Learning from Real Life Data – highlights of the national ABCD programme

Dr Bob Ryder,

Clinical lead, ABCD nationwide audits of new diabetes therapies and devices

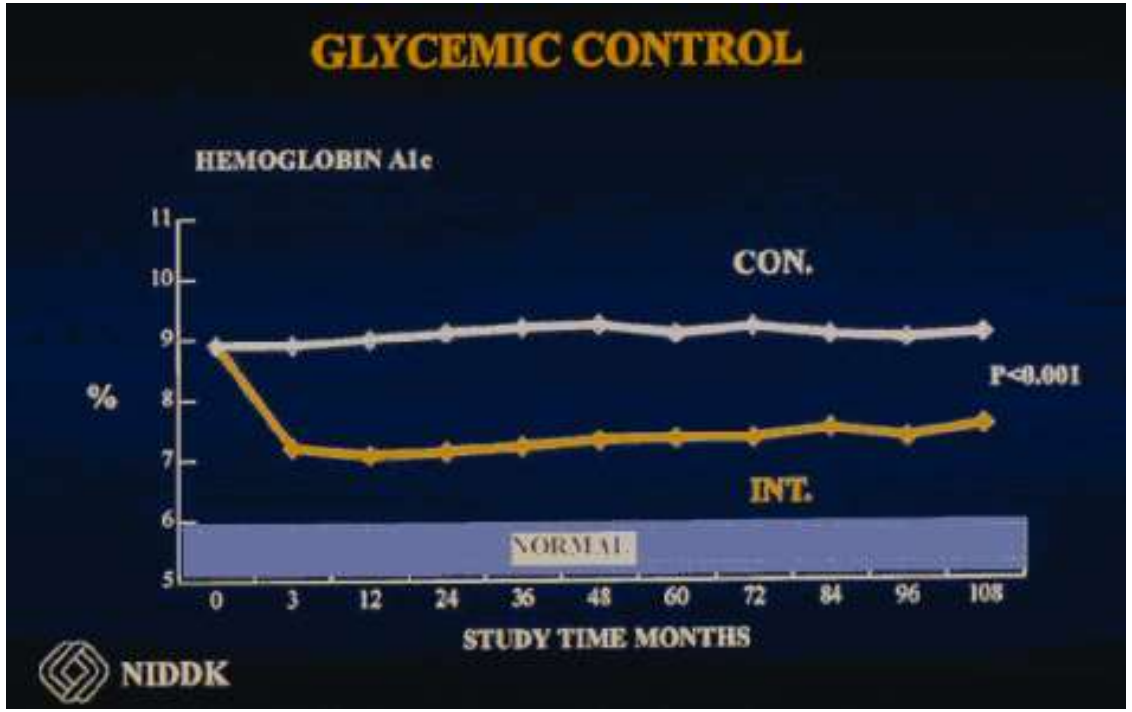
29 October, 2019

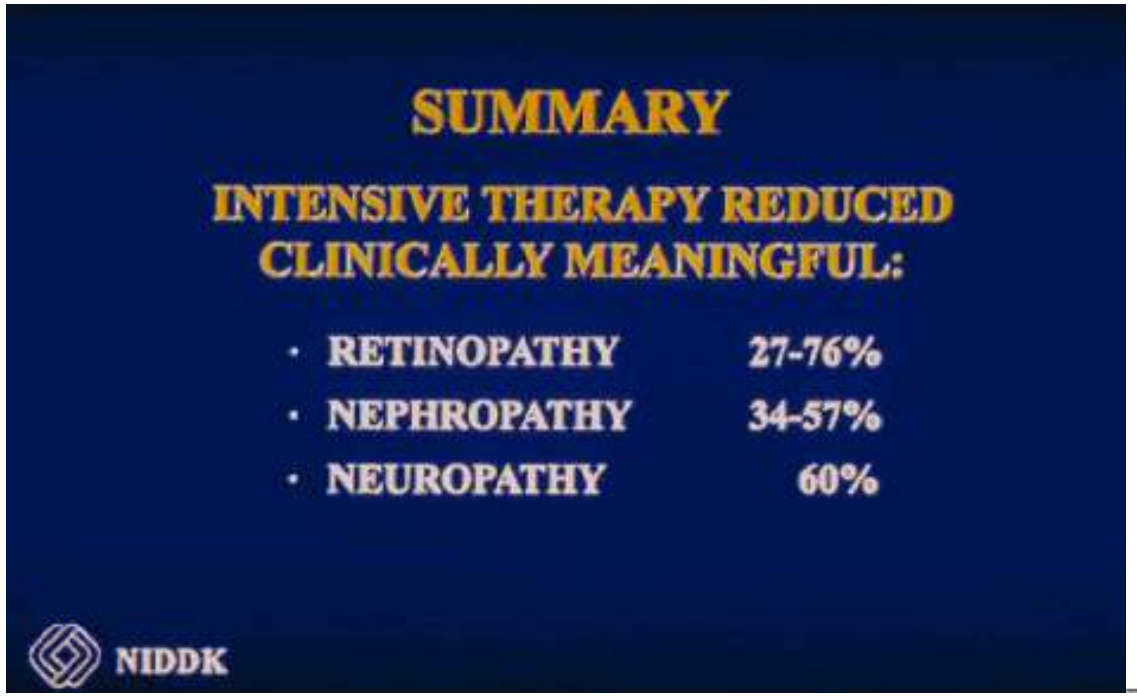
ABCD

Association of British Clinical Diabetologists

ABCD nationwide and worldwide audit programme

- New diabetes medications and devices as they start being used in real clinical practice (as opposed to research)





DCCT – ADA - Las Vegas - 1993

The New England
Journal of Medicine

Volume 329 SEPTEMBER 30, 1993 Number 14

THE EFFECT OF INTENSIVE TREATMENT OF DIABETES ON THE DEVELOPMENT AND PROGRESSION OF LONG-TERM COMPLICATIONS IN INSULIN-DEPENDENT DIABETES MELLITUS

THE DIABETES CONTROL AND COMPLICATIONS TRIAL RESEARCH GROUP*

Abstract *Background.* Long-term microvascular and neurologic complications cause major morbidity and mortality in patients with insulin-dependent diabetes mellitus (IDDM). We examined whether intensive treatment with the goal of maintaining blood glucose concentrations close to the normal range could decrease the frequency and severity of these complications.

Methods. A total of 1441 patients with IDDM — 726 with no retinopathy at base line (the primary-prevention cohort) and 715 with mild retinopathy (the secondary-intervention cohort) were randomly assigned to intensive therapy administered either with an external insulin pump or by three or more daily insulin injections and guided by frequent blood glucose monitoring or to conventional therapy with one or two daily insulin injections. The patients were followed for a mean of 6.5 years, and the appearance and progression of retinopathy and other complications were assessed regularly.

Results. In the primary-prevention cohort, intensive therapy reduced the adjusted mean risk for the development of retinopathy by 76 percent (95 percent confidence interval, 62 to 85 percent), as compared with conventional therapy. In the secondary-intervention cohort, intensive therapy slowed the progression of retinopathy by 54 percent (95 percent confidence interval, 39 to 66 percent) and reduced the development of proliferative or severe nonproliferative retinopathy by 47 percent (95 percent confidence interval, 14 to 67 percent). In the two cohorts combined, intensive therapy reduced the occurrence of microalbuminuria (urinary albumin excretion of >40 mg per 24 hours) by 39 percent (95 percent confidence interval, 21 to 52 percent), that of albuminuria (urinary albumin excretion of >300 mg per 24 hours) by 54 percent (95 percent confidence interval, 19 to 74 percent), and that of clinical neuropathy by 60 percent (95 percent confidence interval, 38 to 74 percent). The chief adverse event associated with intensive therapy was a two-to-threefold increase in severe hypoglycemia.

Conclusions. Intensive therapy effectively delays the onset and slows the progression of diabetic retinopathy, nephropathy, and neuropathy in patients with IDDM. (N Engl J Med 1993;329:977-86.)

INSULIN-dependent diabetes mellitus (IDDM) is accompanied by long-term microvascular, neurologic, and macrovascular complications. Although the daily management of IDDM is burdensome and the specter of metabolic decompensation ever-present, long-term complications, including retinopathy, nephropathy, neuropathy, and cardiovascular disease, have caused the most morbidity and mortality since the introduction of insulin therapy.[1,2] The prevention and amelioration of these complications have been major goals of recent research.

Although studies in animal models of diabetes[3-5] and epidemiologic studies[6-8] implicate hyperglycemia in the pathogenesis of long-term complications, previous clinical trials have not demonstrated a consistent or convincing beneficial effect of intensive therapy on them.[9-11] A recent publication from the Stockholm Diabetes Intervention Study demonstrated a more uniform beneficial effect of intensive therapy in patients with established complications, despite the apparent crossover of most conventionally treated patients to intensive therapy during the trial.[12]

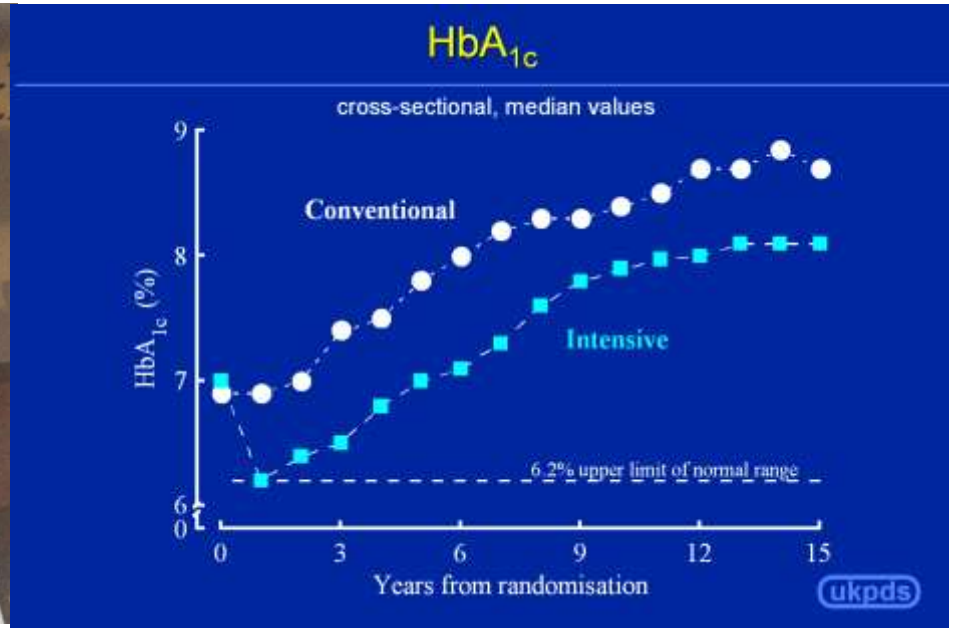
The Diabetes Control and Complications Trial was a multicenter, randomized clinical trial designed to compare intensive with conventional diabetes therapy with regard to their effects on the development and progression of the early vascular and neurologic complications of IDDM.[13-15] The intensive-therapy regimen was designed to achieve blood glucose values as close to the normal range as possible with three or more daily insulin injections or treatment with an insulin pump. Conventional therapy consisted of one or two insulin injections per day. Two cohorts of patients were studied in order to answer two different, but related, questions: Will intensive therapy prevent the development of diabetic retinopathy in patients with no retinopathy (primary prevention), and will inten-

Address reprint requests to the DCCT Research Group, Box NDIC/DCCT, Bethesda, MD 20892.

Supported under cooperative agreements and a research contract with the Division of Diabetes, Endocrinology, and Metabolic Diseases of the National Institute of Diabetes and Digestive and Kidney Diseases and by the National Heart, Lung, and Blood Institute, the National Eye Institute, the National Center for Research Resources, and various corporate sponsors (listed in *Diabetes Care* 1987;10:1-19).

*A complete list of the persons and institutions participating in the Diabetes Control and Complications Trial Research Group appears in the Appendix.

UKPDS – EASD – Barcelona - 1998



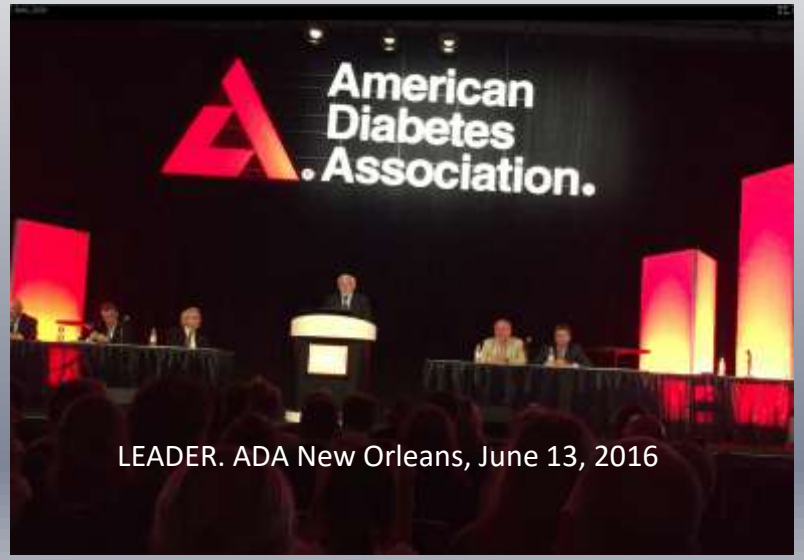
The Lancet

The Lancet

PROactive. EASD Athens, September 12, 2005

EMPA-REG. EASD Stockholm, September 18, 2015

Other great moments in the history of diabetes



LEADER. ADA New Orleans, June 13, 2016

CANVAS. ADA San Diego, June 12, 2017

My favourite moment – satellite symposium,
DUK Glasgow, 2007

Development of Exenatide: An Incretin Mimetic

Exenatide (Exendin-4)

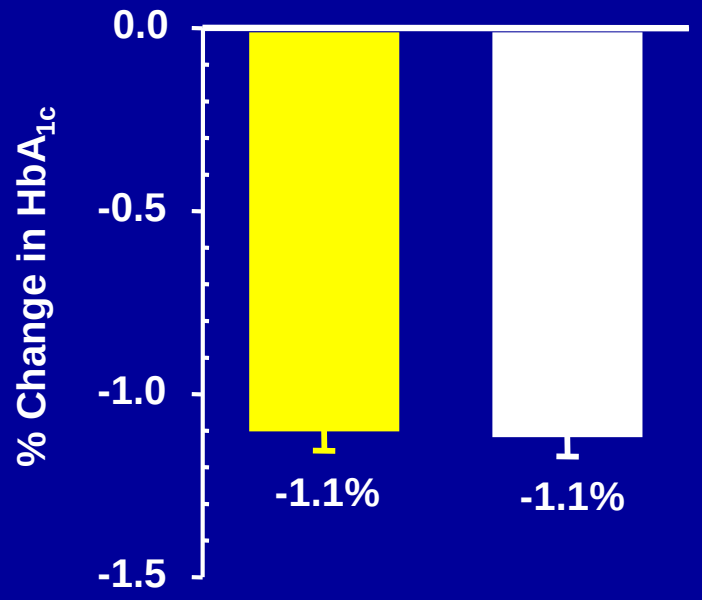
- Synthetic version of salivary protein found in the Gila monster
- Approximately 50% identity with human GLP-1
  - Binds to known human GLP-1 receptors on β cells *in vitro*
  - Resistant to DPP-IV inactivation

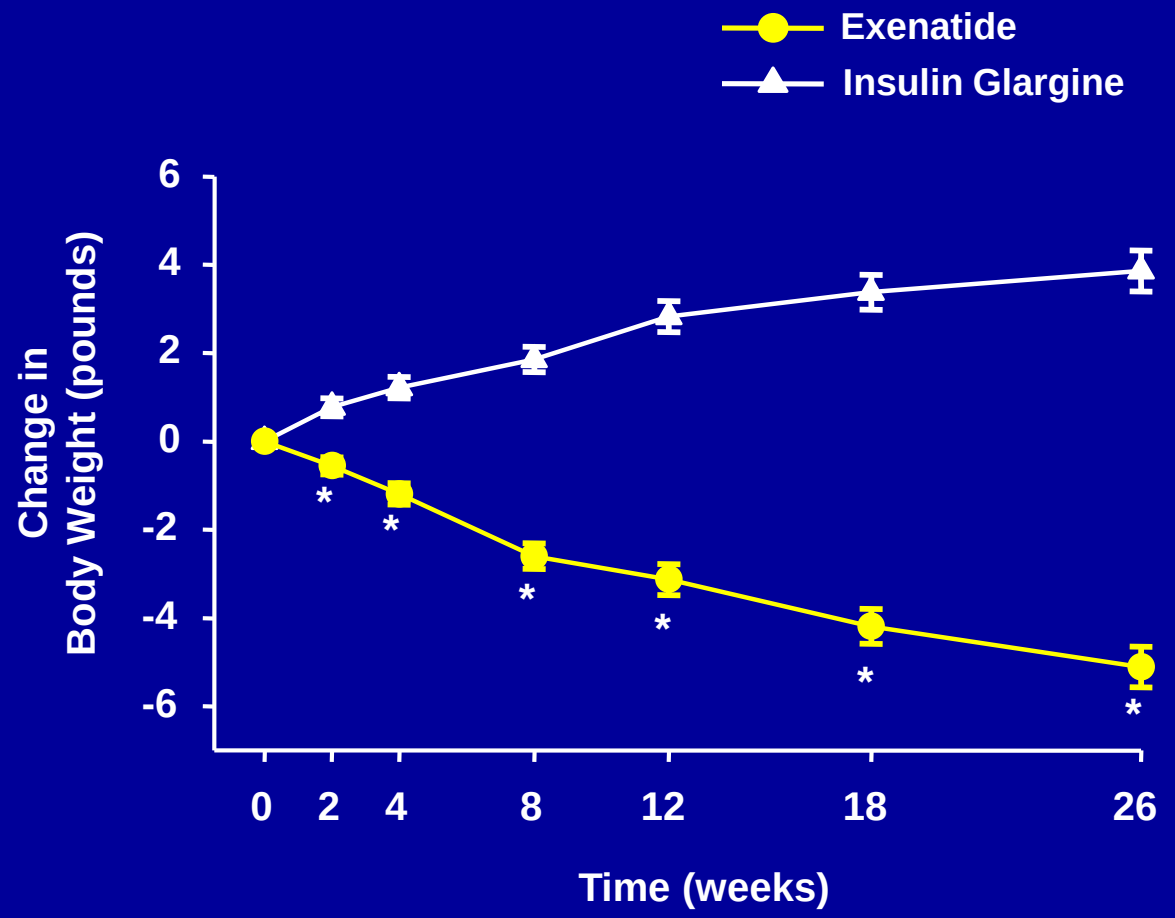
Exenatide	**H G** E G T F T S D **L** S **K Q M** E **E E** A **V R L** F I **E** W L **K N** G **G P S S G A P P P S – NH_2**
GLP-1 Human	H A E G T F T S D V S S Y L E G Q A A K E F I A W L V K G R – NH_2

Site of DPP-IV Inactivation

Adapted from Nielsen LL, et al. *Regulatory Peptides*. 2004;117:77-88.; Fineman MS, et al. *Diabetes Care*. 2003;26:2370-2377. Reprinted from *Regulatory Peptides*, 117, Nielsen LL, et al, Pharmacology of exenatide (synthetic exendin-4): a potential therapeutic for improved glycemic control of type 2 diabetes, 77-88, 2004, with permission from Elsevier.

