadline 7 January 2019

ABCD Nationwide FreeStyle Libre Audit

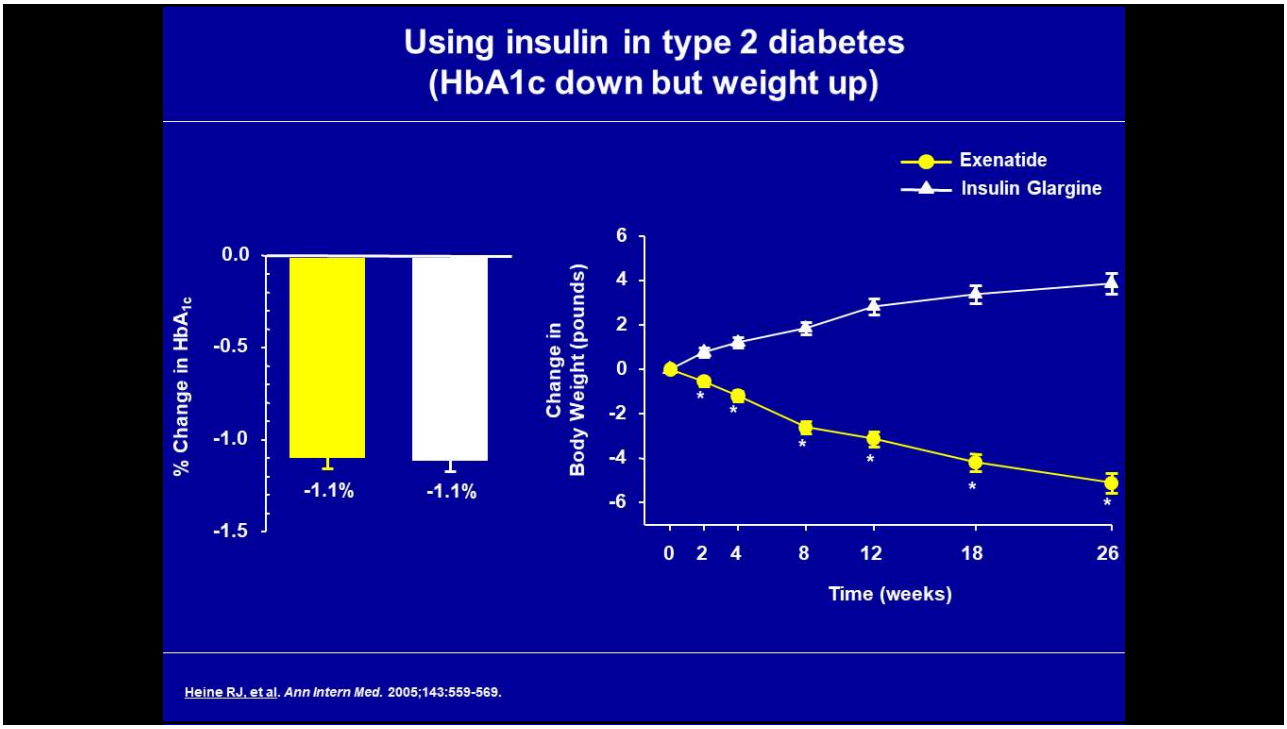
- Audit overview 7 November 2018
  - Total Centres: 85
  - Total Sites: 104
  - Total Users: 146
  - Total Patients: 706
- 706 patients are from 28 centres – only 15 of these 10 or more patients
- 57 centres still to enter any data

ABCD Nationwide FreeStyle Libre Audit

- Countdown to deadline of 15 December 2018 for you to be part of the ADA submission
- Please submit ALL your FSL data before that date
- Countdown emails will be sent weekly as a nudge …..

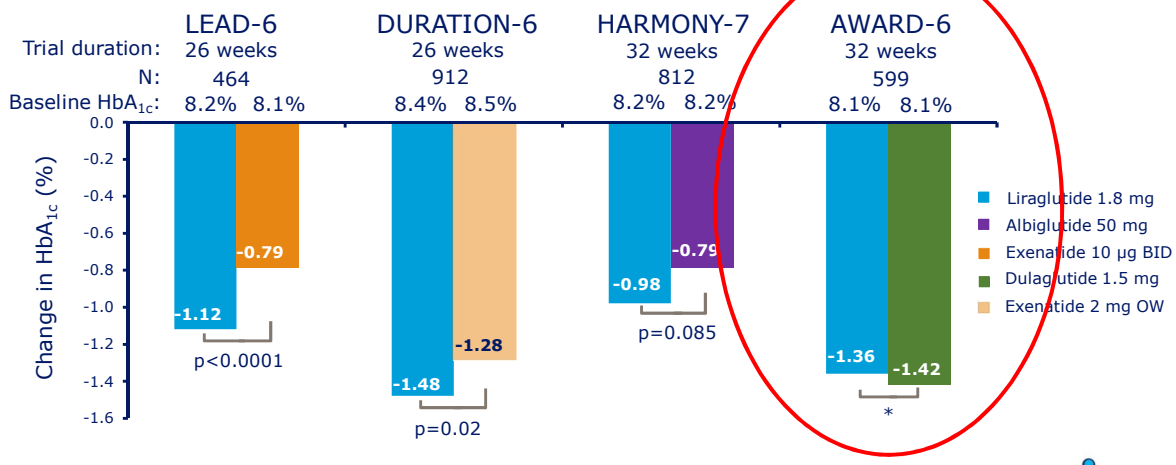
ABCD Nationwide Semaglutide Audit

- Tool being created ready to be ready for use as semaglutide becomes available to prescribe in January 2019
- Why is this a big deal?



UK/VT/0818/0371 Date of Preparation: Sep 2018

Liraglutide: HbA_{1c} reductions vs comparators



*Treatment difference (nominal 95% CI)=-0.06 (-0.19, 0.07), p<0.0001 for non inferiority vs. liraglutide.
Direct comparisons between trials cannot be made due to different trial designs.
BID, twice a day; CI, confidence interval; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycosylated haemoglobin; OW, once weekly.
Buse et al. *Lancet* 2009;374:39–47 (LEAD-6); Buse et al. *Lancet* 2013;381:117–124 (DURATION-6); Pratley et al. *Lancet Diabetes Endocrinol* 2014; 2:289–297 (Harmony-7); Dungan et al. *Lancet* 2014;384(9951):1349–1357 (AWARD-6).

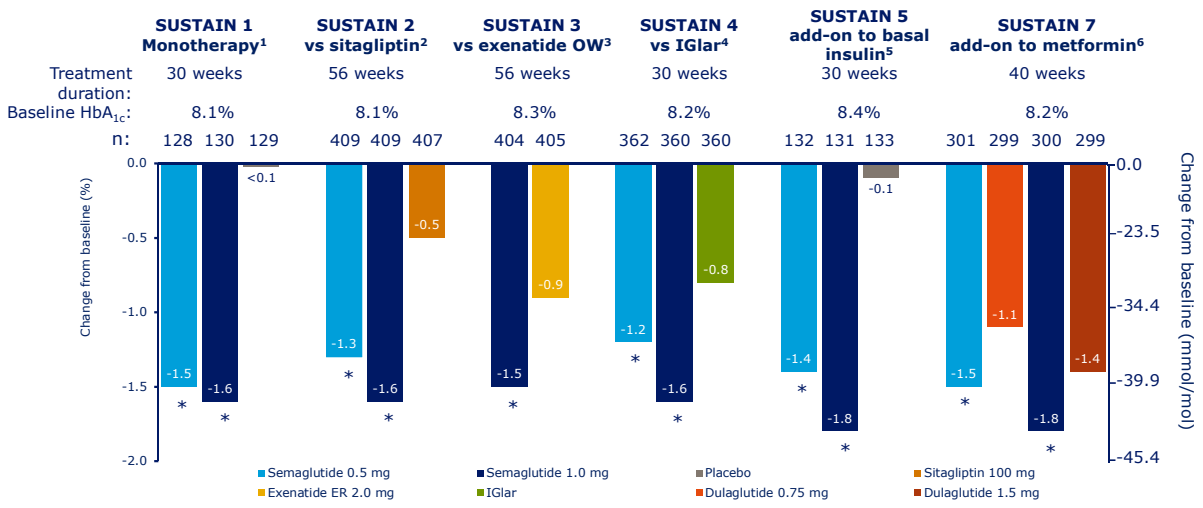
novo nordisk®

Date of preparation: September 2018 Job bag: UK/SM/0218/0069(1)

This slide discusses studies with different designs and comparators; no direct comparisons of data can be made between studies

Consistent efficacy results across SUSTAIN trials

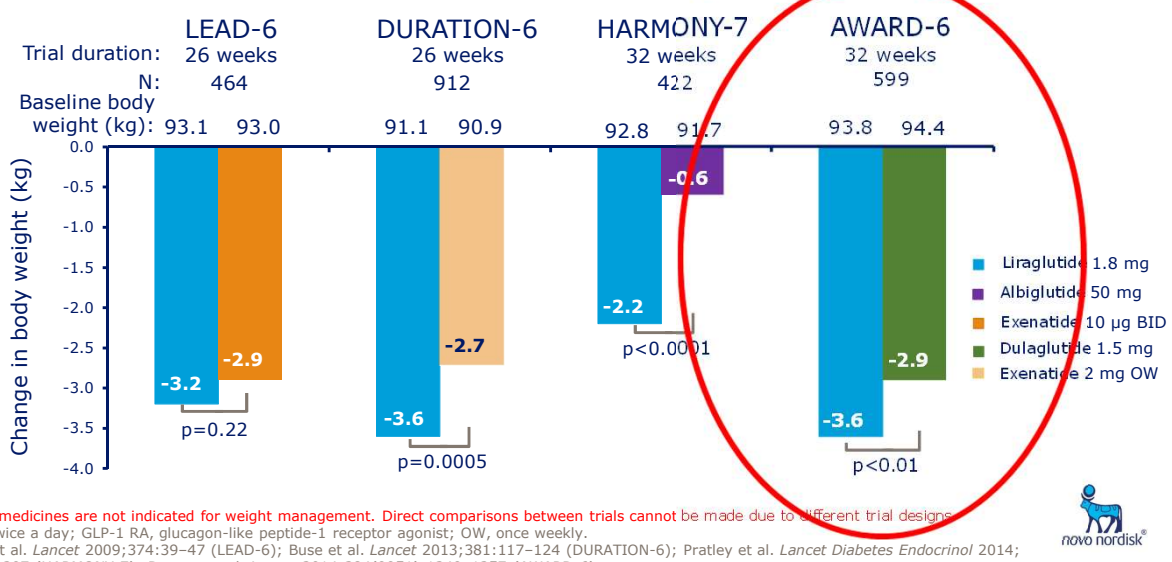
ESTIMATED CHANGE IN HbA_{1c}



*p<0.0001 vs comparator.
Exenatide OW, exenatide once weekly; IGlar, insulin glargine.
1. Sorli et al. *Lancet Diabetes Endocrinol* 2017;5:251–260; 2. Ahrén et al. *Lancet Diabetes Endocrinol* 2017;5:341–354; 3. Ahmann et al. *Diabetes Care* 2018;41:258–266; 4. Aroda et al. *Lancet Diabetes Endocrinol* 2017;5:355–366; 5. Rodbard et al. The Journal of Clinical Endocrinology and Metabolism 2018, 103(6):2291–2301; 6. Pratley et al. Lancet Diabetes Endocrinol 2018; 6(4):275–286