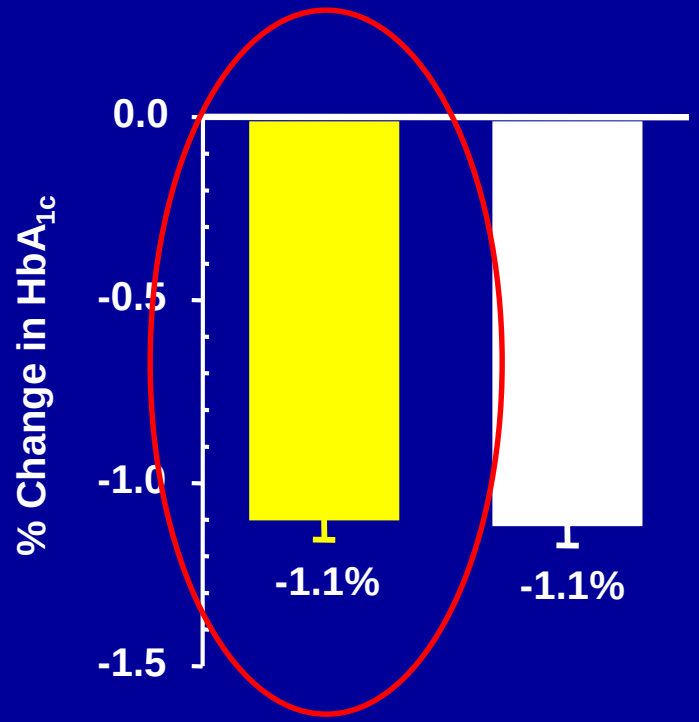
Using insulin in type 2 diabetes (HbA1c down but weight up)

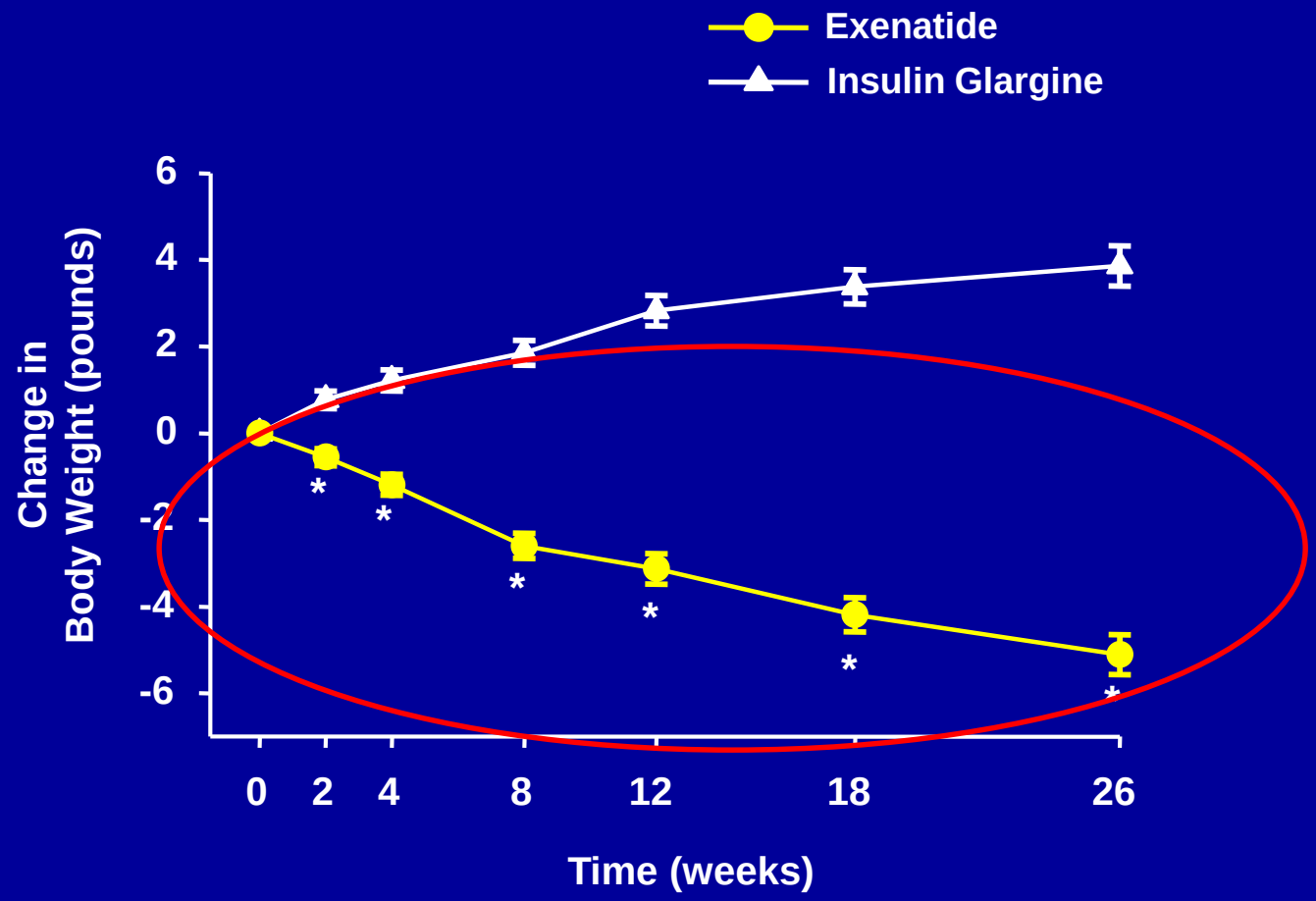




Heine RJ, et al. *Ann Intern Med.* 2005;143:559-569.

Using insulin in type 2 diabetes (HbA1c down but weight up)





Heine RJ, et al. *Ann Intern Med.* 2005;143:559-569.

Exenatide – coming off insulin, improving control, and losing weight

- June 2008
- Wt = 87 kg
- BMI = 35.3
- A1c = 9.0%
- Insulin 82 units, Repaglinide 4mg tds, Metformin 1gm BD

- April 2011
- Wt = 65 kg
- BMI = 26.7
- A1c = 7.2%
- Exenatide 10ug BD, Metformin 1gm BD

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit – launched December 2008

Top contributors > 100 patients

1.	B.M. Singh, U. A. Nayak, J. Govindan, D.N.Kalupahana, New Cross Hospital, Wolverhampton	438
2.	Bob Ryder, Hisham Ibrahim, Peter Davies et al, SWBH NHS Trust	231
3.	Shenaz Ramtoola & Geraint Jones et al, Royal Blackburn Hospital, Blackburn	209
4.	Karen Adamson, Ferelith Green et al, St John's Hospital, Livingston	182
5.	Laila King, Ralph Abraham et al, London Medical, London	180
6.	David Dove et al, Wexham Park Hospital, Slough	163
7.	Jackie Elliott et al, Sheffield Teaching Hospitals, Sheffield	154
8.	Mark Edwards, Helen Doolittle et al, The Hillingdon Hospital, Uxbridge	136
9.	Keith Sands, Lincoln County Hospital, Lincoln	132
10.	Julie Mehaffy Jean MacLeod et al, North Tees General Hospital, Stockton-on-Tees	125
11.	Zin Zin Htike, Anne Kilvert, Brian Mtemererwa et al, Northampton General Hospital	115
12.	Roland Guy et al, Basingstoke and North Hampshire NHS Foundation Trust, Hampshire	111
13.	Jeffrey W Stephens et al, Morriston Hospital, Swansea	110
14.	Richard Paisey et al, Torbay Hospital, Torquay	106
15.	Patrick English et al, Derriford Hospital, Plymouth	104
16.	Alison Melvin, Julia Pledger & Nick Morrish et al, Bedford Hospital, Bedford	103
17.	Phil Coates, Peter Daggett, Gill Green et al, Staffordshire DGH, Stafford	102
18.	Mark Savage, Phil Wiles & Parmeshwara Prakash et al, North Manchester General	101

ABCD
Association of British Clinical Diabetologists

Premier league

1.	Wolverhampton Wonderers	438
2.	West Bromwich Albion	231
3.	Blackburn Rovers	209
4.	Livingston FC	182
5.	Tottenham Hotspurs	180
6.	Slough Town FC	163
7.	Sheffield Wednesday	154
8.	Uxbridge FC	136
9.	Lincoln County	132
10.	Middlesbrough	125
11.	Northampton	115
12.	Basingstoke Town	111
13.	Swansea	110
14.	Torquay United	106
15.	Plymouth Argyle	104
16.	Bedford Town	103
17.	Stafford Town	102
18.	Manchester United	101

Premier league

1.	Wolverhampton Wonderers	438
2.	West Bromwich Albion	231
3.	Blackburn Rovers	209
4.	Livingston FC	182
5.	Tottenham Hotspurs	180
6.	Slough Town FC	163
7.	Sheffield Wednesday	154
8.	Uxbridge FC	136
9.	Lincoln County	132
10.	Middlesbrough	125
11.	Northampton	115
12.	Basingstoke Town	111
13.	Swansea	110
14.	Torquay United	106
15.	Plymouth Argyle	104
16.	Bedford Town	103
17.	Stafford Town	102
18.	Manchester United	101

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit – launched December 2008
- ABCD liraglutide audit – launched Autumn 2009

Liraglutide – coming off insulin, improving control, losing weight and “never felt so good”

- September 2009
- Wt = 93.9 kg
- BMI = 36.7
- A1c = 9.3%
- Insulin 60 units, Metformin 1gm BD

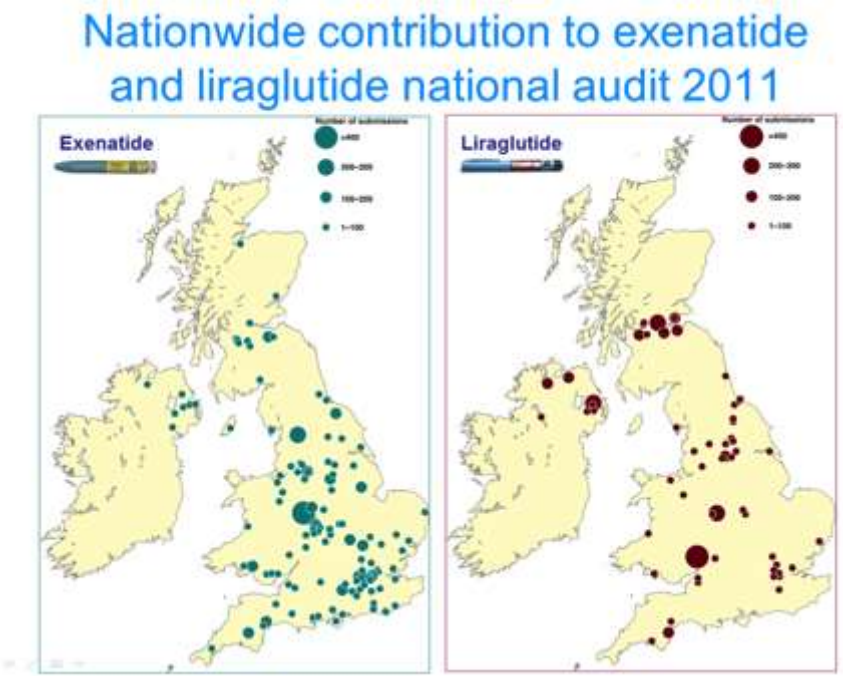
- February 2012
- Wt = 70 kg
- BMI = 26.3
- A1c = 7.2%
- Liraglutide 1.2mg daily, Metformin 1gm BD

ABCD nationwide exenatide and liraglutide audits

Dr Bob Ryder,
Clinical lead, ABCD nationwide audits of new diabetes therapies and devices

29 October, 2019

ABCD nationwide exenatide and liraglutide audits



- Real-life data
  - >13000 patients from
  - >150 centres
  - >500 contributors
- There had been (by 2019)
  - 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

ABCD
Association of British Clinical Diabetologists

ABCD nationwide exenatide audit contributors

The following are those whom we know about.

ABCD nationwide exenatide audit project steering group: *Ryder REJ, Walton C, Rowles S, Adamson K, Dove D, Thozhukat S*

ABCD nationwide exenatide audit – initial setup, maintenance and nationwide analysis: *Ryder REJ, Walton C, Winocour P, Cull ML, Jose B, Sukumar N, Mills AP, Sands K, Shafiq W, Rigby A, Thozhukat S, Thong K. Statistician: Blann A.*

Addenbrookes Hospital: Adler A, Evans M, Simmons D, O'Rahilly S, Coll T, Farooqi S, Park A. **Altnagelvin Area Hospital:** Lindsay J, Kelly J. **Antrim Area Hospital:** Kennedy A, Rooney D. **Barnsley Hospital:** Uchegbu E. **Basildon University Hospital:** Mulcahy M, Krishnan L. **Basingstoke and North Hampshire NHS Foundation Trust:** Guy R, Turner B, Akester K, Lewis G, Harrison O, Tombling S, Lloyd G, Hughes C, Lowe C. **Bedford Hospital:** Morrish N, Melvin A, Pledger J, Barron R. **Bedfordshire & Hertfordshire PGMS, Luton:** Rehman T, Sinclair A. **Belfast City Hospital:** Henry W. **Bolton Diabetes Centre:** Palin S, Kenz R. **Bristol Royal Infirmary:** Raghavan R, Phillips S, Bradley K. **Bronglais Hospital:** Kotonya C, Premawardhana LDKE. **Chesterfield Royal Hospital:** Mohammad M, Robinson RTCE, MacInerney RM. **Chorley & South Ribble Hospital:** Rajbhandari SM, Acharya S. **City Hospital, Birmingham:** Ryder REJ, Basu A, De P, Lee BC, Jose B, Sukumar N, McAloon CJ, Blann A, Mills AP, Cull ML, Lee A, Rawcliffe C, Ryder B, Burbridge W, Irwin S, Cutler J, Zzizinger A, Mehrali T, Bedi T, Stevenson-Mort J. **CMMC Foundation Trust, Manchester:** Jinadev P, Watts R, Abul-Ainine S, Salahuddin S. **Colchester General Hospital:** Bodmer C. **Conquest Hospital, St Leonards on Sea:** Dashora U, Castro E. **Countess of Chester:** Shulwalia R,, Ewins D, Goenka N. **County Hospital, Hereford:** Lloyd J. **Craigavon Area Hospital, Co Armagh:** Ritchie C. **Daisy Hill hospital, Newry:** Adil MM. **Derriford Hospital, Plymouth:** English P, Viney T, Laird O, Rigley R, Babu A, Blackmore M. **Dumfries & Galloway Royal Infirmary:** Bell E., Green F, Banerjee S. **East Surrey Hospital, Redhill:** Foster K, Natarajan G. **Eastbourne District Diabetes Centre:** Bending J, Afolayan J, Sheppard P. **Fairfield Hospital, Bury:** Rowles S, Smithurst HJ. **Falkirk and District Royal Infirmary:** Kelly C, Peden N, Currie J., Buchanan L. **Frimley Park Hospital:** Eliwe MH, Bingham E, Tringham JR. **Furness General, Barrow In Furness:** Chuni P, Hay C, Narayan S, Krishnan S. **Gartnavel General Hospital:** Small M, Jones G, McGrane D, Sainsbury G. **George Eliot Hospital Nuneaton:** Shaikh S, Patel V. **Good Hope Hospital, Sutton Coldfield:** Jones SL, Milles JJ, Griffiths U, Colloby M, Harold C, Rangan S, Morrison J. **Glasgow Royal Infirmary**, Fisher M, McGrane D. **Great Western, Swindon:** Govindan J, Price P, Ahmed S, Gardner A. **Guys & St Thomas Hospital, London:** Brackenbridge A, Reid A, Piper-Smith J, Preston J. **Hammersmith and Charing Cross:** Field BCT, Dornhorst A. **Harrogate Hospital:** Hammond P, Thirumurugan E,. **Heartlands Hospital, Birmingham:** John R, Patel M, Ulnaf S, Begum S. **Hillingdon Hospital, Uxbridge:** Edwards M, Doolittle H, Currie A, O'Sullivan S, Lillystone R. **Hinchinbrooke Hospital, Huntingdon:** Mathews AA. **Hull Royal Infirmary:** Walton C, Ng B, Kumar BK, Bosomworth A. **Ipswich Hospital:** Srinath A, Parkinson C, Fowler D, Morris D, Rayman G, Scott A. **James Paget Hospital, Great Yarmouth:** Grinnell F, Huston N, MacMillian C. **King's College Hospital, London:** Lee M, Amiel S, Nathan Y. **Kingston Hospital:** Oldfield M. **Lagan Valley Hospital, Lisburn:** Au S, Turtle EJ. **Leicester General Hospital:** Tarigopula G, Braithwaite J, Kong M-F, Jackson S, Gregory R. **Leicester Royal Infirmary:** Nisal K, Gallagher A, Davies MJ, McNally PG, Lawrence IG **Lincoln County:** Sands K. **London Medical:** King L, Abraham R, Tomeu J. **Mayday University Hospital, Croydon:** Prentice M. **Medway Maritime Hospital, Gillingham:** Scobie IN. **Monklands Hospital, Airdrie:** Sandeep T. **Morriston Hospital, Swansea:** Stephens JW. **Newcastle General:** Taylor R. **New Cross Hospital, Wolverhampton:** Singh BM, Nayak UA, Govindan J, Kalupahana DN **Newham University Hospital, London:** Gelding S, Rayanagoudar G.. **Ninewells, Dundee:** Petrie J, Al-Dahlaki M. **Nobles Hospital, Isle of Man:** Khan EG, Krishnan A, Clark J, Thondam S. **North Manchester General Hospital:** Rathur H, Savage M, Wiles P, Prakash P. **North Tees & Hartlepool Trust:** MacLeod J, Anthony S, Mehaffy J. **North Wales NHS Trust, Wrexham:** White H. **Northampton General Hospital** Htike ZZ, Kilvert A, Mtemererwa B, Nisal K, Fox C, Rippin J. **Bromley PCT:** Casiglia D. **Pinderfields General, Wakefield:** Nagi DK. **Poole Hospital NHS Foundation Trust:** Masding M, Osborne K, Wallace P. **PRH, Haywards Heath:** Smith A, Mabrook J. **Prince Philip Hospital, Llanelli:** Williams M, Aggarwal N. **Princess Royal, Bromley:** Lulsegged A. **Queen Alexandra, Portsmouth:** Cranston I, Darzy K. **Queen Elizabeth II Hospital, Welwyn Garden City:** Winocour PH. **Queen's Hospital, Burton:** Benn J. **Raigmore Hospital, Inverness:** McLaren L. **Rotherham General:** Franke B. **Royal Berkshire Hospital, Reading:** Simpson H, Reddy N, Barber T. **Royal Blackburn Hospital:** Astin J, Faina J, Whalley G, Ramtoola S, Jones G, Wilkinson R. **Royal Bournemouth:** Richards J, Richardson T. **Royal Cornwall Hospital, Treliske:** Fox T., Foote J, Browne D, Pinkney J **Royal Devon & Exeter:** Bowman P, Hattersley A, Vadiya B. **Royal Glamorgan Hospital, Llantrisant:** Evans P. **Royal Gwent Hospital, Newport:** Obuobie K. **Royal Infirmary of Edinburgh:** Jaap A, Noh R, Richards M. **Royal Liverpool University Hospital:** Vora J, Brake J. **Royal Oldham Hospital:** Mishra BM. **Royal Surrey County Hospital, Guildford:** Hordern V. **Royal United Hospitals, Bath:** Higgs E, Gouni R, Taylor P, Wylie S, Hall B, Hillier N, Neathercote D. **RSCH, Brighton:** Quin J, Robinson N. **Sandwell Hospital, West Bromwich:** Ibrahim H, Robertson D, Davies P, Banerjee P, Li YK, Wong KH, Barker N, Dhallu J, Farell D., R.M. Iqbal **Scunthorpe General:** Moisey R, Malik M, Dromgoole P, Elmalti A. **Selly Oak Hospital, Birmingham:** Creely S, Gough S, Hanif W. **Sheffield Teaching Hospitals:** Elliott J, Scott A. **Smethwick Health Centre:** Pall N, Harrington J. **South East CHCP, Glasgow:** Carson L-A. **Southampton General Hospital:** Sharp P, Brown B. **Southern General Hospital, Glasgow:** Semple C. **St John's Hospital, Livingston:** Adamson K, Green F. **St Mary's Hospital, Isle of Wight:** Kaklamanou M, Al-Mrayat M. **St Peter's Hospital, Chertsey:** Sennik D, Baxter M, Naqvi S, Suresh D, Miras A. **Staffordshire DGH, Stafford:** Coates P, Daggett P, Green F. **Stirling Royal Infirmary:** Kelly C, Mackenzie A, Peden N. **Bronglais Hospital, Aberystwyth:** Kotonya CA. **Sunderland Royal:** Nayar R, Carey P, Aspray T. **Taunton & Somerset:** Close C, Andrews R, Douek I, Watson J., Lambert P. **Torbay Hospital, Torquay:** Paisey R. **University Hospital Coventry Warwickshire:** Anderson S. **Ulster Hospital, Belfast:** Brennan U, Satti N, Harper R, Harding J. **Victoria Infirmary, Glasgow:** Stewart A. **Warwick Hospital** Rao RK, Gopinathan KP, Horrocks P. **Watford General Hospital:** Tharakan G, Simpson K. **West Suffolk Hospital, Bury St. Edmunds:** Majeed J, Clark J, Wijenaike N, Gurnell E, Hartley L, Abdullah H, Marath H. **Western General Hospital, Edinburgh:** Aniello L, McKnight JA, Strachen M, Reynolds R, Nyrenda M. **Berkshire East PCT:** Dove D, Aung T. **Whipps Cross University Hospital, London:** Lakhdar A, Manogaraan B. **Wirral Teaching Hospital, Upton Wirral:** Leong KS, Leong K, Lorains J, Joseph P, Leach J, Fenna I. **Whiteabbey Hospital:** Andrews J, Strrezlecka A. **Wishaw General, Lanarkshire:** O'Brien I, Davidson E. **Worcestershire Acute Hospitals, Worcester:** Newrick P, Jenkins D. **Wrexham Maelor:** Dixon AN, Munigoti S, Stanaway S, Harvey JN. **Wythenshawe Hospital, Manchester:** Younis N. **Yeovil District Hospital:** Bickerton AST, Crocker M, Down S. **York Hospital:** Jennings P, Hudson N.

Acknowledgment

The ABCD nationwide exenatide audit is an independent audit supported by an unrestricted grant from Eli Lilly Ltd

ABCD
Association of British Clinical Diabetologists

ABCD nationwide liraglutide audit contributors *The following are those whom we know about.*

ABCD nationwide liraglutide audit – initial setup, maintenance and nationwide analysis: *Ryder REJ, Walton C, Thong KY, Sen Gupta P, Cull ML, Mills AP. Statistician: Blann A.*

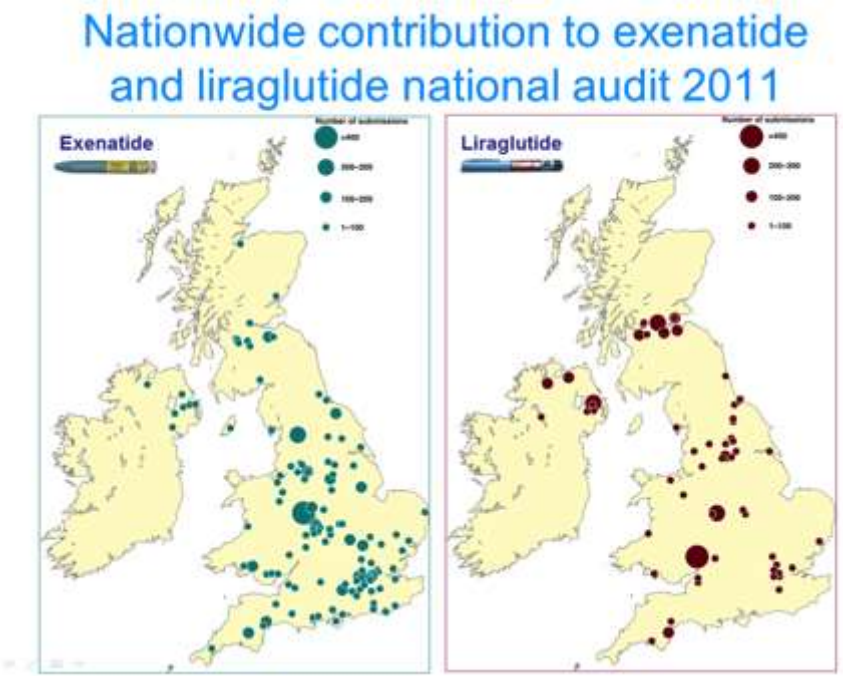
Addenbrookes Hospital: Adler A, Bejinariu E, Myring J, Park A, Parker V, Sarker A, Simmons D. **Altnagelvin Area Hospital:** Black R N, Caskey H, Cooke B, Early R, Giff K, Hamilton L, Helmy A F, King L, Lindsay J R, McCarroll F, McDaid A-M, McIlvor E, Moles K W, Morahan S, O'Kane M, Williams L. **Antrim Area Hospital:** Kennedy A. **BaNES NHS primary care trust:** Catchpole S, Wylie S. **Barnet General, London:** Cohen M, Katz J, Kola B, Tanday R, Seenandan J, Steuer L. **Barnsley Hospital NHS Foundation Trust:** Uchegbu E. **Basildon University Hospital:** Mulcahy M. **Bassetlaw Hospital:** Kela R, Woods H. **Bearwood Medical Practice:** Alderman J, Bhanderi S, Matthews J, Newhouse R, Purcell J, Sen Gupta P. **Belfast City Hospital:** Henry RW, McMullan P, Nugent A. **Bensham General Hospital:** Narayanan K R, Razvi S, Weaver J. **Birmingham Community Healthcare NHS Trust:** Bhanderi S, Cunningham B, Haughton K, Matthews J, Muralidhara K, Sen Gupta P, Shahid S, Thomas A. **Bradford Royal Infirmary:** González S. **Brighton General Hospital:** Duff B. **Brighton Sussex University Hospital NHS Trust, Royal Sussex County Hospital:** Burberry A. **Bristol General Hospital:** Croxson S. **Bristol Royal Infirmary:** John H, Jones L, Pople J A, Richards G. **Bronglais hospital:** Davies C, Evans C, Jones A M, Kotonya C, Phillips L, Powell P, Saunders H. **Calderdale Royal Hospital:** Mon Zin Tun E. **Cape Hill Medical Centre:** Bhanderi S, Child D, Chitnis J, Gardner G, Maan P, Matthews J, Merali A, Sen Gupta P. **Causeway Hospital, Coleraine:** Davidson E, Diong K L, Glass M, Hutchinson K, Kassim S B, McKee M, Ryan M F, Spiers K, Woodend J. **Chase Farm Hospital:** Baynes, C, Lomas J, Russell S. **Cheltenham General Hospital:** Evans A, Gray H, Lock-Pullan P, Phillips S. **City Hospital, Birmingham - Diabetes & Endocrinology Dept (SWBH) + Bearwood GP:** Basu A, Bedi T, Bhanderi S, Blann A, Burbridge W, Cull M L, Cutler J, De P, Guthrie S, Irwin S, Lee B, Lloyd F, Matthews J, Mehrali T, Mills A P, Oakley J, Ryder R E J, Sen Gupta P, Stevenson-Mort J, Thong K, Wyres M, Zzizinger A. **City Hospitals, Sunderland:** Carey P, Coates J A, Lee A, Nayar R, Ogilvie P, Purvis A, Todd J, Walton K. **Conquest Hospital**: Batson D, Castro E, Combes A, Dashora E, Edwards V, Govindan R, Kumar S, Morris R. **Cumberland Infirmary Centre:** Graham S, Higgins N, Mason J, Redgate J, Routledge A, Simpson E, Vithian K. **Darlington Memorial Hospital:** Bishop D. **Derriford Hospital:** English P, Fox T, Tambal A, Wotton F. **Dewsbury District Hospital:** Bissell J, Freeman, Rajeswaran. **Downe Hospital Northern Ireland:** Whitehead H. **East Lancs Hospitals NHS Trust:** Ali A, Demssie Y, Glew M, Jones G, Jostel A, Littley M, Mishra M, Ramtoola S, Wilkinson R. **East Surrey Hospital:** Chinnasamy E, Prajapati C, Sennik D. **Eastbourne District General:** Bending JJ, Lipscombe DW, O'Donnell H. **ELPCT:** McKane C, Procter W, Sarsfield J, Wilkinson R. **Forth Valley Royal Hospital:** Barwell N, Bramley A, Buchanan L, Currie J, Davidson E, Devlin K, Doig J, Kelly C, MacDonald P, Mackenzie A, Mackintosh L, Peden N, Ryan L, Simpson C, Whitty H. **Friarage Hospital:** Kamaruddin M S, Leek C, Owen K. **Frimley Park Hospital:** Beebeejaun M, Tringham J. **Furness General Hospital:** Banerjee M, Obale B, Pearce D, Tong M. **George Eliot Hospital:** Patel V. **Gloucestershire Royal Hospital:** Gan K S, Mahajan T, Saunders S, Ulahannan T. **Guy's and St Thomas' Hospital London (Guy's & St. Thomas' NHS Trust):** McGowan B, Abbas N, Sen Gupta P, Da Costa R, Georgieva E. **Harrogate Hospital:** Brown D, El-Laboudi A, Hammond P, Maguire D, Ray S, Toop M. **Hinchingbrooke Health Care NHS Trust:** Bejinariu E, Krishnan S, Mathews A, Walland K. **Huddersfield Royal Infirmary:** Moisey R. **Hull Royal Infirmary:** Aitkin SL, Allan B, Marinceu D, Masson E, Sathyapalan T, Sugunendran S, Walton C,Wakil A, Waqas S. **Hunslet Health Centre:** Muneer K, Khan. **King's College Hospital:** Amiel, SA, Hunt K F, Lee M, Nathan Y, Pernet A, Raeburn J, Sen Gupta P, Stothard B, Vitello S. **Lagan Valley Hospital:** Au S, Brennan U, Carr S, Harding J, Harper R, MacDonald P, McLaughlin D, Moore L, Mulligan C, Whitehead H. **Lancashire Teaching Hospital, Chorley Hospital:** Rajbhandari S M, Whittaker J. **Lancashire Teaching Hospital, Royal Preston Hospital:** Rajbhandari S M, Whittaker J. **Leicester General Hospital:** Davies M, Gregory R, Jackson S, Kong M-F, Nisal K, Tarigopula G. **Leicester Royal Infirmary:** Htike ZZ. **Leigh Infirmary:** Fatima J, Pearce S. **Lister Hospital:** Barker L, O' Donnell L. **Llandridod Wells:** Powell P. **London Medical (Private Medical Centre):** Abraham C, Abraham R, Bowden J, Cavan D, Genovezos S, King L, Levy D, Lunken C, Oakley N, Press M, Spahiu E, Thomas S. **Mid Yorkshire Hospitals NHS Trust (Pinderfield Hospital, Wakefield, West Yorkshire):** D'Costa R, Kadis T, Maycock J, Nagi D, Seddon L. **Minerva Centre:** Caunce K. **Monklands Hospital:** Sandeep T C, White A. **Musgrove Park Hospital (Taunton & Somerset NHS Foundation Trust):** Adams S, Andrews R, Close C, Douek I, Dunlop A, Lambert P, Thomas J, Watson J. **New Cross Hospital Wolverhampton:** Katreddy V, Khalid Y, Krishnasamy S, Nayak A U, Singh B M. **Newham University Hospital:** Balakumar Y, Gelding S, Menon R, Rayanagoudar G. **NHS Tayside (Ninewells Hospital/Perth Royal Infirmary):** Brennan G, Connagher A, Dutton A, George P, Leese G, Mackie A, Malcom E, McCrimmon R, Morris, Pearson E. **Northumbria Diabetes Service:** Strey C. **Norvic Family Practice (SWBH),Victoria Health Centre**: Baker O, Ely C, Pathan H, **Orpington Hospital:** Allinson R, Casiglia D, Danby T, Fisher N, Hussey S, Lovie K, Lovegrove-Saville L, Mackay F. **Pendyffryn Medical Group, Prestatyn (GP Practice):** Morrison C L. **Pennine Acute Hospitals Trust:** Adams L, Aherne D, Ahmad M, Allen G, Anderson K, Asam M, Atherton L, Balmuri M, Bennion J, Benton M, Berry M J, Bhatnagar D, Bood A, Broude H, Byrom J, Cheer K, Dang C, Emsley C, Farook S, Fletcher M, Flight W, Garg R, Hafeez K, Hall D, Higham C, Holland K, Hunsdale D, Jagadhish, Jani M, Jennings R, Jostel A, Joyce P, Kalavalapalli S, Khan S, Khurana R, Kouta S, Kumar S, Lea S, Lewthwaite P, MacDonald L, Malik I, Mawdsley J, Marsden S, McAllister G, Meredith K, Meth-Cohn D, Mishra B, Moore J, Mustafa A, Narasimhan S, Naray S T K, Nazir K, Norris A, Nune A, Picton M, Prakash P K, Prouten J, Rathur H, Roberts K, Rothwell N, Rowles S, S Rashid S, Savage M, Shah S, Shingler W, Smith G, Smith K V, Smithurst H, S-Samavi M, Stott R, Sudagani J, Suliman M, Tarpey S, Taylor A, Taylor E, Weaver A, West A, Wild J, Wiles P. **Pilgrim Hospital:** Htwe N, Jacob K. **Pontefract General Infirmary:** Bissell J, Howell J, White C. **QE 2 Hospital, Welwyn Garden City:** Ali S, Chirayath H, Darzy K, Ford M, George S, Kaplan F, Lecamwasam V, Perera S, Qureshi S A, Scott R, Htay T, Winocour P, Wyman D, Zalin B. **Queens Romford:** Khan K, Nkonge F. **Roebuck House (Surgery 1):** Dicker C, Rowan J, White T. **Rotherham General Hospital:** Franke B, Muzulu S, Salam S. **Royal Blackburn Hospital:** Demssie Y, Glew M, Jones G, Jostel, A, Littley M, Mishra M, Prouten J, Ramtoola S, Wilkinson R. **Royal Devon and Exeter Hospital:** Aziz A, Babiker T, Brooks A, Lockett H. **Royal Gwent Hospital:** DaCruz T, Kamath C, Obuobie K. **Royal Infirmary of Edinburgh:** Inkster B, McLaren J, Zammitt N. **Royal Sussex County Hospital, Brighton:** Burberry A. **Royal United Hospital Bath:** Allen K, Higgs E, Naik S, Robinson A, Ward A. **Royal Victoria Hospital Belfast:** Cooke B, Hunter S, McCance D, McErlean U. **Sandwell General Hospital (SWBH):** Bhanderi S, Davies P, Matthews J, Rock K, Sen Gupta P, Thong K Y. **Sedlescombe House Surgery St. Leonards-on-Sea:** Cooper S, Joyce L, Kaliniecki J. **Singleton Hospital, Swansea:** Sorensen M, Udiawar M. **Smethwick Medical Centre (GP) (SWBH):** Bhanderi S, Harrington J, Matthews J, Sen Gupta P. **Southern General Hospital:** Gallagher S, Hutchieson A, Kennon B, Kernohan A, Semple C, Struthers S. **Southmead Hospital:** Gaffar I. **St Bartholomew's and The London NHS Trust:** Coppack S, Gouveia C, Khan R, Waugh J. **St Georges Hospital NHS Trust:** Ahmed F W, Bano G, Firth P, Flanagan A, O'Brien J, Patel N, Wilson Z. **St John's Hospital Livingston:** Adamson K, Teoh W L. **St Marys Hospital, IOW:** Al-Mrayat M, Verlekar P. **St Mary's Hospital, London:** Qureshi S A. **St Stephens Gate Medical Practice (Norfolk PCT) (SSGMP):** Haylock C. **Stepping Hill Hospital:** Kong N, Mumby C. **Stirling Community Hospital (Stirling Royal Infirmary):**, Barwell N, Bramley A, Buchanan L, Currie J, Davidson E, Devlin K, Dewar L, Doig J, Kelly C, MacDonald P, Mackenzie A, Mackintosh L, Peden N, Ryan L, Simpson C, Whitty H.**Stobhill Hospital, Glasgow:** Acquah R, Drummond R, Gordon D, Leggett G, MacEwen A, McKenzie J, McLaren J, Panarelli M, Smith C. **Stoke Mandeville:** Stokes V. **The Ipswich Hospital:** Astle J, Fowler D, Morris D, Parkinson C, Rayman G, Thomas M. **Torbay Hospital:** Dimitropoulos I, Dyer R, Lissett K, Paisey R, Smith J, Weekes C. **Trafford General Hospital:** Adamson C, George A, Hopewell L, Marchi C, Snell A, Stephens W P. **Tyrone County Hospital:** Bradley P, Evans H, Hameed A, Helmy A, McGirr B, Monaghan S, Patterson H. **Ulster Hospital:** Au S, Brennan U, Carr S, Donnelly R, Harding J, Harper R, MacDonald P, McIlwaine W, McLaughlin D, Moore L, Mulligan C, Trinick T, Whitehead H. **University College Hospital, London:** Lunken C, Patel D. **University Hospital of Durham:** Kashif M. **University Hospital of Hartlepool:** Anthony S, Ijaz S, Jones S, Sinclair J, Worrall E. **University Hospital of North Tees:** Dobson M, MacLeod J, Manohar S P, Mehaffy J, Presgrave M, Pye S, Robinson M, Roper N, Worrall E. **Victoria Hospital Kirkcaldy (Kirkcaldy Acute Hospitals NHS Trust):** Baird J, Burns D, Chalmers J, Creagh M, Duncan C, Patterson C, Swaminathan K. **Warrior Square Surgery:** Adams S, Dunlop A, Ottaway L. **West Suffolk Hospital:** Clarke J, Moss A. **Western General Hospital:** Inkster B, Kochhar R S, Mathur S, Mclaren, Zammitt N. **Western Isles Hospital:** Achar K N. **Westmoreland General Hospital:** Banerjee M, Obale B, Pearce D, Tong M. **Wharfedale Hospital:** Amery C. **Wiltshire NHS Primary Care Trust:** Hall B, Hillier N. **Wrexham Maelor:** Dixon A, Lansdowne A. **Wythenshawe Hospital (UHSM):** Younis N. **Yeovil District Hospital NHS Foundation Trust:** Bickerton A, Crocker M, Pramodh S. **Ysbyty Ystrad Mynach:** Premawardhana L D.

Acknowledgment

The ABCD nationwide liraglutide audit is an independent audit supported by an unrestricted grant from Novo Nordisk Ltd

Association of British Clinical Diabetologists

ABCD nationwide exenatide and liraglutide audits



- Real-life data
  - >13000 patients from
  - >150 centres
  - >500 contributors
- There had been (by 2019)
  - 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

ABCD
Association of British Clinical Diabetologists

What did we learn from these audits?

Association of British Clinical Diabetologists

ABCD GLP1-RA audits v clinical trials

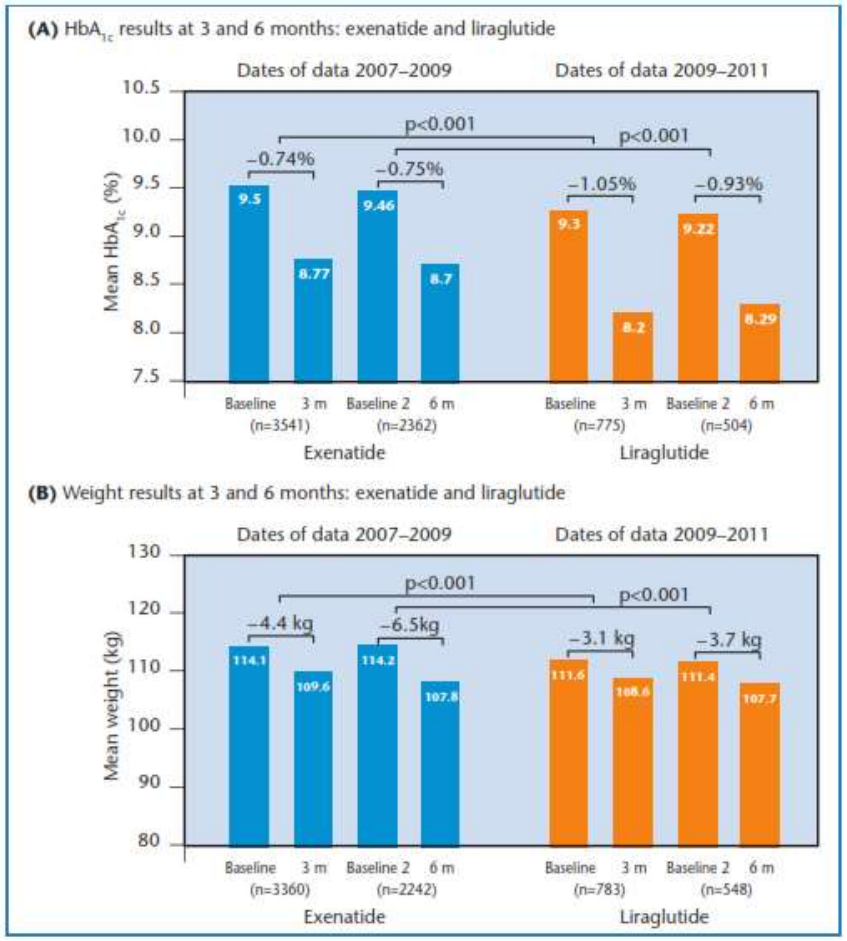
	Clinical trials combined	Real clinical use in UK (ABCD audit)
	Baseline HbA_{1c} (%)	
Exenatide	8.37	9.47
Liraglutide	8.5	9.40
	Baseline BMI (kg/m^2)	
Exenatide	32.72	39.8
Liraglutide	31	39.0

- The patients treated with GLP1-RAs in real clinical practice are much heavier and with much poorer glycaemic control than in clinical trials of these agents
- Nevertheless the agents have proven to be very effective

Ryder and Thong. In Hot topics in diabetes, 5th edition, Vora J, ed. Synergy, London, 2012: 49-61: http://www.diabetologists-abcd.org.uk/GLP1_Audits/ABCD_Hot_Topics_2012.pdf

ABCD
Association of British Clinical Diabetologists

Difference in HbA1c and weight responses – exenatide v liraglutide audits

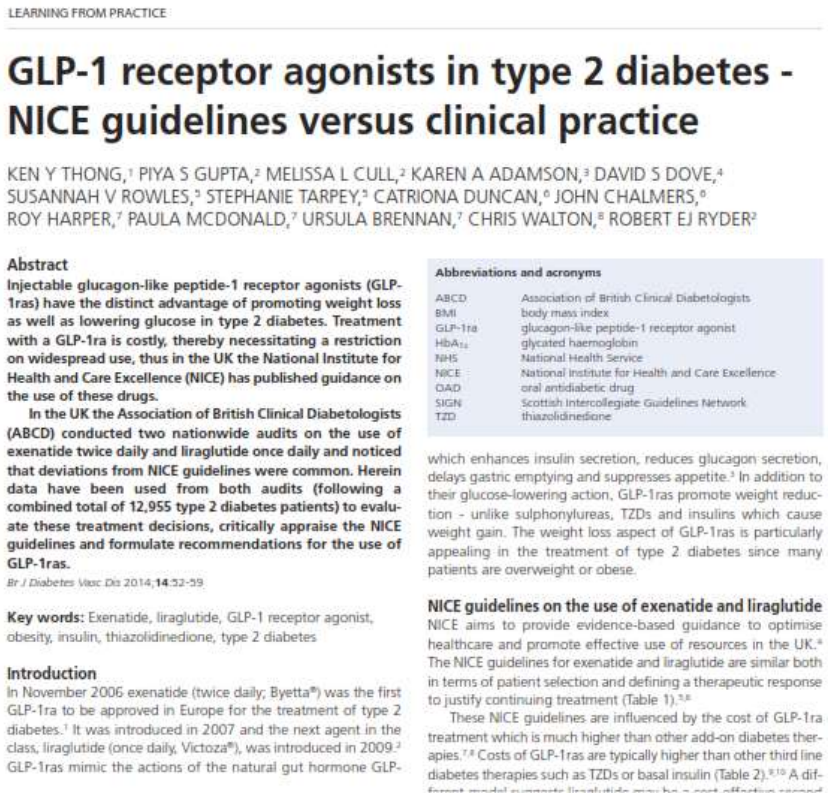


- Patients appear to achieve greater HbA1c reduction but lesser weight reduction in the liraglutide audit as compared with the exenatide audit
- However, there was much less insulin and TZD discontinuation in the liraglutide audit
- Contributors may have learnt from the previous use of exenatide (2007-2009) to avoid over-reduction of diabetes treatment when initiating liraglutide (2009-2011)

Ryder and Thong. In Hot topics in diabetes, 5th edition, Vora J, ed. Synergy, London, 2012: 49-61: http://www.diabetologists-abcd.org.uk/GLP1_Audits/ABCD_Hot_Topics_2012.pdf

ABCD
Association of British Clinical Diabetologists

Reality versus NICE guidelines



LEARNING FROM PRACTICE

GLP-1 receptor agonists in type 2 diabetes - NICE guidelines versus clinical practice

KEN Y THONG,[1] PIYA S GUPTA,[2] MELISSA L CULL,[2] KAREN A ADAMSON,[3] DAVID S DOVE,[4] SUSANNAH V ROWLES,[5] STEPHANIE TARPEY,[5] CATRIONA DUNCAN,[6] JOHN CHALMERS,[6] ROY HARPER,[7] PAULA MCDONALD,[7] URSULA BRENNAN,[7] CHRIS WALTON,[8] ROBERT EJ RYDER[2]

Abstract

Injectable glucagon-like peptide-1 receptor agonists (GLP-1ras) have the distinct advantage of promoting weight loss as well as lowering glucose in type 2 diabetes. Treatment with a GLP-1ra is costly, thereby necessitating a restriction on widespread use, thus in the UK the National Institute for Health and Care Excellence (NICE) has published guidance on the use of these drugs.

In the UK the Association of British Clinical Diabetologists (ABCD) conducted two nationwide audits on the use of exenatide twice daily and liraglutide once daily and noticed that deviations from NICE guidelines were common. Herein data have been used from both audits (following a combined total of 12,955 type 2 diabetes patients) to evaluate these treatment decisions, critically appraise the NICE guidelines and formulate recommendations for the use of GLP-1ras.