UK/VT/0818/0371 Date of Preparation: Sep 2018

Liraglutide: weight loss vs comparators



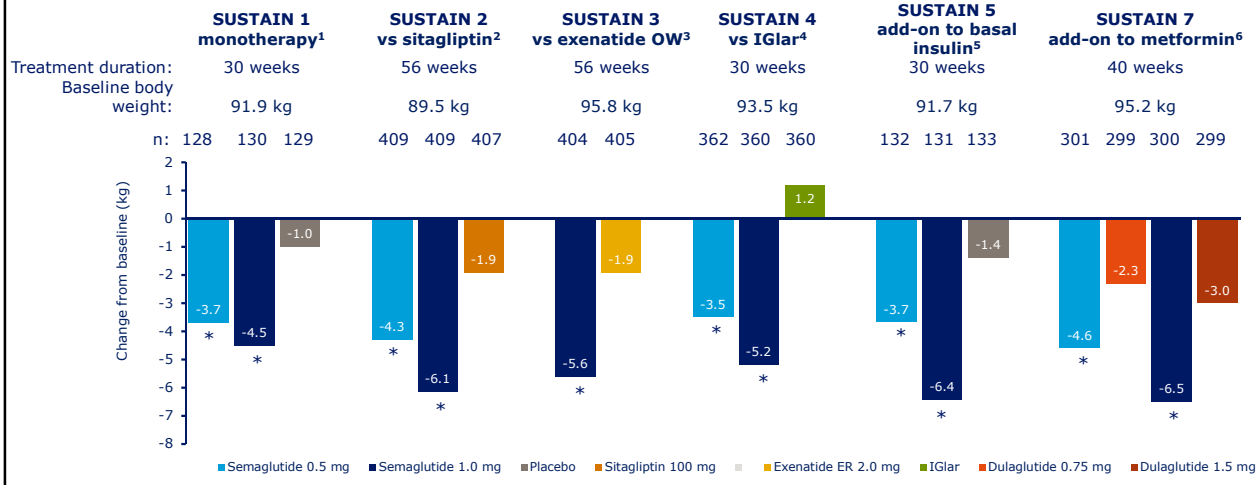
These medicines are not indicated for weight management. Direct comparisons between trials cannot be made due to different trial designs.
BID, twice a day; GLP-1 RA, glucagon-like peptide-1 receptor agonist; OW, once weekly.
Buse et al. *Lancet* 2009;374:39–47 (LEAD-6); Buse et al. *Lancet* 2013;381:117–124 (DURATION-6); Pratley et al. *Lancet Diabetes Endocrinol* 2014; 2:289–297 (HARMONY-7); Dungan et al. *Lancet* 2014;384(9951):1349–1357 (AWARD-6).

Date of preparation: September 2018 Job bag: UK/SM/0218/0069(1)

This slide discusses studies with different designs and comparators; no direct comparisons of data can be made between studies

Consistent efficacy results across SUSTAIN trials

ESTIMATED MEAN CHANGE IN BODY WEIGHT



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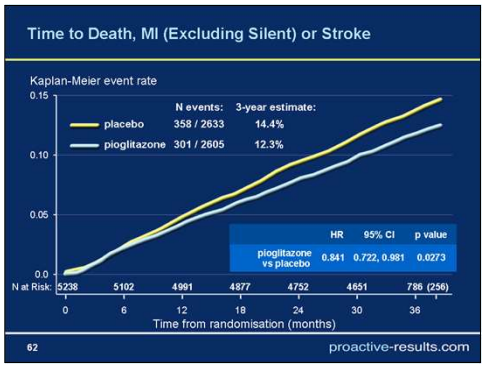
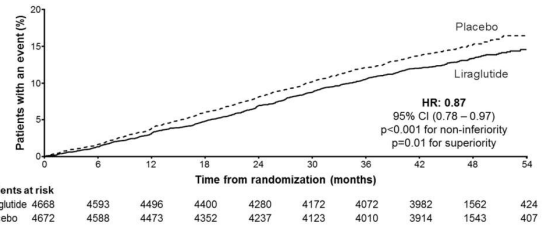
3-point MACE outcome in 4 studies of patients at high CV risk



CV death, non-fatal myocardial infarction, or non-fatal stroke



Patients at risk

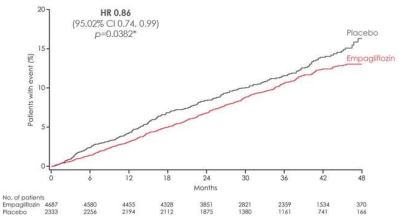
Liraglutide	4668	4593	4496	4400	4280	4172	4072	3982	1562	424
Placebo	4672	4588	4473	4352	4237	4123	4010	3914	1543	407

LEADER®

The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke. The cumulative incidences were estimated with the use of the Kaplan–Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months. CI: confidence interval; CV: cardiovascular; HR: hazard ratio.