Br J Diabetes Vasc Dis 2014;**14**:52-59

Key words: Exenatide, liraglutide, GLP-1 receptor agonist, obesity, insulin, thiazolidinedione, type 2 diabetes

Abbreviations and acronyms

ABCD	Association of British Clinical Diabetologists
BMI	body mass index
GLP-1ra	glucagon-like peptide-1 receptor agonist
HbA_{1c}	glycated haemoglobin
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OAD	oral antidiabetic drug
SIGN	Scottish Intercollegiate Guidelines Network
TZD	thiazolidinedione

Introduction

In November 2006 exenatide (twice daily; Byetta®) was the first GLP-1ra to be approved in Europe for the treatment of type 2 diabetes.[1] It was introduced in 2007 and the next agent in the class, liraglutide (once daily, Victoza®), was introduced in 2009.[2] GLP-1ras mimic the actions of the natural gut hormone GLP-1, which enhances insulin secretion, reduces glucagon secretion, delays gastric emptying and suppresses appetite.[3] In addition to their glucose-lowering action, GLP-1ras promote weight reduction - unlike sulphonylureas, TZDs and insulins which cause weight gain. The weight loss aspect of GLP-1ras is particularly appealing in the treatment of type 2 diabetes since many patients are overweight or obese.

NICE guidelines on the use of exenatide and liraglutide

NICE aims to provide evidence-based guidance to optimise healthcare and promote effective use of resources in the UK.[4] The NICE guidelines for exenatide and liraglutide are similar both in terms of patient selection and defining a therapeutic response to justify continuing treatment (Table 1).[5,6]

These NICE guidelines are influenced by the cost of GLP-1ra treatment which is much higher than other add-on diabetes therapies.[7,8] Costs of GLP-1ras are typically higher than other third line diabetes therapies such as TZDs or basal insulin (Table 2).[9,10] A dif-

- Exenatide and liraglutide used outside NICE guidelines in substantial numbers of patients
- Proven effective in outside NICE guidelines
- In particular used with insulin (40% in the nationwide liraglutide audit) with good effect in many patients
- The NICE 6 month weight loss (≥ 3% initial body weight) and HbA1c fall (≥ 1%) criteria are too restrictive by not taking into account the diversity of patients and their responses which can be much more one criterion than the other

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

ABCD
Association of British Clinical Diabetologists

Off licence use with insulin

original article

Diabetes, Obesity and Metabolism 13: 703–710, 2011.

Safety, efficacy and tolerability of exenatide in combination with insulin in the Association of British Clinical Diabetologists nationwide exenatide audit*

ORIGINAL ARTICLE

K. Y. Thong[1], B. Jose[1], N. Sukumar[1], M. L. Cull[1], A. P. Mills[1], T. Sathyapalan[2], W. Shafiq[2], A. S. Rigby[2], C. Walton[2] & R. E. J. Ryder[1] on behalf of the ABCD nationwide exenatide audit contributors†

[1]Department of Diabetes, City Hospital, Birmingham, UK
[2]Department of Diabetes, Hull Royal Infirmary, Hull, UK

Aim: To assess the extent, safety, efficacy and tolerability of reported off-licence exenatide use through a nationwide audit.
Methods: The Association of British Clinical Diabetologists hosted a password-protected, online collection of anonymized data of exenatide use in real clinical practice. Three hundred and fifteen contributors from 126 centres across UK provided data on 6717 patients. HbA1c and weight changes, exenatide discontinuation, adverse events and treatment satisfaction were compared between non-insulin and insulin-treated patients.
Results: Four thousand eight hundred and fifty-seven patients had baseline and follow-up treatment status with mean (±s.d.) baseline HbA1c 9.45 ± 1.69% and BMI 40.0 ± 8.2 kg/m^2. Of the 4857 patients, 1921 (39.6%) used exenatide with insulin. Comparing patients who continued insulin with exenatide with non-insulin-treated patients, mean (±s.e.) latest HbA1c and weight reduction (median 26 weeks) were 0.51 ± 0.06 versus 0.94 ± 0.04% ($p < 0.001$) and 5.8 ± 0.2 versus 5.5 ± 0.1 kg ($p = 0.278$). Insulin-treated patients had higher rates of exenatide discontinuation (31.0 vs. 13.9%, $p < 0.001$), hypoglycaemia (8.9 vs. 6.1%, $p < 0.001$), gastrointestinal side effects (28.4 vs. 25.0%, $p = 0.008$) and treatment dissatisfaction (20.8 vs. 5.7%, $p < 0.001$). However, 34.2% of the patients continuing insulin still achieved HbA1c reduction ≥1%. There was significant insulin discontinuation, dose reduction and greater sulphonylurea discontinuation among insulin-treated patients.
Conclusions: Addition of exenatide to obese, insulin-treated patients can improve glycaemia and weight. Adverse events were statistically but probably not clinically significantly higher, but combination treatment was less well tolerated. Overall, exenatide was less effective in lowering HbA1c among insulin-treated patients, although significant number of insulin-treated patients still achieved significant HbA1c, weight and insulin reductions. Further research into identifying obese, insulin-treated patients who will tolerate and benefit from exenatide treatment is urgently needed.
Keywords: exenatide, GLP-1 analogue, incretin therapy, insulin therapy, type 2 diabetes

Date submitted 29 December 2010; date of first decision 7 February 2011; date of final acceptance 9 March 2011

- Off licence exenatide with insulin safe and effective in real clinical practice
- Reduction in insulin dose frequently occurred
- Weight fell
- 1 in 6 patients came off insulin

Thong et al. Diabetes, Obesity and Metabolism 2011; 13(8): 703-710

Association of British Clinical Diabetologists

An important safety issue uncovered

DIABETES RESEARCH AND CLINICAL PRACTICE 93 (2011) e87–e91

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

ELSEVIER

International Diabetes Federation

Brief report

Response at 3 months to insulin dose decisions made at exenatide initiation in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit

K.Y. Thong [a,1,*], B. Jose [a,1], A.D. Blann [a,1], M.L. Cull [a,1], A.P. Mills [a,1], T. Sathyapalan [b,1], C. Walton [b,1], R.E.J. Ryder [a,1]

[a] City Hospital, Birmingham, United Kingdom
[b] Hull Royal Infirmary, Hull, United Kingdom

ARTICLE INFO

Article history:
Received 20 February 2011
Received in revised form
12 April 2011
Accepted 5 May 2011
Published on line 1 June 2011

Keywords:
Exenatide
GLP-1 agonist
Insulin treatment
Obesity
Type 2 diabetes

ABSTRACT

It is uncertain what should be done with insulin dose if starting exenatide. In the ABCD nationwide exenatide audit, many patients with type 2 diabetes had worsened glycaemia when insulin was stopped. If starting exenatide, insulin should not be stopped but weaned off only if there is significant glycaemic response.

- Some clinicians attempted to stop insulin when starting exenatide in order to stay within guidelines
- This led to harm to the patient in some instances
- For example there are 11 reported cases of ketosis or diabetic ketoacidosis - 7 of these occurred to patients who stopped insulin at the time of exenatide initiation
- Analysis of audit data allowed us to recommend that when starting a GLP1-RA in an insulin-treated patient not to stop the insulin but rather to tail the insulin off during treatment if response to treatment allowed

Thong et al. Diabetes Res Clin Pract. 2011; 93(2): e87-e91

ABCD
Association of British Clinical Diabetologists

Pancreatitis


BMJ

FEATURE

DIABETES DRUGS

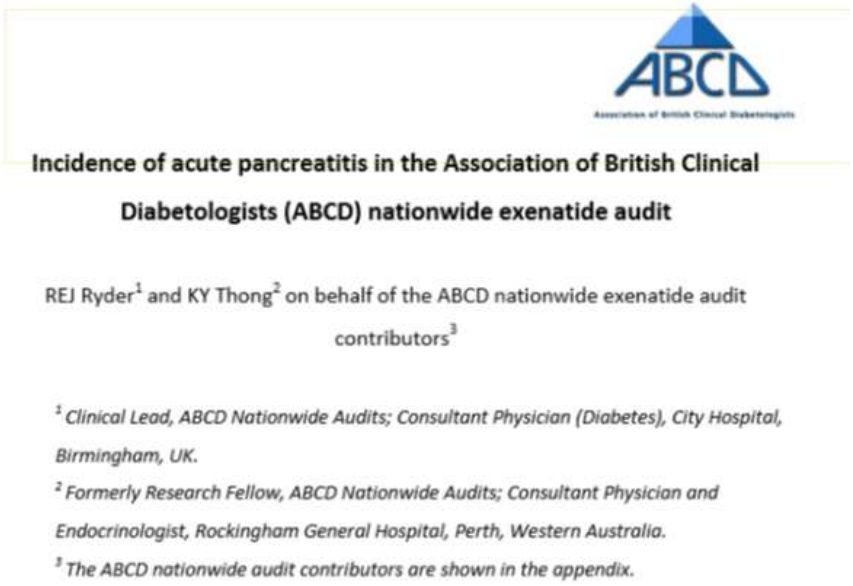
Has pancreatic damage from glucagon suppressing diabetes drugs been underplayed?

Cohen D. Br Med J 2013; 346: f3680

- Alarm raised (BMJ and Channel 4 Dispatches TV programme) in 2013 that incretin therapies might cause pancreatic damage
- We have been able to contribute by publishing data suggesting that in the ABCD audits there is no evidence of such a side effect:

ABCD
Association of British Clinical Diabetologists

Rates of acute pancreatitis in people with type 2 diabetes



Incidence of acute pancreatitis in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit

REJ Ryder[1] and KY Thong[2] on behalf of the ABCD nationwide exenatide audit contributors[3]

[1] *Clinical Lead, ABCD Nationwide Audits; Consultant Physician (Diabetes), City Hospital, Birmingham, UK.*

[2] *Formerly Research Fellow, ABCD Nationwide Audits; Consultant Physician and Endocrinologist, Rockingham General Hospital, Perth, Western Australia.*

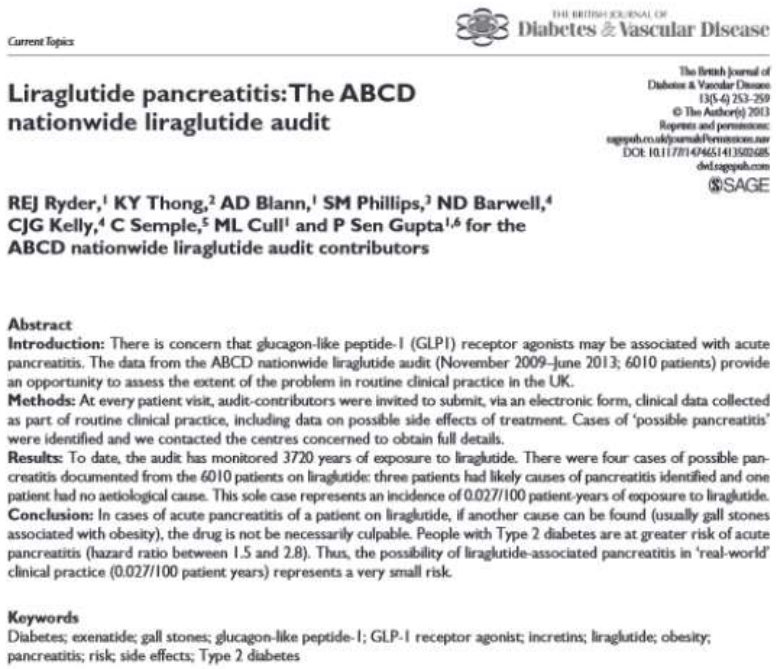
[3] *The ABCD nationwide audit contributors are shown in the appendix.*

- Not on GLP-1 based therapy:
  - between 5 and 56 per 10,000 person years
- ABCD nationwide exenatide audit
  - 12 per 10,000 person year
- ABCD nationwide liraglutide audit
  - 10.8 per 10,000 person years

http://www.diabetologists-abcd.org.uk/GLP1_Audits/pancreatitis_incidence_exenatide_audit.pdf

Association of British Clinical Diabetologists

Rates of acute pancreatitis in people with type 2 diabetes



Current Topics

THE BRITISH JOURNAL OF Diabetes & Vascular Disease

The British Journal of Diabetes & Vascular Disease
13(5-6) 253-259

DOI: 10.1177/1474651413502685
dvd.sagepub.com
SAGE

Liraglutide pancreatitis: The ABCD nationwide liraglutide audit

REJ Ryder,[1] KY Thong,[2] AD Blann,[1] SM Phillips,[3] ND Barwell,[4] CJG Kelly,[4] C Semple,[5] ML Cull[1] and P Sen Gupta[1,6] for the ABCD nationwide liraglutide audit contributors

Abstract

Introduction: There is concern that glucagon-like peptide-1 (GLP1) receptor agonists may be associated with acute pancreatitis. The data from the ABCD nationwide liraglutide audit (November 2009–June 2013; 6010 patients) provide an opportunity to assess the extent of the problem in routine clinical practice in the UK.

Methods: At every patient visit, audit-contributors were invited to submit, via an electronic form, clinical data collected as part of routine clinical practice, including data on possible side effects of treatment. Cases of 'possible pancreatitis' were identified and we contacted the centres concerned to obtain full details.

Results: To date, the audit has monitored 3720 years of exposure to liraglutide. There were four cases of possible pancreatitis documented from the 6010 patients on liraglutide: three patients had likely causes of pancreatitis identified and one patient had no aetiological cause. This sole case represents an incidence of 0.027/100 patient-years of exposure to liraglutide.

Conclusion: In cases of acute pancreatitis of a patient on liraglutide, if another cause can be found (usually gall stones associated with obesity), the drug is not be necessarily culpable. People with Type 2 diabetes are at greater risk of acute pancreatitis (hazard ratio between 1.5 and 2.8). Thus, the possibility of liraglutide-associated pancreatitis in 'real-world' clinical practice (0.027/100 patient years) represents a very small risk.

Keywords

Diabetes; exenatide; gall stones; glucagon-like peptide-1; GLP-1 receptor agonist; incretins; liraglutide; obesity; pancreatitis; risk; side effects; Type 2 diabetes

- Rates of acute pancreatitis in the ABCD exenatide and liraglutide audits are at the low end of the rates expected for people with type 2 diabetes in general.

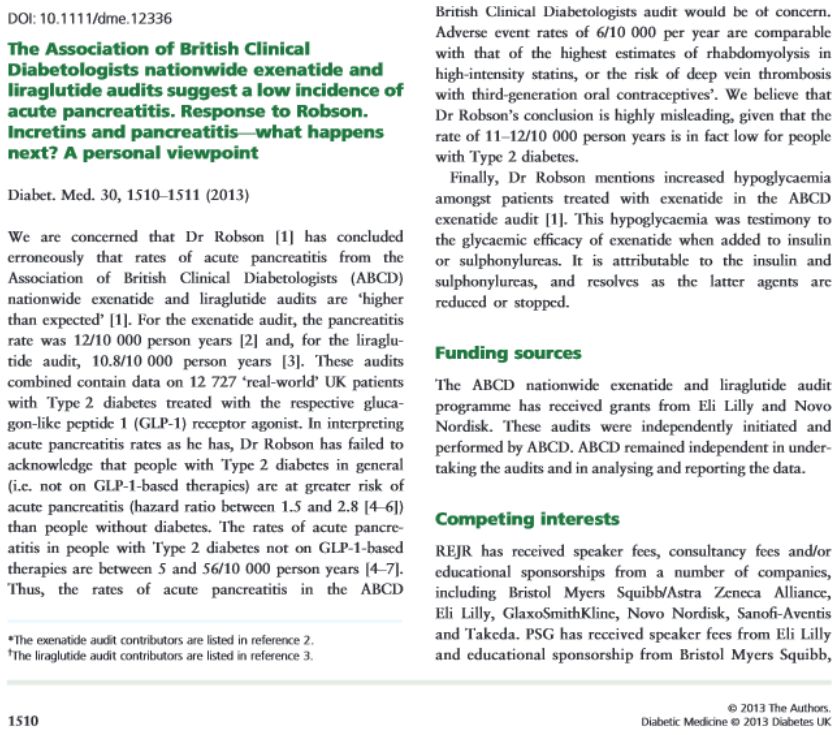
AND

- 75% of the cases of acute pancreatitis in the ABCD exenatide and liraglutide audits had other causes for acute pancreatitis, in particular gall bladder disease

Ryder and Thong. Br J Diabetes Vasc Dis 2013; 13: 253-259

ABCD
Association of British Clinical Diabetologists

Otherwise unexplained pancreatitis – is it likely to be due to the GLP-1RA?



DOI: 10.1111/dme.12336

The Association of British Clinical Diabetologists nationwide exenatide and liraglutide audits suggest a low incidence of acute pancreatitis. Response to Robson. Incretins and pancreatitis—what happens next? A personal viewpoint

Diabet. Med. 30, 1510–1511 (2013)

We are concerned that Dr Robson [1] has concluded erroneously that rates of acute pancreatitis from the Association of British Clinical Diabetologists (ABCD) nationwide exenatide and liraglutide audits are 'higher than expected' [1]. For the exenatide audit, the pancreatitis rate was 12/10 000 person years [2] and, for the liraglutide audit, 10.8/10 000 person years [3]. These audits combined contain data on 12 727 'real-world' UK patients with Type 2 diabetes treated with the respective glucagon-like peptide 1 (GLP-1) receptor agonist. In interpreting acute pancreatitis rates as he has, Dr Robson has failed to acknowledge that people with Type 2 diabetes in general (i.e. not on GLP-1-based therapies) are at greater risk of acute pancreatitis (hazard ratio between 1.5 and 2.8 [4–6]) than people without diabetes. The rates of acute pancreatitis in people with Type 2 diabetes not on GLP-1-based therapies are between 5 and 56/10 000 person years [4–7]. Thus, the rates of acute pancreatitis in the ABCD British Clinical Diabetologists audit would be of concern. Adverse event rates of 6/10 000 per year are comparable with that of the highest estimates of rhabdomyolysis in high-intensity statins, or the risk of deep vein thrombosis with third-generation oral contraceptives'. We believe that Dr Robson's conclusion is highly misleading, given that the rate of 11–12/10 000 person years is in fact low for people with Type 2 diabetes.

Finally, Dr Robson mentions increased hypoglycaemia amongst patients treated with exenatide in the ABCD exenatide audit [1]. This hypoglycaemia was testimony to the glycaemic efficacy of exenatide when added to insulin or sulphonylureas. It is attributable to the insulin and sulphonylureas, and resolves as the latter agents are reduced or stopped.

Funding sources

The ABCD nationwide exenatide and liraglutide audit programme has received grants from Eli Lilly and Novo Nordisk. These audits were independently initiated and performed by ABCD. ABCD remained independent in undertaking the audits and in analysing and reporting the data.

Competing interests

REJR has received speaker fees, consultancy fees and/or educational sponsorships from a number of companies, including Bristol Myers Squibb/Astra Zeneca Alliance, Eli Lilly, GlaxoSmithKline, Novo Nordisk, Sanofi-Aventis and Takeda. PSG has received speaker fees from Eli Lilly and educational sponsorship from Bristol Myers Squibb,

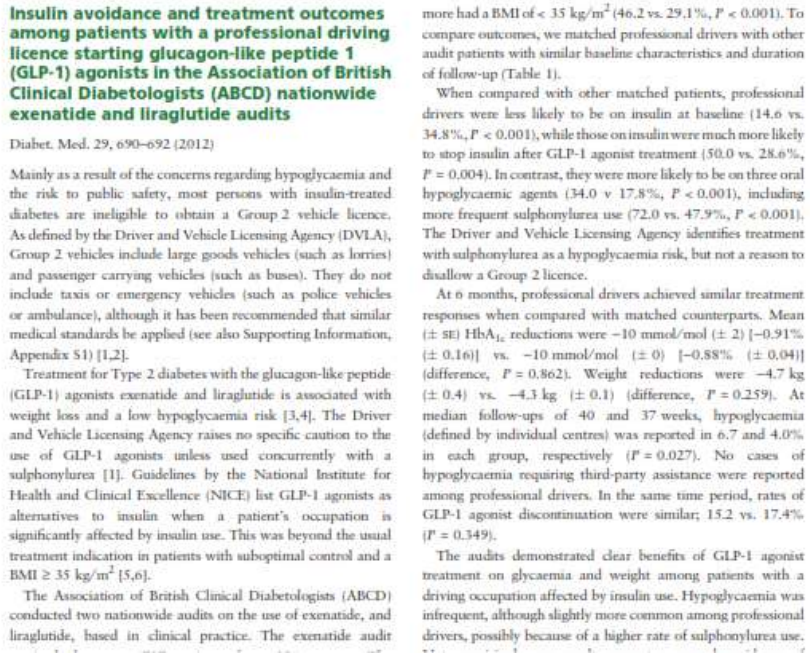
*The exenatide audit contributors are listed in reference 2.
†The liraglutide audit contributors are listed in reference 3.

- ….it is worth remembering that many cases of acute pancreatitis are "idiopathic" ….
- ….hence exenatide or liraglutide may not be the actual cause even if no other cause is found

Ryder et al. Diabetic Medicine 2013; 30(12): 1510-1511

ABCD
Association of British Clinical Diabetologists

GLP1-RAs in professional drivers



Insulin avoidance and treatment outcomes among patients with a professional driving licence starting glucagon-like peptide 1 (GLP-1) agonists in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide and liraglutide audits

Diabet. Med. 29, 690–692 (2012)

Mainly as a result of the concerns regarding hypoglycaemia and the risk to public safety, most persons with insulin-treated diabetes are ineligible to obtain a Group 2 vehicle licence. As defined by the Driver and Vehicle Licensing Agency (DVLA), Group 2 vehicles include large goods vehicles (such as lorries) and passenger carrying vehicles (such as buses). They do not include taxis or emergency vehicles (such as police vehicles or ambulance), although it has been recommended that similar medical standards be applied (see also Supporting Information, Appendix S1) [1,2].

Treatment for Type 2 diabetes with the glucagon-like peptide (GLP-1) agonists exenatide and liraglutide is associated with weight loss and a low hypoglycaemia risk [3,4]. The Driver and Vehicle Licensing Agency raises no specific caution to the use of GLP-1 agonists unless used concurrently with a sulphonylurea [1]. Guidelines by the National Institute for Health and Clinical Excellence (NICE) list GLP-1 agonists as alternatives to insulin when a patient's occupation is significantly affected by insulin use. This was beyond the usual treatment indication in patients with suboptimal control and a BMI ≥ 35 kg/m^2 [5,6].