Presented at the American Diabetes Association 76th Scientific Sessions, Session 3-CT-SY24, June 13 2016, New Orleans, LA, USA.

Primary outcome:
3-point MACE



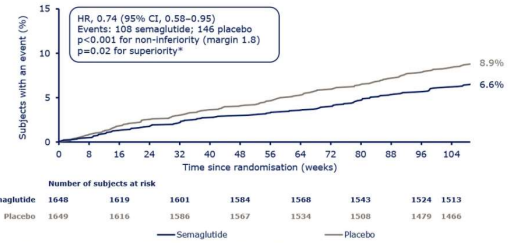
No. of patients

Empagliflozin	4687	4580	4455	4328	3851	2821	2359	1534	370
Placebo	2333	2256	2194	2112	1875	1380	1161	741	166

Cumulative incidence function; MACE, Major Adverse Cardiovascular Event; HR, hazard ratio.
* Two-sided tests for superiority were conducted (statistical significance was indicated if p≤0.0496)

EMPA-REG OUTCOME®

FIRST OCCURRENCE OF CV DEATH, NON-FATAL MI OR NON-FATAL STROKE



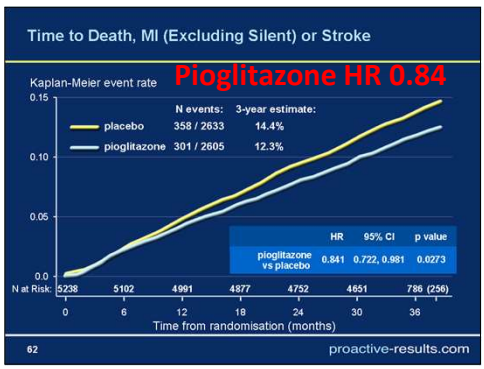
Number of subjects at risk

Semaglutide	1648	1619	1601	1584	1568	1543	1524	1513
Placebo	1649	1616	1586	1567	1534	1508	1479	1466

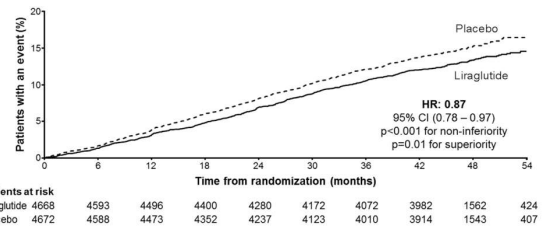
Semaglutide Placebo

Kaplan Meier plot for first event adjudication committee-confirmed CV death, non-fatal MI and non-fatal stroke using 'in-trial' data from subjects in the full analysis set.
*Not prespecified.
CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction.

3-point MACE outcome in 4 studies of patients at high CV risk



CV death, non-fatal myocardial infarction, or non-fatal stroke



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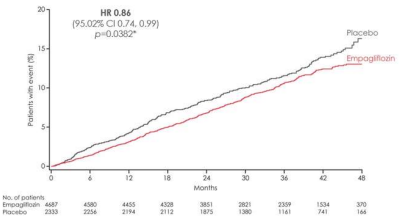

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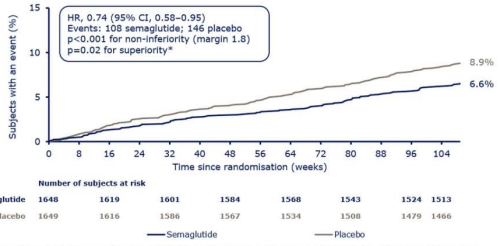

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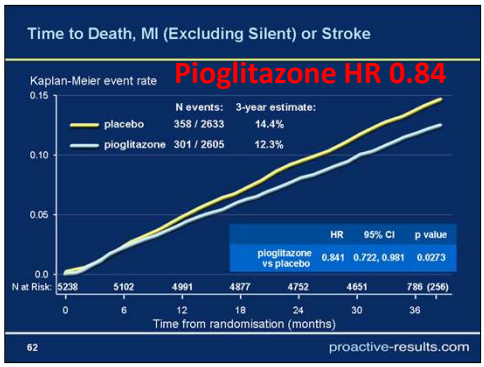
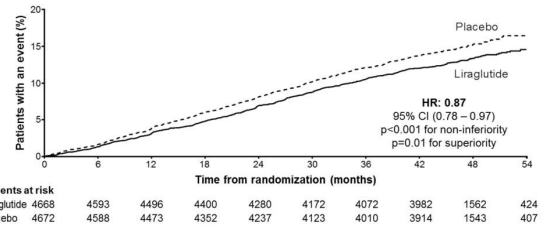


CV death, non-fatal myocardial infarction, or non-fatal stroke



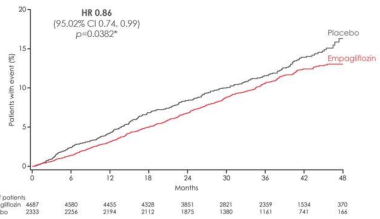
LEADER®

The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke. The cumulative incidences were estimated with the use of the Kaplan–Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months. CI: confidence interval; CV: cardiovascular; HR: hazard ratio.

Presented at the American Diabetes Association 76th Scientific Sessions, Session 3-CT-SY24, June 13 2016, New Orleans, LA, USA.

Primary outcome:
3-point MACE

Empagliflozin HR 0.86



Cumulative incidence function; MACE, Major Adverse Cardiovascular Event; HR, hazard ratio.
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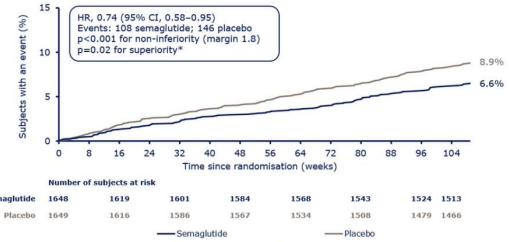
EMPA-REG OUTCOME®

FIRST OCCURRENCE OF CV DEATH, NON-FATAL MI OR NON-FATAL STROKE



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*Not prespecified.
CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction.

3-point MACE outcome in 4 studies of patients at high CV risk

Time to Death, MI (Excluding Silent) or Stroke
Pioglitazone HR 0.84
Kaplan-Meier event rate
N events: 3-year estimate:
placebo 358 / 2633 14.4%
pioglitazone 301 / 2605 12.3%
HR 95% CI p value
pioglitazone vs placebo 0.841 0.722, 0.981 0.0273
N at Risk: 5238 5102 4991 4877 4752 4651 786 (256)
Time from randomisation (months)
62
proactive-results.com

CV death, non-fatal myocardial infarction, or non-fatal stroke

Liraglutide HR 0.87
Patients with an event (%)
Placebo
Liraglutide
HR: 0.87
95% CI (0.78 – 0.97)
p<0.001 for non-inferiority
p=0.01 for superiority
Time from randomization (months)
Patients at risk
Liraglutide 4668 4593 4496 4400 4280 4172 4072 3982 1562 424
Placebo 4672 4588 4473 4352 4237 4123 4010 3914 1543 407

LEADER®

The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke. The cumulative incidences were estimated with the use of the Kaplan–Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months. CI: confidence interval; CV: cardiovascular; HR: hazard ratio.

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Primary outcome:
3-point MACE

Empagliflozin HR 0.86

HR 0.86
(95.02% CI 0.74, 0.99)
p=0.0382*
Placebo
Empagliflozin
Patients with event (%)
Months
No. of patients
Empagliflozin 4687 4580 4455 4328 3851 2821 2359 1534 370
Placebo 2333 2256 2194 2112 1875 1380 1161 741 166

Cumulative incidence function; MACE, Major Adverse Cardiovascular Event; HR, hazard ratio.
* Two-sided tests for superiority were conducted (statistical significance was indicated if p≤0.0495)

EMPA-REG OUTCOME®

FIRST OCCURRENCE OF CV DEATH, NON-FATAL MI OR NON-FATAL STROKE

HR, 0.74 (95% CI, 0.58–0.95)
Events: 108 semaglutide; 146 placebo
p<0.001 for non-inferiority (margin 1.8)
p=0.02 for superiority*
Subjects with an event (%)
8.9%
6.6%
Time since randomisation (weeks)
Number of subjects at risk
Semaglutide 1648 1619 1601 1584 1568 1543 1524 1513
Placebo 1649 1616 1586 1567 1534 1508 1479 1466
Semaglutide
Placebo

Kaplan Meier plot for first event adjudication committee-confirmed CV death, non-fatal MI and non-fatal stroke using 'in-trial' data from subjects in the full analysis set.
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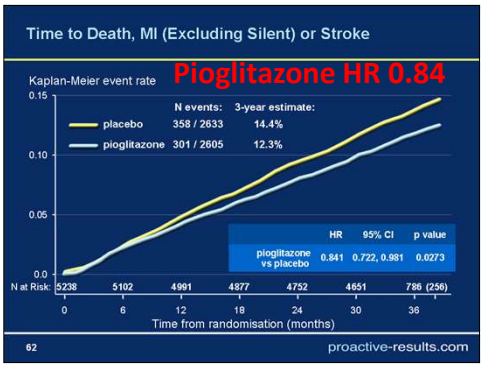

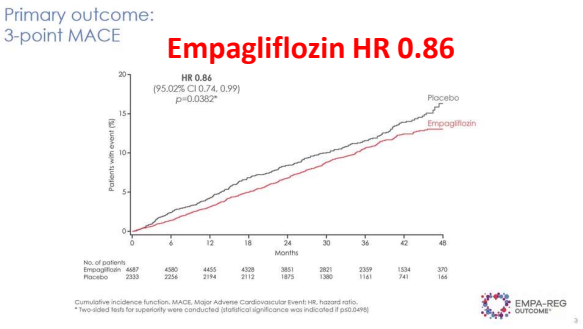

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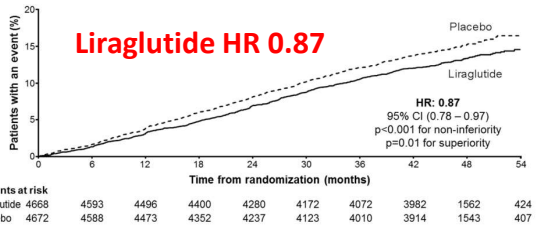

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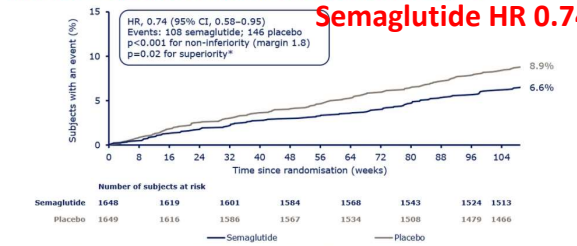

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*Not prespecified.
CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction.