The Association of British Clinical Diabetologists (ABCD) conducted two nationwide audits on the use of exenatide, and liraglutide, based in clinical practice. The exenatide audit

more had a BMI of < 35 kg/m^2 (46.2 vs. 29.1%, $P < 0.001$). To compare outcomes, we matched professional drivers with other audit patients with similar baseline characteristics and duration of follow-up (Table 1).

When compared with other matched patients, professional drivers were less likely to be on insulin at baseline (14.6 vs. 34.8%, $P < 0.001$), while those on insulin were much more likely to stop insulin after GLP-1 agonist treatment (50.0 vs. 28.6%, $P = 0.004$). In contrast, they were more likely to be on three oral hypoglycaemic agents (34.0 v 17.8%, $P < 0.001$), including more frequent sulphonylurea use (72.0 vs. 47.9%, $P < 0.001$). The Driver and Vehicle Licensing Agency identifies treatment with sulphonylurea as a hypoglycaemia risk, but not a reason to disallow a Group 2 licence.

At 6 months, professional drivers achieved similar treatment responses when compared with matched counterparts. Mean (± SE) HbA_{1c} reductions were −10 mmol/mol (± 2) [−0.91% (± 0.16)] vs. −10 mmol/mol (± 0) [−0.88% (± 0.04)] (difference, $P = 0.862$). Weight reductions were −4.7 kg (± 0.4) vs. −4.3 kg (± 0.1) (difference, $P = 0.259$). At median follow-ups of 40 and 37 weeks, hypoglycaemia (defined by individual centres) was reported in 6.7 and 4.0% in each group, respectively ($P = 0.027$). No cases of hypoglycaemia requiring third-party assistance were reported among professional drivers. In the same time period, rates of GLP-1 agonist discontinuation were similar; 15.2 vs. 17.4% ($P = 0.349$).

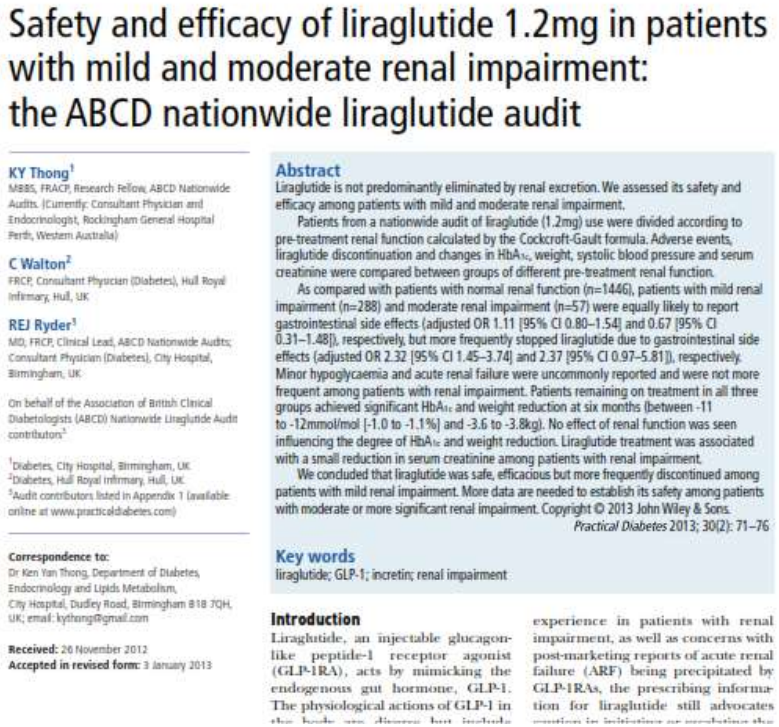
The audits demonstrated clear benefits of GLP-1 agonist treatment on glycaemia and weight among patients with a driving occupation affected by insulin use. Hypoglycaemia was infrequent, although slightly more common among professional drivers, possibly because of a higher rate of sulphonylurea use.

- Many patients with a professional drivers licence who would lose their jobs if they went onto insulin, have been able to avoid insulin, and maintain similar glycaemic outcomes and keep their jobs by using exenatide or liraglutide

Thong et al. Diabetic Medicine 2012; 29(5): 690-692

Association of British Clinical Diabetologists

Liraglutide in renal impairment



Safety and efficacy of liraglutide 1.2mg in patients with mild and moderate renal impairment: the ABCD nationwide liraglutide audit

KY Thong[1]
MBBS, FRACP, Research Fellow, ABCD Nationwide Audits. (Currently: Consultant Physician and Endocrinologist, Rockingham General Hospital Perth, Western Australia)

C Walton[2]
FRCP, Consultant Physician (Diabetes), Hull Royal Infirmary, Hull, UK

REJ Ryder[1]
MD, FRCP, Clinical Lead, ABCD Nationwide Audits; Consultant Physician (Diabetes), City Hospital, Birmingham, UK

On behalf of the Association of British Clinical Diabetologists (ABCD) Nationwide Liraglutide Audit contributors[3]

[1]Diabetes, City Hospital, Birmingham, UK
[2]Diabetes, Hull Royal Infirmary, Hull, UK
[3]Audit contributors listed in Appendix 1 (available online at www.practicaldiabetes.com)

Correspondence to:
Dr Ken Yan Thong, Department of Diabetes, Endocrinology and Lipids Metabolism, City Hospital, Dudley Road, Birmingham B18 7QH, UK; email: kythong@gmail.com

Received: 26 November 2012
Accepted in revised form: 3 January 2013

Abstract

Liraglutide is not predominantly eliminated by renal excretion. We assessed its safety and efficacy among patients with mild and moderate renal impairment.

Patients from a nationwide audit of liraglutide (1.2mg) use were divided according to pre-treatment renal function calculated by the Cockcroft-Gault formula. Adverse events, liraglutide discontinuation and changes in HbA_{1c}, weight, systolic blood pressure and serum creatinine were compared between groups of different pre-treatment renal function.

As compared with patients with normal renal function (n=1446), patients with mild renal impairment (n=288) and moderate renal impairment (n=57) were equally likely to report gastrointestinal side effects (adjusted OR 1.11 [95% CI 0.80–1.54] and 0.67 [95% CI 0.31–1.48]), respectively, but more frequently stopped liraglutide due to gastrointestinal side effects (adjusted OR 2.32 [95% CI 1.45–3.74] and 2.37 [95% CI 0.97–5.81]), respectively. Minor hypoglycaemia and acute renal failure were uncommonly reported and were not more frequent among patients with renal impairment. Patients remaining on treatment in all three groups achieved significant HbA_{1c} and weight reduction at six months (between -11 to -12mmol/mol [-1.0 to -1.1%] and -3.6 to -3.8kg). No effect of renal function was seen influencing the degree of HbA_{1c} and weight reduction. Liraglutide treatment was associated with a small reduction in serum creatinine among patients with renal impairment.

We concluded that liraglutide was safe, efficacious but more frequently discontinued among patients with mild renal impairment. More data are needed to establish its safety among patients with moderate or more significant renal impairment.

Practical Diabetes 2013; 30(2): 71–76

Key words
liraglutide; GLP-1; incretin; renal impairment

Introduction

Liraglutide, an injectable glucagon-like peptide-1 receptor agonist (GLP-1RA), acts by mimicking the endogenous gut hormone, GLP-1. The physiological actions of GLP-1 in

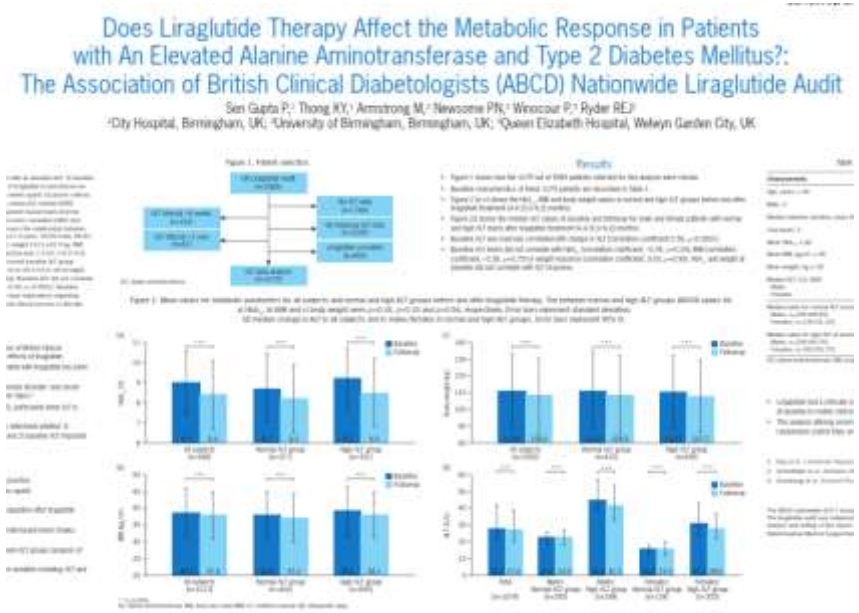
experience in patients with renal impairment, as well as concerns with post-marketing reports of acute renal failure (ARF) being precipitated by GLP-1RAs, the prescribing information for liraglutide still advocates

- Liraglutide was safe and effective among patients with moderate renal impairment, which was an exclusion for use at the time

Thong et al. Practical Diabetes 2013; 30(2): 71-76

Association of British Clinical Diabetologists

Diabetes and NAFLD – impact on ALT



Does Liraglutide Therapy Affect the Metabolic Response in Patients with An Elevated Alanine Aminotransferase and Type 2 Diabetes Mellitus?: The Association of British Clinical Diabetologists (ABCD) Nationwide Liraglutide Audit

Sen Gupta P,[1] Thong KY,[1] Armstrong M,[2] Newsome PN,[3] Winocour P,[4] Ryder RE[5]

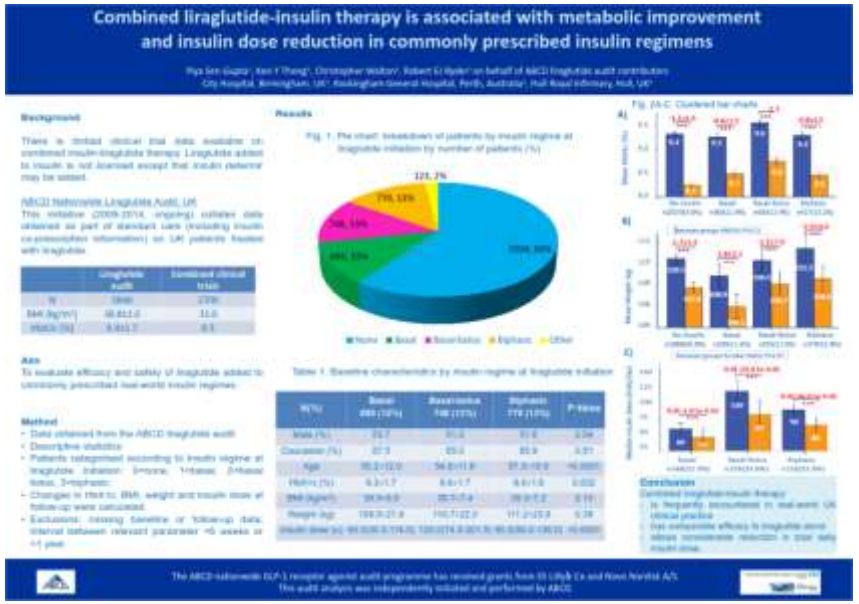
[1]City Hospital, Birmingham, UK; [2]University of Birmingham, Birmingham, UK; [3]Queen Elizabeth Hospital, Welwyn Garden City, UK

- Liraglutide can reduce ALT when it is elevated – ALT being an index of fat in the liver ….

Sen Gupta et al. Diabetes 2013; 62 (Suppl. 1): 1037P

Association of British Clinical Diabetologists

Liraglutide with different insulin regimes

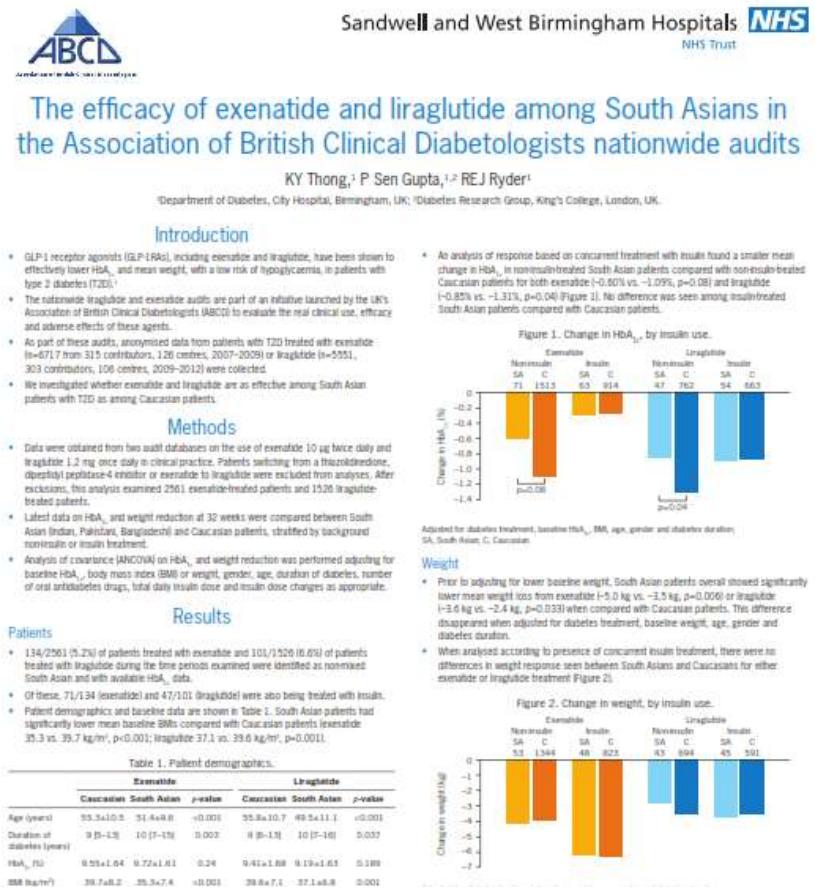


- Liraglutide was effective with all the common insulin regimes - i.e. with:
  - Basal
  - Basal bolus
  - Biphasic

Sen Gupta et al.Diabetes 2014; 63 (Suppl. 1): 1023-P

Association of British Clinical Diabetologists

Effectiveness in South Asians



Sandwell and West Birmingham Hospitals NHS
NHS Trust

The efficacy of exenatide and liraglutide among South Asians in the Association of British Clinical Diabetologists nationwide audits

KY Thong,[1] P Sen Gupta,[1,2] REJ Ryder[1]
[1]Department of Diabetes, City Hospital, Birmingham, UK; [2]Diabetes Research Group, King's College, London, UK.

Introduction

- GLP-1 receptor agonists (GLP-1RAs), including exenatide and liraglutide, have been shown to effectively lower HbA_{1c} and mean weight, with a low risk of hypoglycaemia, in patients with type 2 diabetes (T2D).[1]
- The nationwide liraglutide and exenatide audits are part of an initiative launched by the UK's Association of British Clinical Diabetologists (ABCD) to evaluate the real clinical use, efficacy and adverse effects of these agents.
- As part of these audits, anonymised data from patients with T2D treated with exenatide (n=6717 from 315 contributors, 126 centres, 2007–2009) or liraglutide (n=5551, 303 contributors, 106 centres, 2009–2012) were collected.
- We investigated whether exenatide and liraglutide are as effective among South Asian patients with T2D as among Caucasian patients.

Methods

- Data were obtained from two audit databases on the use of exenatide 10 µg twice daily and liraglutide 1.2 mg once daily in clinical practice. Patients switching from a thiazolidinedione, dipeptidyl peptidase-4 inhibitor or exenatide to liraglutide were excluded from analyses. After exclusions, this analysis examined 2561 exenatide-treated patients and 1526 liraglutide-treated patients.
- Latest data on HbA_{1c} and weight reduction at 32 weeks were compared between South Asian (Indian, Pakistani, Bangladeshi) and Caucasian patients, stratified by background non-insulin or insulin treatment.
- Analysis of covariance (ANCOVA) on HbA_{1c} and weight reduction was performed adjusting for baseline HbA_{1c}, body mass index (BMI) or weight, gender, age, duration of diabetes, number of oral antidiabetes drugs, total daily insulin dose and insulin dose changes as appropriate.

Results

Patients

- 134/2561 (5.2%) of patients treated with exenatide and 101/1526 (6.6%) of patients treated with liraglutide during the time periods examined were identified as non-mixed South Asian and with available HbA_{1c} data.
- Of these, 71/134 (exenatide) and 47/101 (liraglutide) were also being treated with insulin.
- Patient demographics and baseline data are shown in Table 1. South Asian patients had significantly lower mean baseline BMIs compared with Caucasian patients (exenatide 35.3 vs. 39.7 kg/m², p<0.001; liraglutide 37.1 vs. 39.6 kg/m², p=0.001).

Table 1. Patient demographics.

	Exenatide			Liraglutide		
	Caucasian	South Asian	*p*-value	Caucasian	South Asian	*p*-value
Age (years)	55.3±10.5	51.4±9.8	<0.001	55.8±10.7	49.5±11.1	<0.001
Duration of diabetes (years)	3 [0–13]	10 [7–13]	0.003	4 [0–13]	10 [7–16]	0.037
HbA_{1c} (%)	8.55±1.64	8.72±1.61	0.24	8.41±1.88	8.19±1.63	0.189
BMI (kg/m²)	39.7±8.2	35.3±7.4	<0.001	39.6±7.1	37.1±6.8	0.001

- An analysis of response based on concurrent treatment with insulin found a smaller mean change in HbA_{1c} in non-insulin-treated South Asian patients compared with non-insulin-treated Caucasian patients for both exenatide (–0.60% vs. –1.09%, p=0.08) and liraglutide (–0.85% vs. –1.31%, p=0.04) (Figure 1). No difference was seen among insulin-treated South Asian patients compared with Caucasian patients.

Figure 1. Change in HbA_{1c}, by insulin use.

Adjusted for: diabetes treatment, baseline HbA_{1c}, BMI, age, gender and diabetes duration; SA, South Asian; C, Caucasian.

Weight

- Prior to adjusting for lower baseline weight, South Asian patients overall showed significantly lower mean weight loss from exenatide (–5.0 kg vs. –3.5 kg, p=0.006) or liraglutide (–3.6 kg vs. –2.4 kg, p=0.033) when compared with Caucasian patients. This difference disappeared when adjusted for diabetes treatment, baseline weight, age, gender and diabetes duration.
- When analysed according to presence of concurrent insulin treatment, there were no differences in weight response seen between South Asians and Caucasians for either exenatide or liraglutide treatment (Figure 2).

Figure 2. Change in weight, by insulin use.

- GLP1-RAs may be less effective at improving glycaemic control amongst non-insulin treated South Asians

Thong et al. Abstract Book, 22nd World Diabetes Congress, IDF, Melbourne, Australia, 2-6 December 2013

Association of British Clinical Diabetologists

Liraglutide – predicting treatment response

LEARNING FROM PRACTICE

Insulin treatment and longer diabetes duration both predict poorer glycaemic response to liraglutide treatment in type 2 diabetes: the Association of British Clinical Diabetologists Nationwide Liraglutide Audit

KEN Y THONG,[1] BARBARA M MCGOWAN,[2] THEIN HTAY,[3] ANDREW PERNET,[4] CHRIS KELLY,[5] CHINNADORAI RAJESWARAN,[6] JILL HOWELL,[7] CATRIONA DUNCAN,[8] BERIT INKSTER,[9] LINDA BUCHANAN,[10] SAIFUL KASSIM,[11] RAHUL NAYER,[12] NICHOLAS D BARWELL,[13] CHRISTOPHER WALTON,[12] ROBERT EJ RYDER,[14] ABCD NATIONWIDE LIRAGLUTIDE AUDIT CONTRIBUTORS[15]

Abstract

Background: Liraglutide may be less effective in patients with more advanced type 2 diabetes. This study from the Association of British Clinical Diabetologists Nationwide Liraglutide Audit analysed changes in HbA_{1c} of patients after 26 weeks of treatment with liraglutide 1.2 mg, stratified according to the intensity of their background diabetes therapy, or according to their duration of diabetes.

Methods: Patients using liraglutide as add-on therapy were stratified for receipt to one, two or three oral antidiabetic agents (OADs) or insulin (± OAD), or for diabetes duration of 0–5 years, 6–10 years, or >10 years. Changes in HbA_{1c} were compared across groups after adjusting for baseline HbA_{1c}.

Results: After exclusions to standardise comparisons, 932 patients with background diabetes treatment and 802 patients with recorded diabetes duration were analysed. Least-squares adjusted mean changes in HbA_{1c} (± SEM) were −1.8% ± 0.1 for 135 patients on one OAD, −1.7% ± 0.1 for 284 patients on two OADs, −1.9% ± 0.1 for 94 patients on three OADs (n=94) and −1.0% ± 0.1 for 424 patients receiving insulin. HbA_{1c} changes did not differ significantly between OAD groups, but all OAD groups had greater HbA_{1c} reductions compared with the insulin group (all p<0.00001). Adjusted mean HbA_{1c} changes were −2.0% ± 0.1 for patients with diabetes duration 0–5 years (n=147, p≤0.05 vs. longer diabetes durations), −1.6% ± 0.1 for 6–10 years (n=256), and −1.2% ± 0.1 for >10 years (n=399).

Conclusion: The need for insulin and long diabetes duration, but not the number of OADs taken, predicted a smaller treatment response to liraglutide.