ABCD Nationwide Semaglutide Audit

- Many interesting things to learn from the audit as semaglutide moves into real clinical use
- You can do your own local analyses whilst contributing to the national effort

ABCD
Association of British Clinical Diabetologists

Previous ABCD GLP1 RA Nationwide Audits

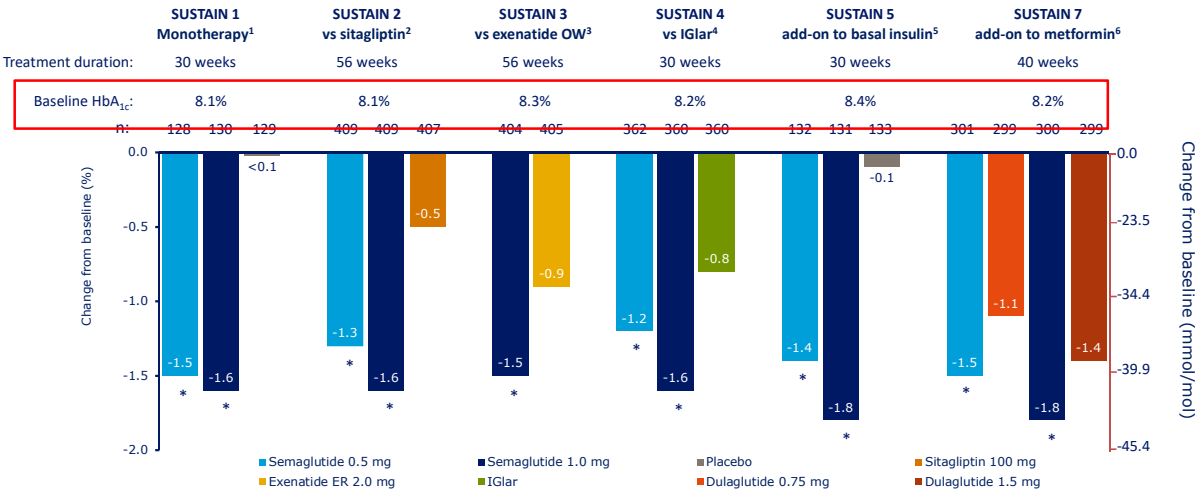
- Combined trials v real world

	Clinical trials combined	Real clinical use in UK (ABCD audit)
	Baseline HbA_{1c} (%)	
Exenatide	8.37	9.47
Liraglutide	8.5	9.40
	Baseline BMI (kg/m^2)	
Exenatide	32.72	39.8
Liraglutide	31	39.0

This slide discusses studies with different designs and comparators; no direct comparisons of data can be made between studies

Consistent efficacy results across SUSTAIN trials

ESTIMATED CHANGE IN HbA_{1c}



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ABCD liraglutide audit – the higher the baseline HbA1c the bigger the fall

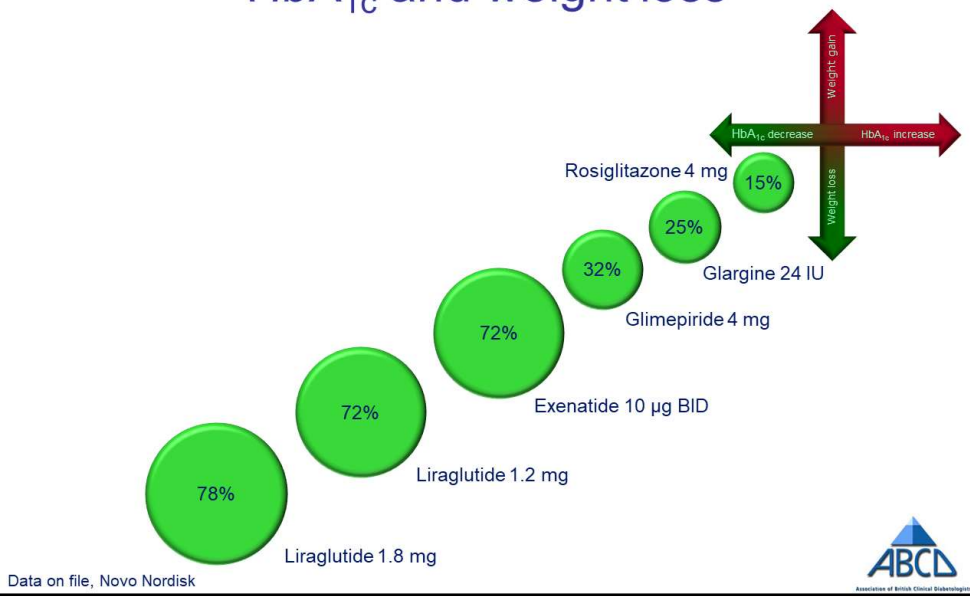
Table 3 Median HbA_{1c} change, proportion of patients achieving HbA_{1c} reduction of ≥1% and proportion of patients achieving target HbA_{1c} of 7% among patients treated with liraglutide in the ABCD audit; results stratified by baseline HbA_{1c} and use of insulin.