Key words: type 2 diabetes, liraglutide, insulin, diabetes duration, oral antidiabetic drug

Introduction

Guidelines for the management of type 2 diabetes place a strong emphasis on the need for personalised antidiabetic treatment.[1] Accordingly, it is important to identify factors which predispose to an optimum treatment response to a given antidiabetic therapy. Liraglutide is a once-daily GLP-1 receptor agonist approved for use alongside diet and exercise in combination with one or more oral antidiabetic agents (OADs) or with basal insulin for the management of type 2 diabetes.[2,3]

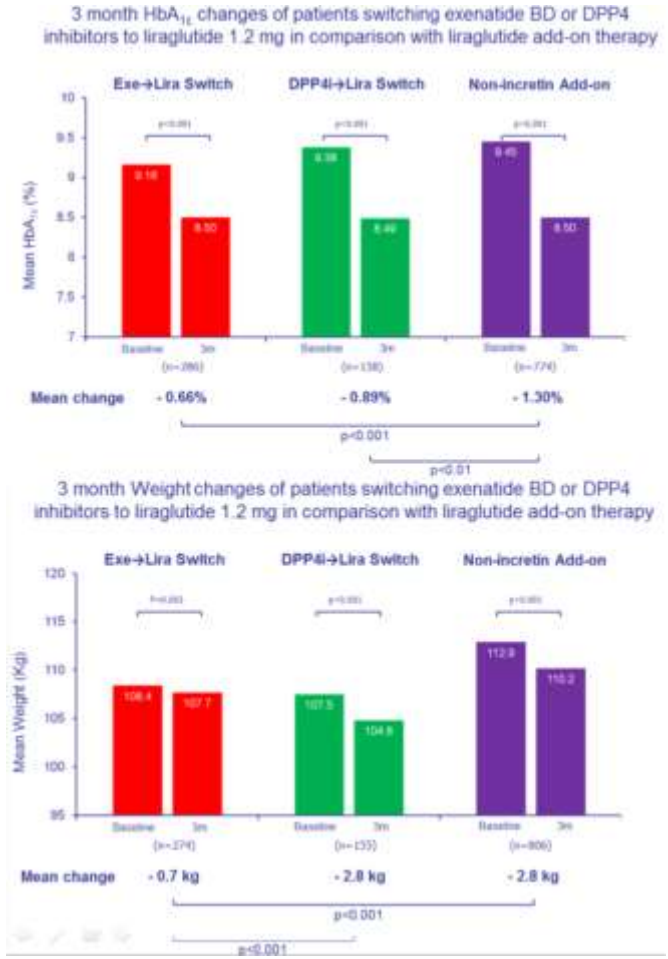
Studies currently reported in abstract form point towards a

- Long duration of diabetes and insulin use both predict reduced response

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

Association of British Clinical Diabetologists

Switching to liraglutide from BD exenatide or from DPP4 inhibitor



- Improvements in HbA1c and weight are seen when switching from exenatide and DPP4 inhibitors to liraglutide

Ryder and Gough. Presentation at IDF Scientific Update Satellite Meeting, Dubai, December 6 2011
http://www.diabetologists-abcd.org.uk/liraglutide_audit/Shared%20Documents/IDF_Dubai2011_SUM.pdf

ABCD
Association of British Clinical Diabetologists

Influence of age and non-use of metformin on GI side effects with liraglutide

DIABETES RESEARCH AND CLINICAL PRACTICE 109 (2015) 124–129

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

ELSEVIER

International Diabetes Federation

The influence of age and metformin treatment status on reported gastrointestinal side effects with liraglutide treatment in type 2 diabetes

K.Y. Thong [a,*], P. Sen Gupta [b], A.D. Blann [c], R.E.J. Ryder [b]

[a] School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia
[b] Diabetes Centre, City Hospital, Birmingham, England, United Kingdom
[c] University of Birmingham Centre for Cardiovascular Science, Department of Medicine, City Hospital, Birmingham, England, United Kingdom

ARTICLE INFO

Article history:
Received 21 January 2015
Received in revised form
23 March 2015
Accepted 14 April 2015
Available online 20 April 2015

Keywords:
GLP-1
Liraglutide
Metformin
Gastrointestinal side effects

ABSTRACT

Aim: Treatment of type 2 diabetes with glucagon-like peptide-1 (GLP-1) receptor agonists may be limited by gastrointestinal side effects (GISE) in some patients. Risk factors for developing GISE are not known. We analysed patient characteristics that were associated with GISE among patients treated with the GLP-1 receptor agonist liraglutide.

Methods: Data was obtained from an audit database of liraglutide use based in clinical practice in the UK. Patients were grouped into those who did not report GISE, those who reported GISE but continued liraglutide and those who discontinued liraglutide due to GISE within 26 weeks of treatment. Baseline variables of age, diabetes duration, HbA_{1c}, weight, BMI, blood pressure, lipids, gender, ethnicity, alanine transaminotransferase, estimated glomerular filtration rate (eGFR) and diabetes treatment types were tested for possible associations with GISE outcome. Significant variables in univariate analyses were entered into ordinal logistic regression analyses.

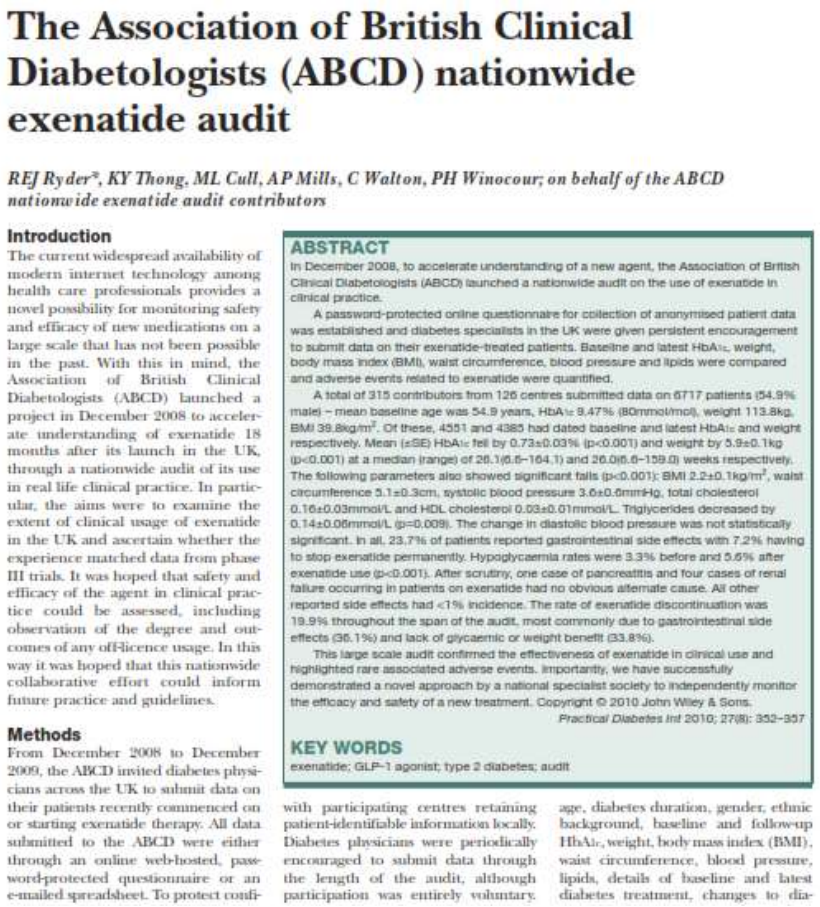
Results: A total of 4442 patients were suitable for analysis. A total of 3905 (87.9%) did not report GISE, 297 (6.7%) and 240 (5.4%) had GISE and continued and discontinued treatment, respectively. Age, weight, eGFR, metformin status and insulin status were associated with GISE outcome in univariate analyses (P all <0.05). In the final regression model, age (adjusted OR 1.15 [95%CI 1.05,1.26], $P = 0.002$) and non-metformin use (adjusted OR 0.76 [95%CI

- Older age and non-metformin use were associated with more significant GISE leading to discontinuation of liraglutide treatment.
- Reasons for these findings are unclear

Thong et al. Diabetes Res Clin Pract. 2015; 109: 124-129

Association of British Clinical Diabetologists

Safety



The Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit

REJ Ryder, KY Thong, ML Cull, AP Mills, C Walton, PH Winocour; on behalf of the ABCD nationwide exenatide audit contributors*

ABSTRACT

In December 2008, to accelerate understanding of a new agent, the Association of British Clinical Diabetologists (ABCD) launched a nationwide audit on the use of exenatide in clinical practice.

A password-protected online questionnaire for collection of anonymised patient data was established and diabetes specialists in the UK were given persistent encouragement to submit data on their exenatide-treated patients. Baseline and latest HbA1c, weight, body mass index (BMI), waist circumference, blood pressure and lipids were compared and adverse events related to exenatide were quantified.

A total of 315 contributors from 126 centres submitted data on 6717 patients (54.9% male) – mean baseline age was 54.9 years, HbA1c 9.47% (80mmol/mol), weight 113.8kg, BMI 39.8kg/m^2. Of these, 4551 and 4385 had dated baseline and latest HbA1c and weight respectively. Mean (±SE) HbA1c fell by 0.73±0.03% ($p<0.001$) and weight by 5.9±0.1kg ($p<0.001$) at a median (range) of 26.1(6.6–164.1) and 26.0(6.6–159.0) weeks respectively. The following parameters also showed significant falls ($p<0.001$): BMI 2.2±0.1kg/m^2, waist circumference 5.1±0.3cm, systolic blood pressure 3.6±0.6mmHg, total cholesterol 0.16±0.03mmol/L and HDL cholesterol 0.03±0.01mmol/L. Triglycerides decreased by 0.14±0.06mmol/L ($p=0.009$). The change in diastolic blood pressure was not statistically significant. In all, 23.7% of patients reported gastrointestinal side effects with 7.2% having to stop exenatide permanently. Hypoglycaemia rates were 3.3% before and 5.6% after exenatide use ($p<0.001$). After scrutiny, one case of pancreatitis and four cases of renal failure occurring in patients on exenatide had no obvious alternate cause. All other reported side effects had <1% incidence. The rate of exenatide discontinuation was 19.9% throughout the span of the audit, most commonly due to gastrointestinal side effects (36.1%) and lack of glycaemic or weight benefit (33.8%).

This large scale audit confirmed the effectiveness of exenatide in clinical use and highlighted rare associated adverse events. Importantly, we have successfully demonstrated a novel approach by a national specialist society to independently monitor the efficacy and safety of a new treatment.

Practical Diabetes Int 2010; 27(8): 352–357

KEY WORDS

exenatide; GLP-1 agonist; type 2 diabetes; audit

Introduction

The current widespread availability of modern internet technology among health care professionals provides a novel possibility for monitoring safety and efficacy of new medications on a large scale that has not been possible in the past. With this in mind, the Association of British Clinical Diabetologists (ABCD) launched a project in December 2008 to accelerate understanding of exenatide 18 months after its launch in the UK, through a nationwide audit of its use in real life clinical practice. In particular, the aims were to examine the extent of clinical usage of exenatide in the UK and ascertain whether the experience matched data from phase III trials. It was hoped that safety and efficacy of the agent in clinical practice could be assessed, including observation of the degree and outcomes of any off-licence usage. In this way it was hoped that this nationwide collaborative effort could inform future practice and guidelines.

Methods

From December 2008 to December 2009, the ABCD invited diabetes physicians across the UK to submit data on their patients recently commenced on or starting exenatide therapy. All data submitted to the ABCD were either through an online web-hosted, password-protected questionnaire or an e-mailed spreadsheet. To protect confidentiality with participating centres retaining patient-identifiable information locally. Diabetes physicians were periodically encouraged to submit data through the length of the audit, although participation was entirely voluntary. age, diabetes duration, gender, ethnic background, baseline and follow-up HbA1c, weight, body mass index (BMI), waist circumference, blood pressure, lipids, details of baseline and latest diabetes treatment, changes to dia-

- In some patients the nausea, vomiting or diarrhoea was so severe that they developed transient acute kidney injury
- There have been no other new safety issues uncovered

Ryder et al. Practical Diabetes International 2010; 27(8): 352-357

Association of British Clinical Diabetologists

Conclusion

- We learned a lot from these audits
- Lets do some more audits!

Association of British Clinical Diabetologists

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD
Association of British Clinical Diabetologists

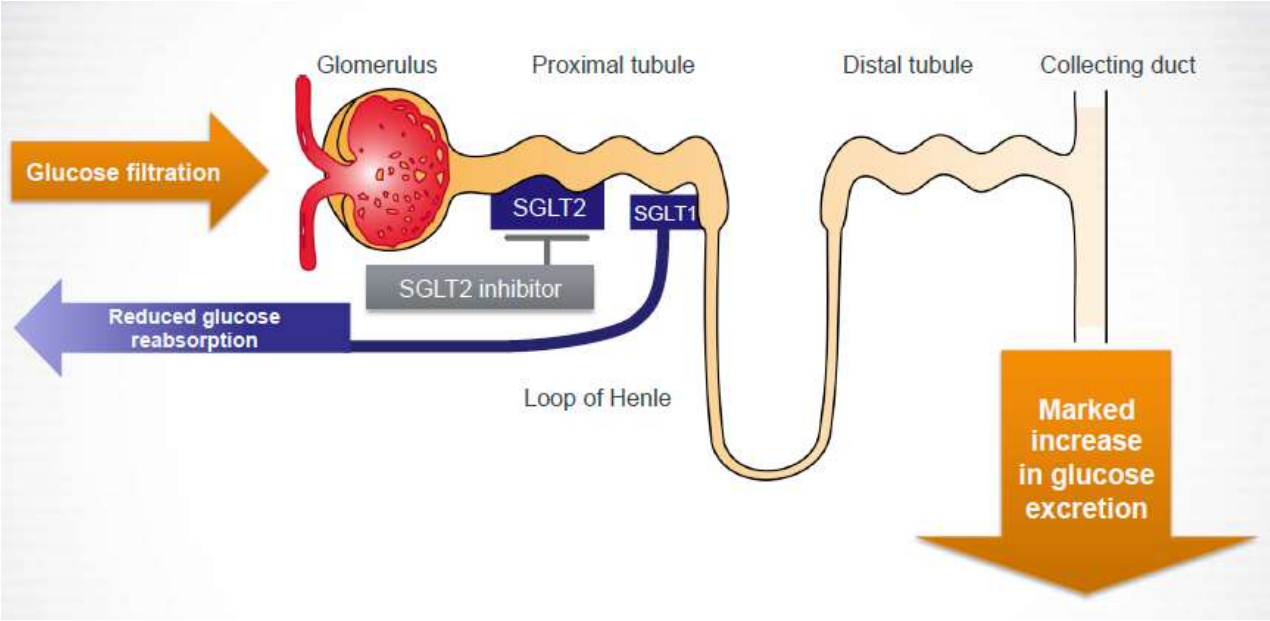
ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD
Association of British Clinical Diabetologists

ABCD nationwide dapagliflozin audit

- Launched October 2014
- Findings so far …..



Year 1 Audit Overview – October 2015

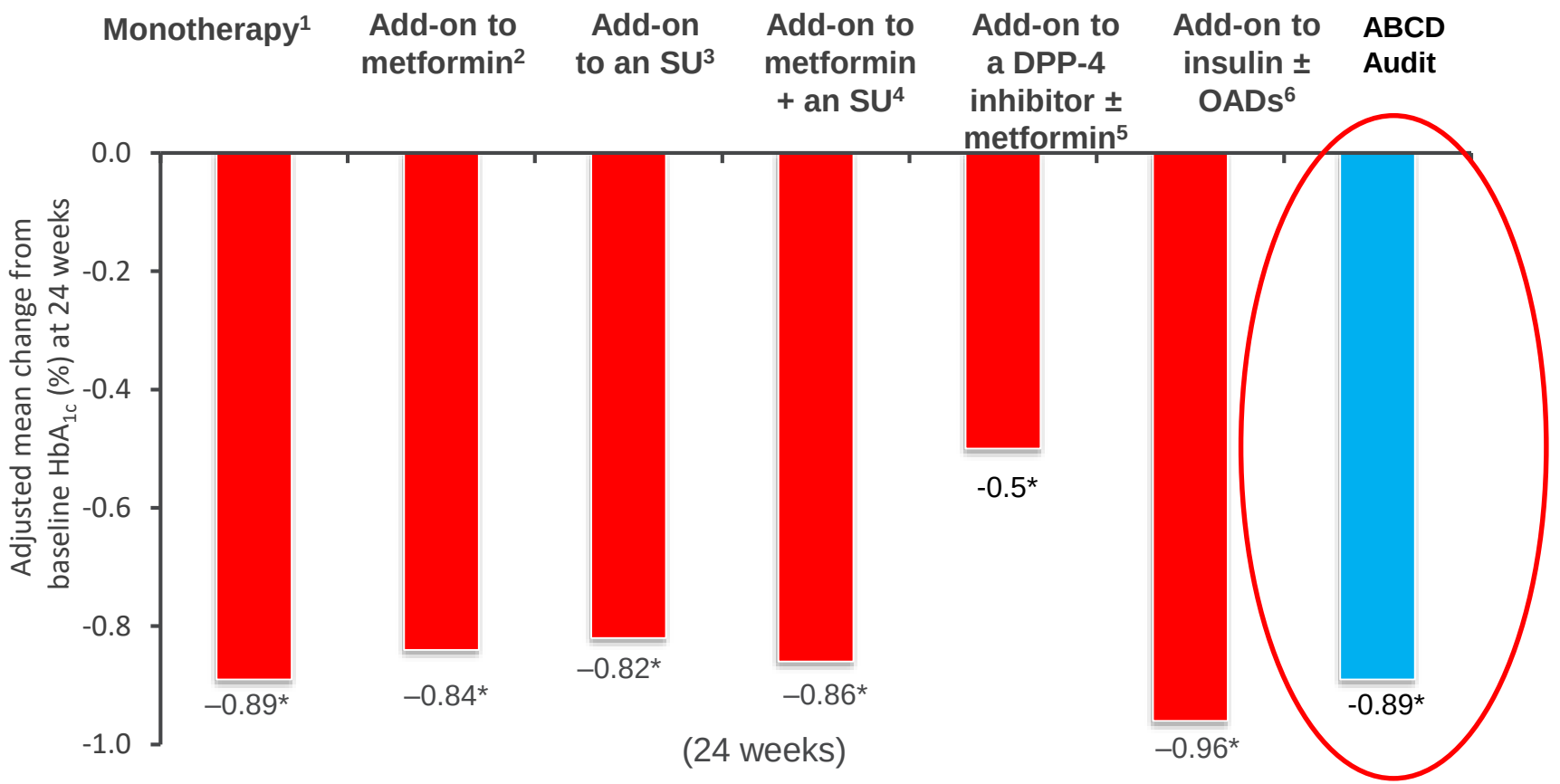
Data Input	Oct 2014 – Oct 2015	vs Combined Clinical Trials – Dapagliflozin
Centres	44	
Contributors	129	
Number of Patients	943	
Age (years)	56.7±10.4	
Sex [Males(%)]	55.9%	
Duration of diabetes (years)*	11.4 (6–16)	
Baseline HbA_{1c} (mmol/mol)	80.2±16.1	
Baseline HbA_{1c}(%)	9.5±1.5	8.0
BMI (kg/m²)	37.0±13.3	32.2
Baseline weight (kg)	103.3±22.7	
Duration of follow up (months)*	6.4 (0–12.3)	

Reported as mean±SD or median (IQR)*

Data presented at ABCD autumn meeting, November 2015

ABCD
Association of British Clinical Diabetologists

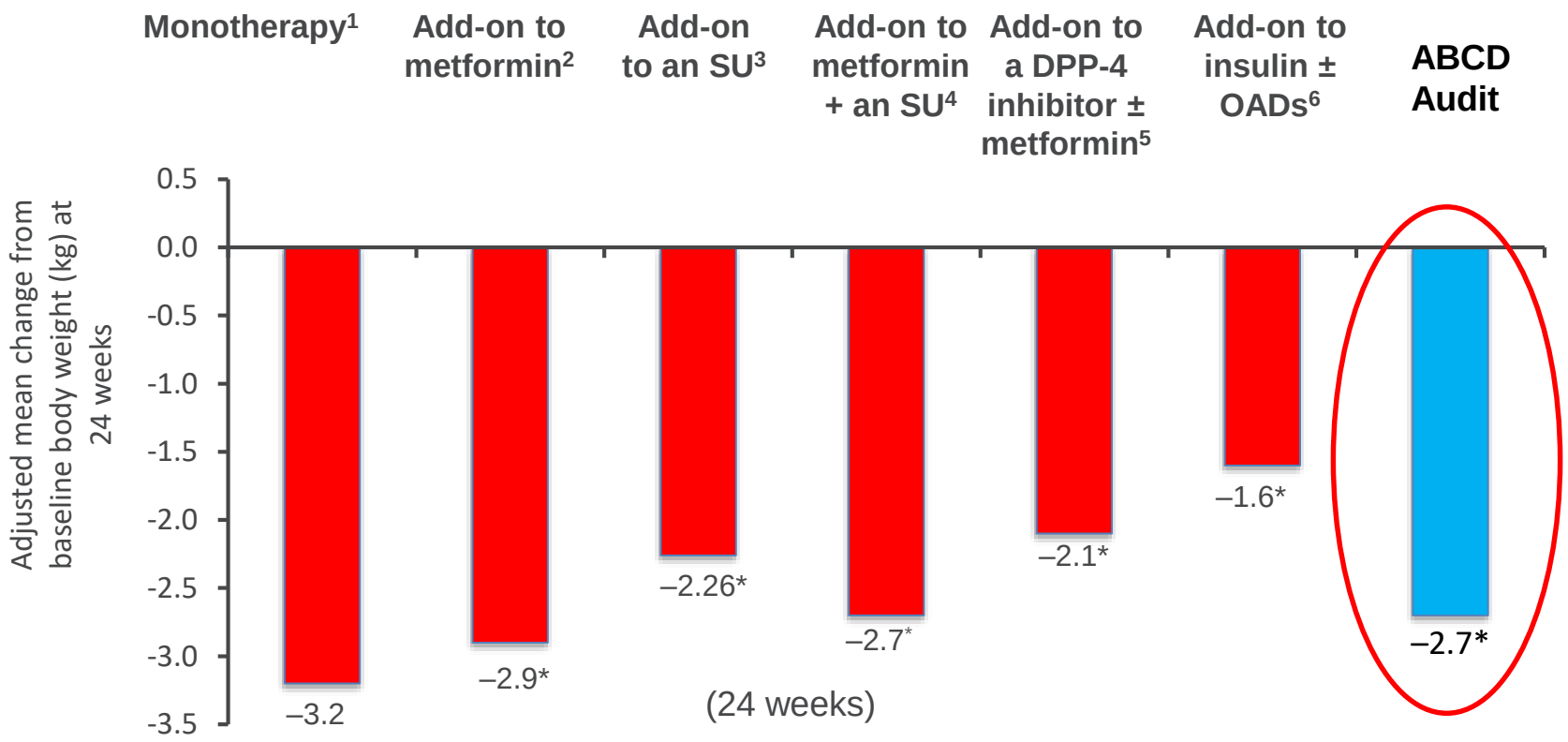
Reductions in HbA_{1c}: RCT data vs. ABCD audit