	Baseline HbA_{1c} (%)							
	7.0-7.9	8.0-8.9	9.0-9.9	10.0-10.9	11.0-11.9	12.0-12.9	13.0-13.9	P value
Non-insulin-treated								
n	91	158	161	106	60	35	11	
Median HbA_{1c} change, (%)	-0.7 [-1.1,-0.1]	-1.1 [-1.7,-0.5]	-1.4 [-2.2,-0.4]	-1.9 [-3.2,-0.9]	-2.6 [-3.9,-1.6]	-3.1 [-1.3,-4.5]	-2.0 [-0.3,-4.9]	< 0.001
Proportion achieving ≥1% reduction, n(%)	30 (33.0)	95 (60.1)	103 (64.0)	77 (72.6)	51 (85.0)	28 (80.0)	8 (72.7)	< 0.001
Proportion achieving HbA_{1c} of 7%, n(%)	50 (55.0)	58 (36.7)	35 (21.7)	25 (23.6)	11 (18.3)	4 (11.4)	1 (9.1)	< 0.001
Insulin-treated								
n	73	124	156	98	61	35	10	
Median HbA_{1c} change, (%)	-0.2 [-0.7,0.4]	-0.5 [-1.2,0.3]	-1.1 [-2.0,-0.2]	-1.3 [-2.6,-0.5]	-1.3 [-2.5,-0.5]	-1.8 [-3.4,-0.6]	-3.6 [-4.7,-1.6]	< 0.001
Proportion achieving ≥1% reduction, n(%)	11 (15.1)	41 (33.1)	82 (52.6)	61 (62.2)	36 (59.0)	24 (68.6)	9 (90.0)	< 0.001
Proportion achieving HbA_{1c} of 7%, n(%)	28 (38.4)	18 (14.5)	21 (13.5)	8 (8.2)	3 (4.9)	1 (2.9)	2 (20.0)	< 0.001

Median HbA_{1c} change results are shown as median [interquartile range]

Results show patients are more likely to achieve ≥1% HbA_{1c} reduction when baseline HbA_{1c} is higher and conversely more likely to achieve target HbA_{1c} of 7% if baseline HbA_{1c} is lower.

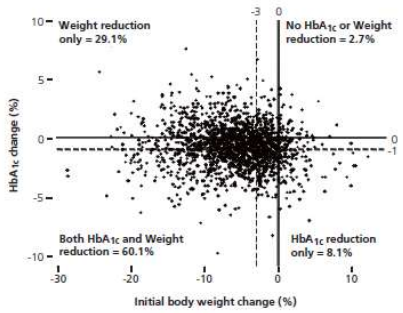
Percentage of subjects achieving fall in HbA_{1c} and weight loss



Data on file, Novo Nordisk

Patients improving weight AND HbA1c in previous audits

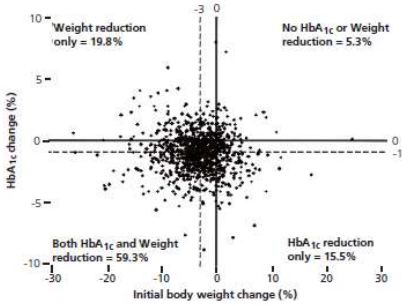
Figure 5. Scatterplot of HbA_{1c} change and initial body weight change at 20-32 weeks of 1882 patients treated with exenatide



Dotted line indicates criteria of ≥1% HbA1c reduction and ≥3% IBW reduction require by NICE for continuation of therapy – while 60.1% of patients achieved both HbA1c and weight reduction, only 28.6% achieved this to the criteria level set by NICE.

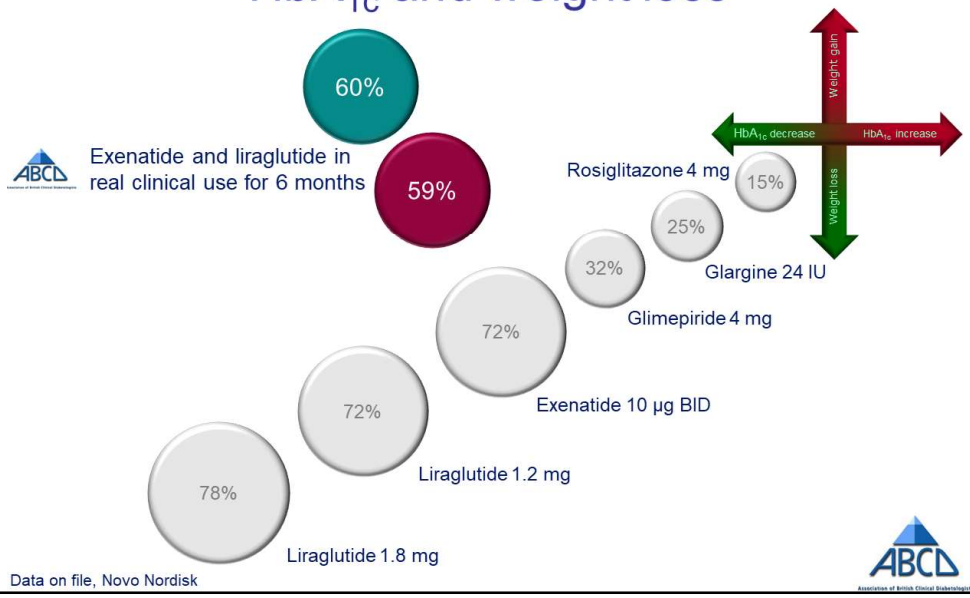
KY Thong et al. Br J Diabetes 2014; 14: 52-59

Figure 6. Scatterplot of HbA_{1c} change and initial body weight change at 20-32 weeks of 1023 patients treated with liraglutide