1. Ferrannini E et al (2010) *Diabetes Care* **33**: 2217–24; 2. Bailey CJ et al (2010) *Lancet* **375**: 2223–33; 3. Strojek K et al (2011) *Diabetes Obes M* 928–38; 4. Matthaei S et al (2015) *Diabetes Care* **38**: 365–72; 5. Jabbour SA et al (2014) *Diabetes Care* **37**: 740–50; 6. Wilding JPH et al (2012) *Ann Ir Med* **156**: 405–15

Data presented at ABCD autumn meeting, November 2015

Weight loss: : RCT data vs. ABCD audit

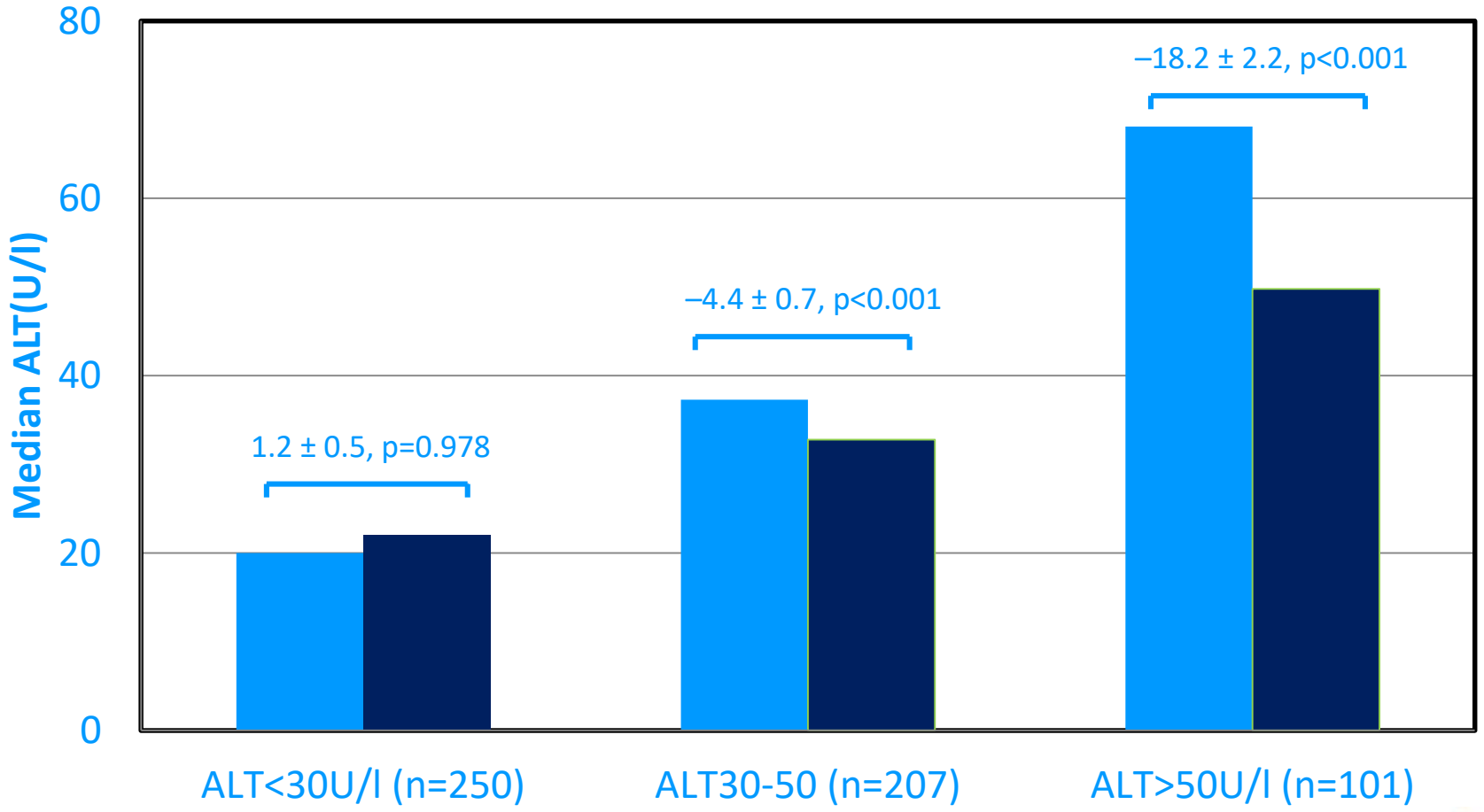


Baseline weight (kg)	94.2	86.3	80. 6	88.6	91.0	94.5	94.5

1. Ferrannini E et al (2010) *Diabetes Care* **33**: 2217–24; 2. Bailey CJ et al (2010) *Lancet* **375**: 2223–33; 3. Strojek K et al (2011) *Diabetes Obes Metab* **13**: 928–38; 4. Matthaei S et al (2015) *Diabetes Care* **38**: 365–72; 5. Jabbour SA et al (2014) *Diabetes Care* **37**: 740–50; 6. Wilding JPH et al (2012) *Ann Intern Med* **156**: 405–15;

Data presented at ABCD autumn meeting, November 2015

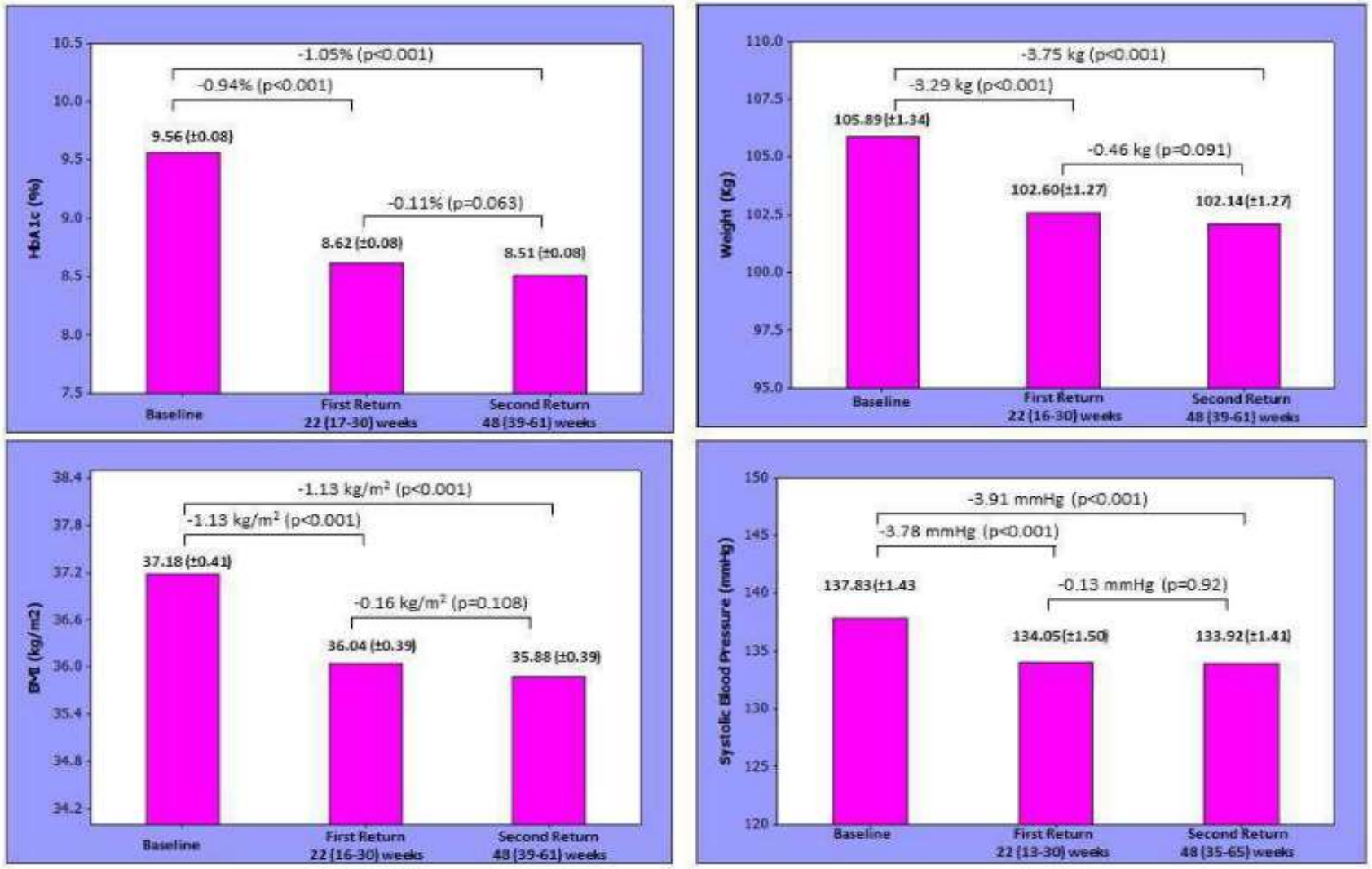
ALT response to dapagliflozin



Data presented at DUK annual professional conference, Glasgow, March 2016

ABCD
Association of British Clinical Diabetologists

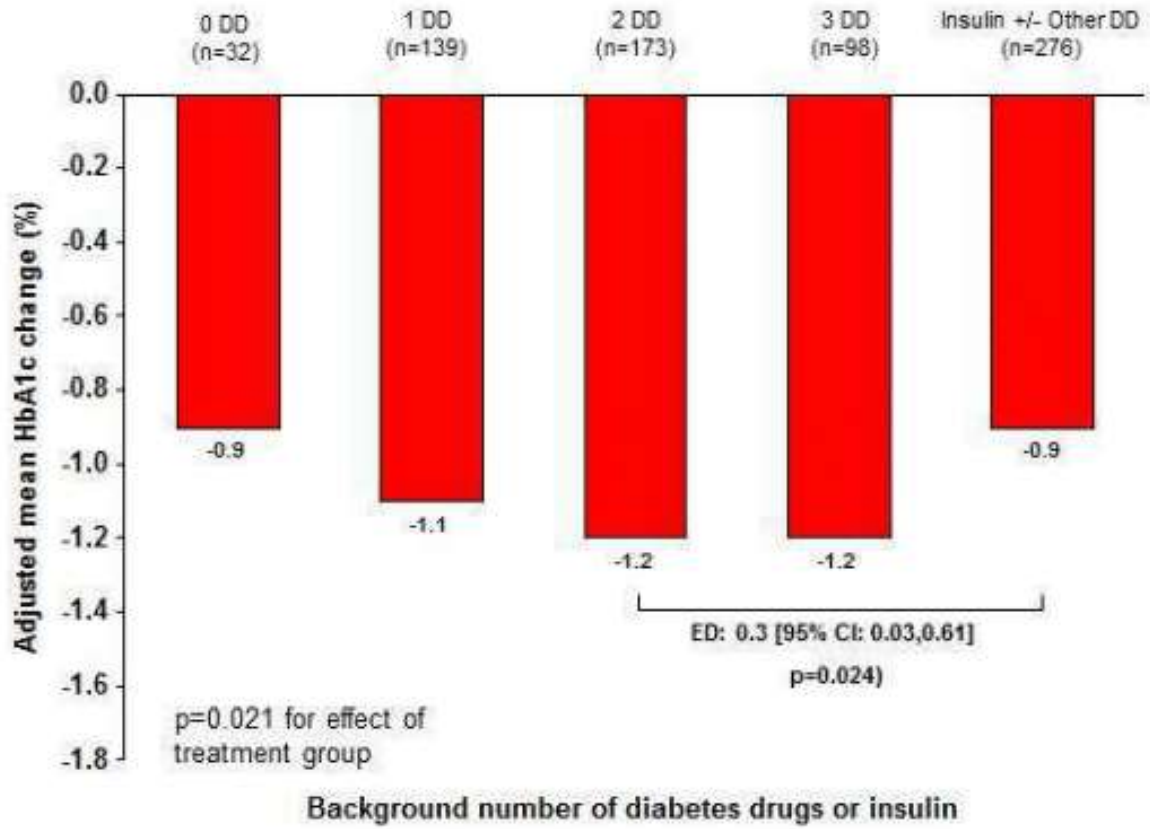
Dapagliflozin – improvements sustained



Data presented at ADA meeting, New Orleans, June 2016

ABCD
Association of British Clinical Diabetologists

Figure 1: Change in HbA1c stratified by background diabetes therapy



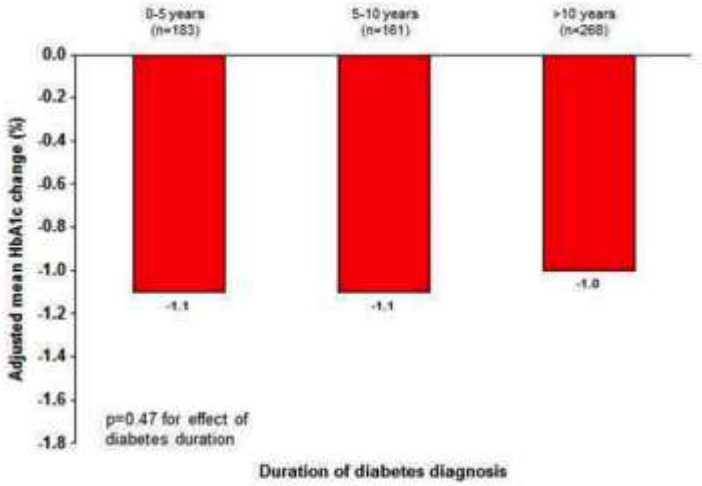
Data are adjusted mean and estimated difference (ED) were analysed by ANCOVA with baseline HbA1c and eGFR as covariates.
DD; diabetes drugs

Data presented at ADA meeting, New Orleans, June 2016

ABCD
Association of British Clinical Diabetologists

ABCD dapagliflozin audit

Figure 2: Change in HbA1c stratified by duration of diabetes

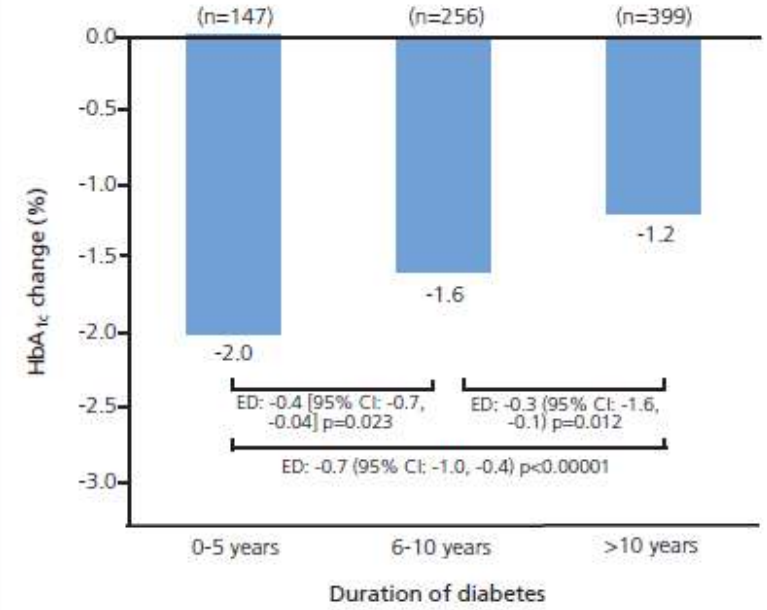


Data are adjusted mean analysed by ANCOVA with baseline HbA1c and eGFR as covariates.

Data presented at ADA meeting, New Orleans, June 2016

ABCD liraglutide audit

Figure 2. Mean HbA_{1c} changes after 26 weeks of liraglutide treatment, stratified according to duration of diabetes



Columns show adjusted mean changes analysed by ANCOVA with baseline HbA_{1c} as a covariate. ED: estimated difference; CI: confidence interval

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

Similar results between the ABCD canagliflozin and dapagliflozin* audits

Figure 1: Change in HbA1c at median (IQR) 4.1 (3-6.1) months after starting canagliflozin, stratified by duration of diabetes

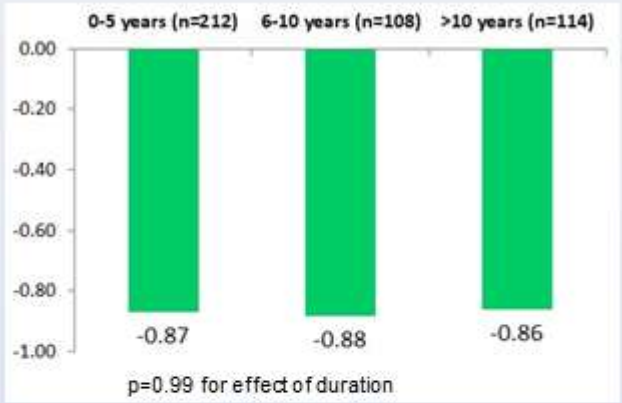
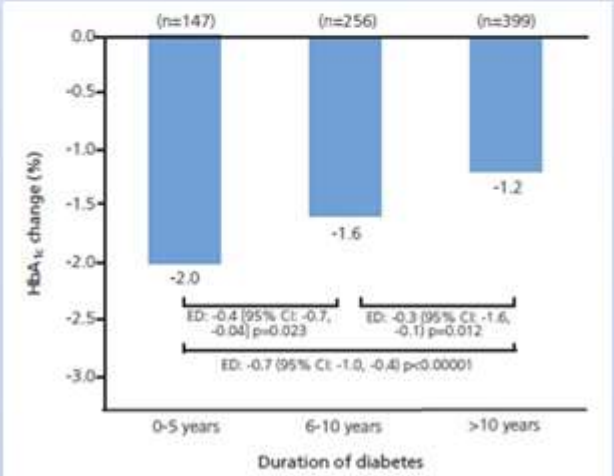
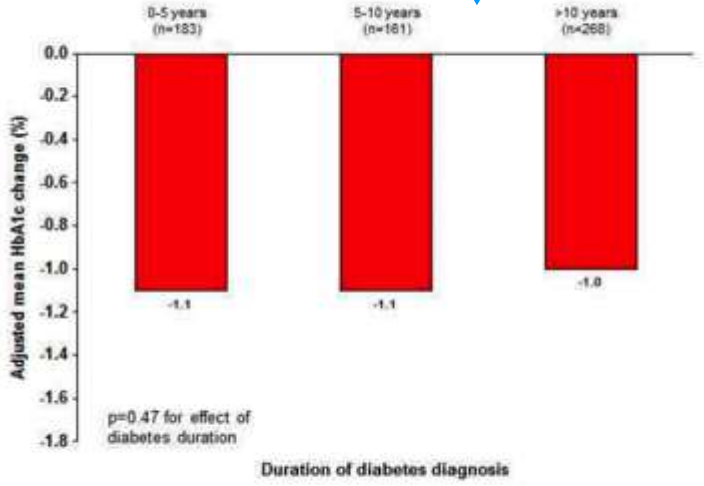


Figure 2: Change in HbA1c at 6 (3-9) months after starting liraglutide, stratified by duration of diabetes (From ABCD nationwide liraglutide audit[1] – see abstract 1038-P, ADA 2012) .