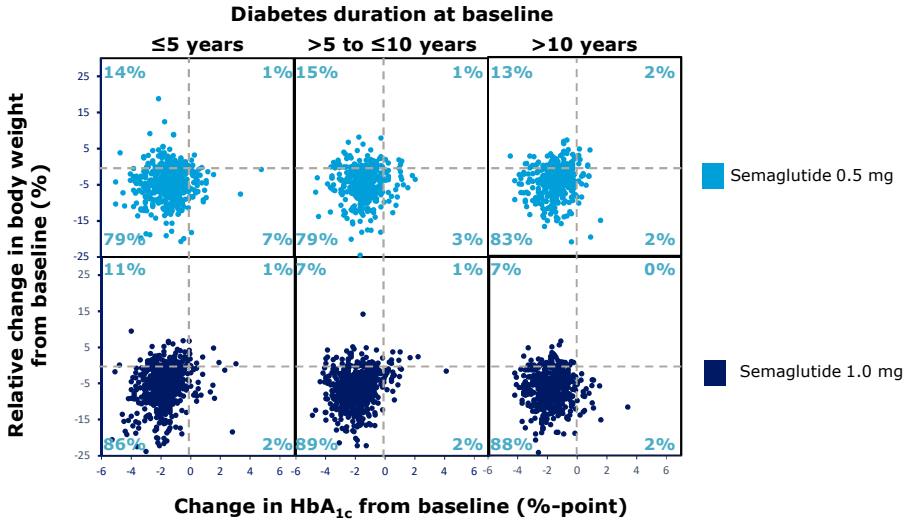


Dotted line indicates criteria of ≥1% HbA_{1c} reduction and ≥3% IBW reduction require by NICE for continuation of therapy – while 59.3% of patients achieved both HbA_{1c} and weight reduction, only 25.0% achieved this to the criteria level set by NICE.

Percentage of subjects achieving fall in HbA_{1c} and weight loss

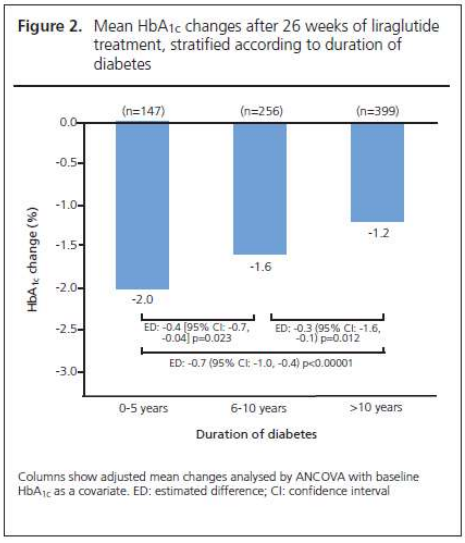


Changes in HbA_{1c} vs body weight by baseline diabetes duration



Data presented are based on observed on-treatment without rescue medication data, with MMRM predictions for missing HbA_{1c} and body weight values, from the six trials.
MMRM, Mixed Model Repeat Measurements.
Rosenstock J et al. Presented at the 78th Scientific Sessions of the American Diabetes Association, 22–26 June, 2018, Orlando, Florida, USA: Poster Presentation 1081-P.

ABCD liraglutide audit HbA1c changes according to duration of diabetes

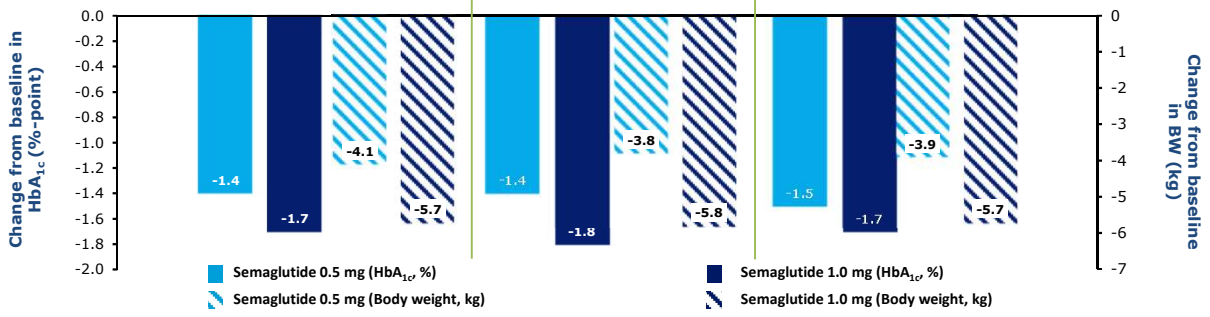


Thong KY et al. Br J Diabetes Vasc Dis 2015; 15(4): 169–172

National GLP-1 advisory board

Estimated change in HbA_{1c} and body weight by baseline diabetes duration

Diabetes duration	≤5 years				>5 to ≤10 years				>10 years			
Change from baseline:	HbA_{1c} (%)		Body weight (kg)		HbA_{1c} (%)		Body weight (kg)		HbA_{1c} (%)		Body weight (kg)	
N	533	641	533	641	423	565	423	565	376	528	376	528
Baseline	8.1	8.1	95.9	95.9	8.2	8.2	93.5	93.5	8.3	8.3	89.8	89.8
End of treatment	6.6	6.4	91.8	90.1	6.8	6.4	89.6	87.7	6.8	6.5	85.8	84.1



Data presented are estimated change from baseline to week 30 or week 40 based on a meta-analysis of data from the six trials. BW, body weight; N, number of subjects in the full analysis set.
Rosenstock J et al. Presented at the 78th Scientific Sessions of the American Diabetes Association, 22–26 June, 2018, Orlando, Florida, USA: Poster Presentation 1081-P.

ABCD Nationwide Semaglutide Audit

- As you start to use semaglutide please enter ALL your patients into the nationwide audit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