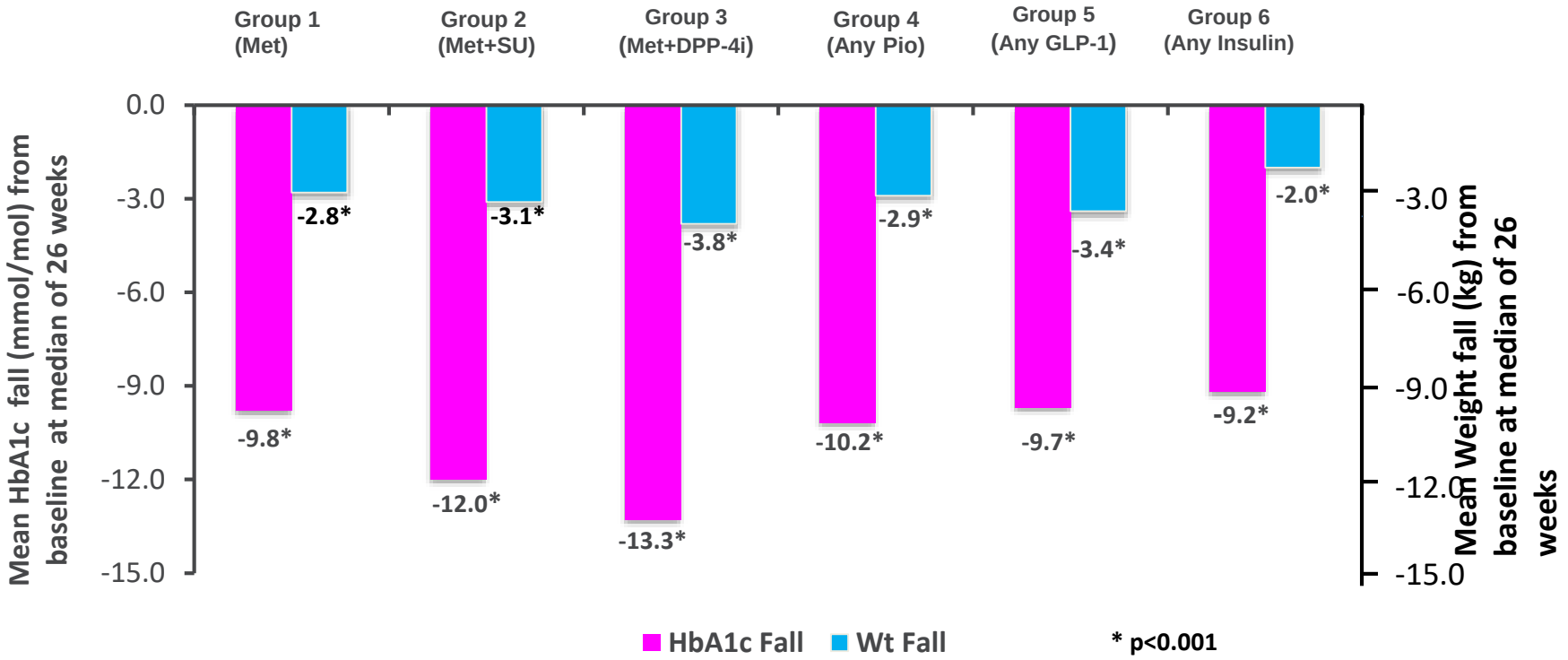
Columns show adjusted mean changes analysed by ANCOVA with baseline HbA_{1c} as a covariate. ED: estimated difference; CI: confidence interval



*Dapagliflozin audit data presented at ADA meeting, New Orleans, June 2016

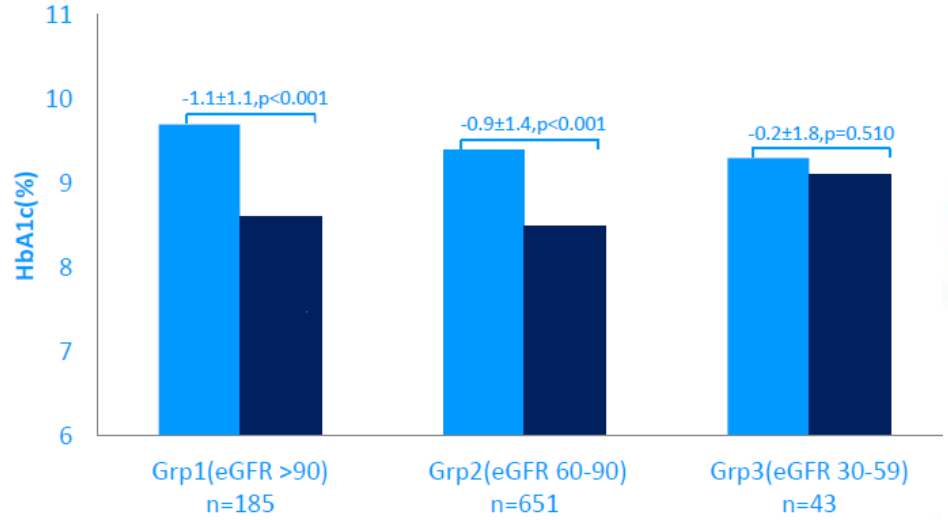
ABCD
Association of British Clinical Diabetologists

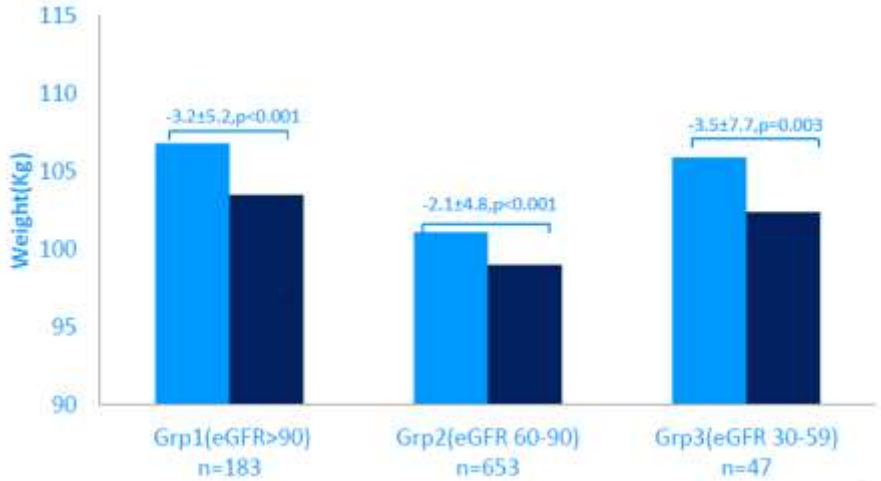
Effect of dapagliflozin on HbA1c and weight after its addition to various combinations of other diabetes medications: ABCD nationwide dapagliflozin audit*

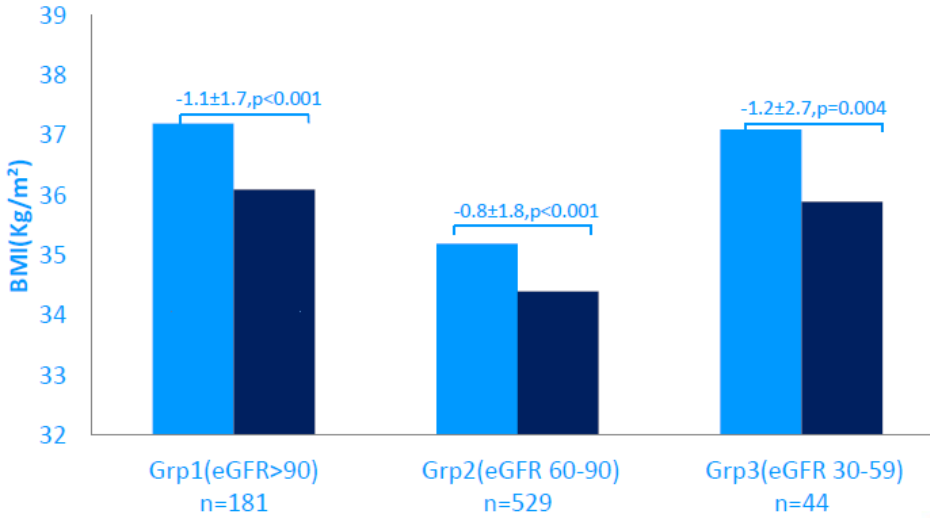


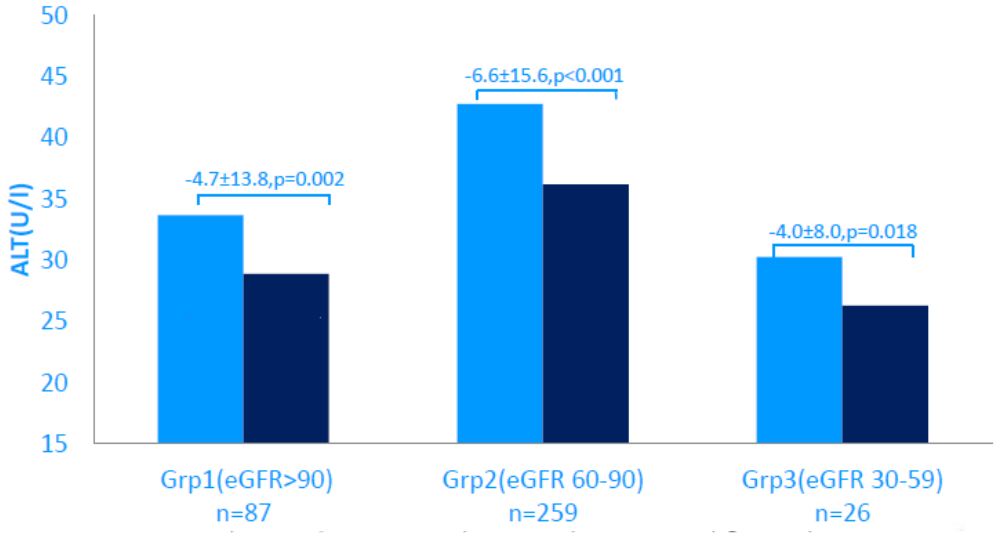
Association of British Clinical Diabetologists

* EASD 2016 Poster Presentation: M. Yadagiri, P. Sen Gupta, R.E.J. Ryder et al on behalf of all ABCD nationwide dapagliflozin audit contributors

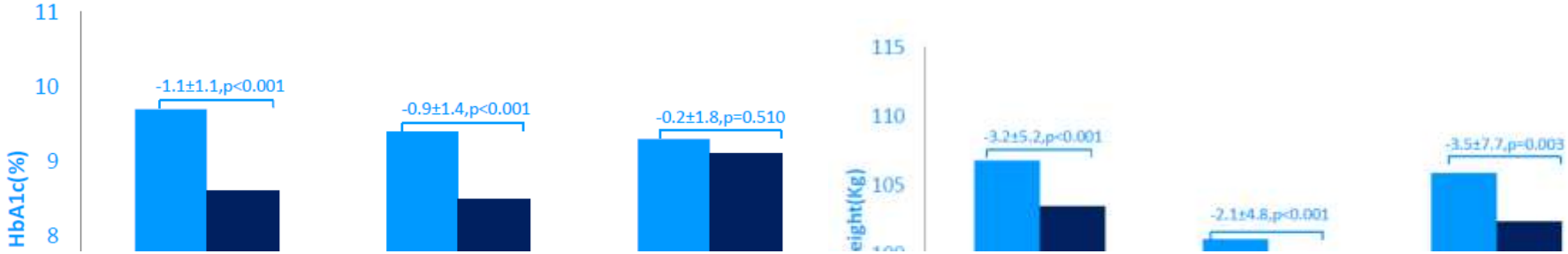






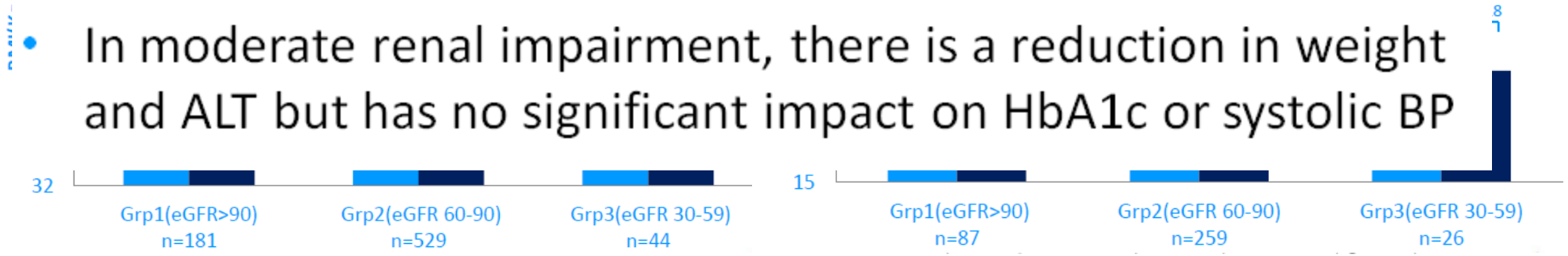


Data presented at ADA meeting, San Diego, June 2017



Conclusion

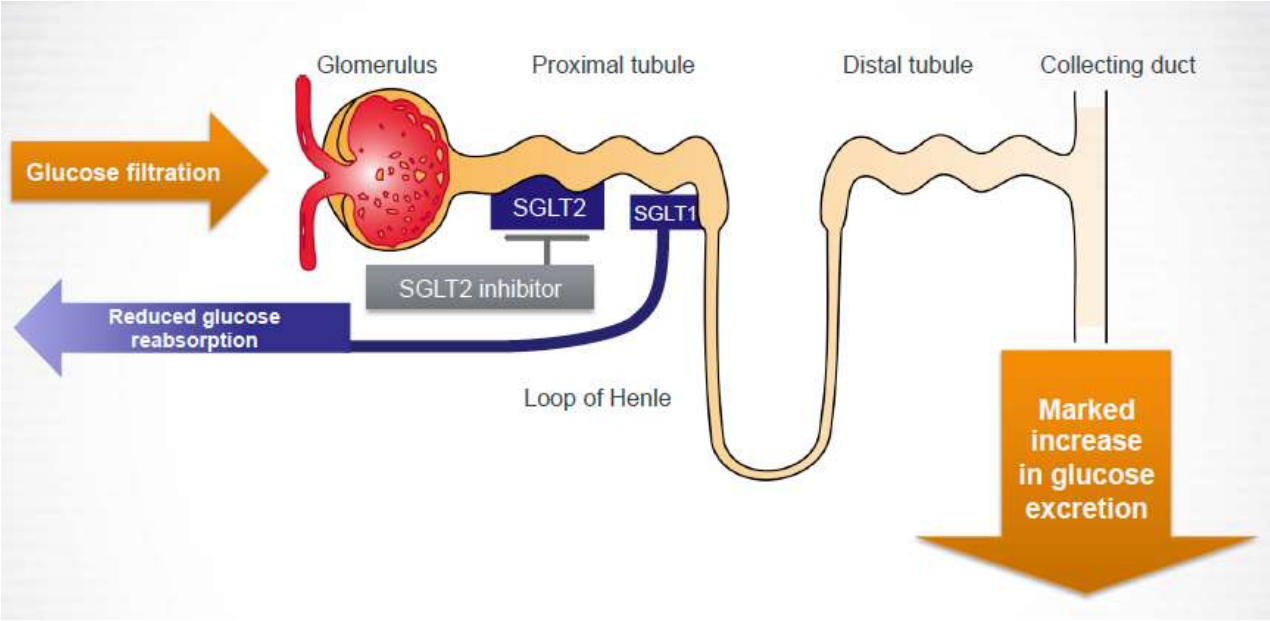
- Dapagliflozin reduces HbA1c,weight, BMI, systolic BP and ALT by statistically and clinically significant amounts in normal and mild renal impairment
- In moderate renal impairment, there is a reduction in weight and ALT but has no significant impact on HbA1c or systolic BP



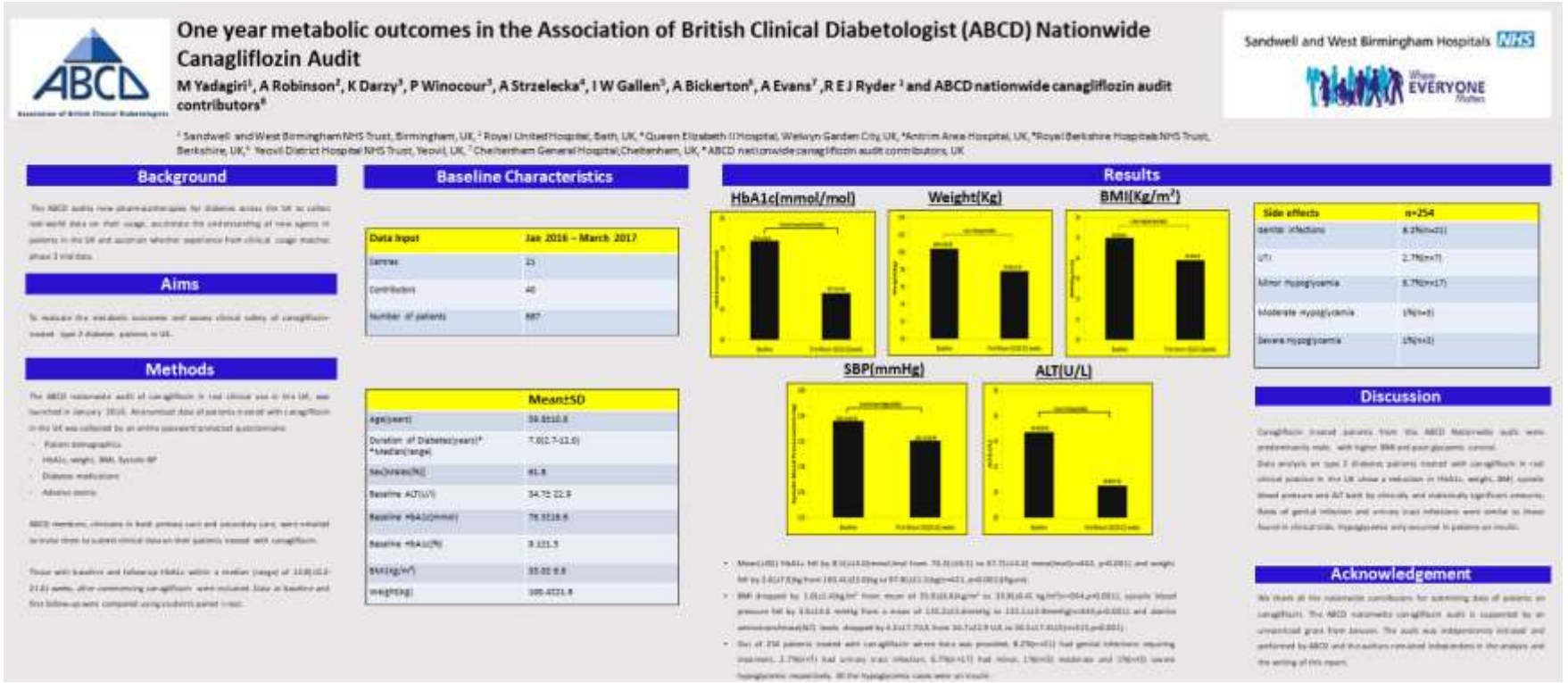
Data presented at ADA meeting, San Diego, June 2017

ABCD nationwide canagliflozin audit

- Launched January 2016
- Findings so far …..



ABCD nationwide canagliflozin audit - findings so far 1



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

M Yadagiri[1], A Robinson[2], K Darzy[3], P Winocour[3], A Strzelecka[4], I W Gallen[5], A Bickerton[6], A Evans[7], R E J Ryder[1] and ABCD nationwide canagliflozin audit contributors[8]

[1] Sandwell and West Birmingham NHS Trust, Birmingham, UK, [2] Royal United Hospital, Bath, UK, [3] Queen Elizabeth II Hospital, Welwyn Garden City, UK, [4] Antrim Area Hospital, UK, [5] Royal Berkshire Hospitals NHS Trust, Berkshire, UK, [6] Yeovil District Hospital NHS Trust, Yeovil, UK, [7] Cheltenham General Hospital, Cheltenham, UK, [8] ABCD nationwide canagliflozin audit contributors, UK

Sandwell and West Birmingham Hospitals NHS

Where EVERYONE Matters

Background

Aims

Methods

Baseline Characteristics

Data Input	Jan 2016 – March 2017
Centres	21
Contributors	40
Number of patients	887

	Mean±SD
Age(years)	59.8±10.8
Duration of Diabetes(years)* *Median(range)	7.0(3.7-12.0)
Sex(Female)(%)	41.8
Baseline ALT(U/l)	34.75 22.9
Baseline HbA1c(mmol/mol)	78.9±16.6
Baseline HbA1c(%)	9.1±1.5
BMI(kg/m²)	35.02 6.8
Weight(kg)	100.4±21.9

Results

HbA1c(mmol/mol)

Weight(Kg)

BMI(Kg/m²)

Side effects	n=254
Genital infections	6.2%(n=21)
UTI	2.7%(n=7)
Minor Hypoglycaemia	6.7%(n=17)
Moderate Hypoglycaemia	1%(n=3)
Severe Hypoglycaemia	1%(n=3)

SBP(mmHg)

ALT(U/L)

- Mean(±SD) HbA1c fell by 8.3(±14.2)mmol/mol from 78.9(±16.6) to 87.7(±14.2) mmol/mol(n=443, p<0.001) and weight fell by 2.6(±7.8)kg from 100.4(±21.9)kg to 97.8(±21.1)kg(n=421, p<0.001)(figure).
- BMI dropped by 1.0(±2.4)kg/m² from mean of 35.0(±8.8)kg/m² to 33.9(±8.4) kg/m²(n=394,p<0.001), systolic blood pressure fell by 3.6(±14.6 mmHg from a mean of 135.2(±15.6)mmHg to 131.1(±13.8)mmHg(n=443,p<0.001) and alanine aminotransferase(ALT) levels dropped by 4.3(±17.7)U/L from 34.7(±22.9 U/L to 30.5(±17.0)U/L(n=415,p<0.001).
- Out of 254 patients treated with canagliflozin where data was provided, 6.2%(n=21) had genital infections requiring treatment, 2.7%(n=7) had urinary tract infection, 6.7%(n=17) had minor, 1%(n=3) moderate and 1%(n=3) severe hypoglycaemic episodes(figure). All the hypoglycaemia cases were on insulin.

Discussion

Acknowledgement

By first return to clinic at median 14 weeks after starting canagliflozin

- Mean HbA1c fell by 0.8% from 9.1% to 8.3%
- Mean weight fell by 2.6 kg from 100.4 kg to 97.8 kg
- Significant falls in BMI, systolic blood pressure and alanine aminotransferase

EASD 2017 Poster Presentation: M. Yadagiri et al, on behalf of all ABCD nationwide canagliflozin audit contributors

Association of British Clinical Diabetologists

ABCD nationwide canagliflozin audit - findings so far 2

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, [6] ABCD nationwide canagliflozin audit contributors, UK

Background

The ABCD audits new pharmacotherapies for diabetes across the UK to collect real-world data on their usage, accelerate the understanding of new agents in patients in the UK and ascertain whether experience from clinical usage matches phase 3 trial data. The ABCD nationwide canagliflozin audit was launched in January 2016 to evaluate the efficacy of canagliflozin in a real world setting of clinical use in the United Kingdom (UK).

Aims

To evaluate the metabolic outcomes and assess clinical safety of canagliflozin-treated type 2 diabetes patients in UK.

Methods

The ABCD nationwide audit of canagliflozin in real clinical use in the UK, was launched in January 2016. Anonymized data of patients treated with canagliflozin in the UK was collected by an online password protected questionnaire:

- Patient demographics
- HbA1c, weight, BMI, Systolic BP
- Diabetes medications
- Adverse events

Two year follow up data from 21 centres across the UK on 690 patients treated with canagliflozin. Male 60.2%, mean age (±SD) 58.9 ± 10.9 years, weight 101.3 ±22.2 kg, BMI 34.0 ±6.9, Hba1c 76.3 ±16.3 mmol/mol. Patients with baseline, first return and second return follow up data were included in the analysis.

ABCD members, clinicians in both primary care and secondary care, were emailed to invite them to submit clinical data on their patients treated with canagliflozin.

Those with baseline and follow-up HbA1c within a median (range) of 14.8(10.2-21.0) weeks, after commencing canagliflozin were included. Data at baseline and first follow-up were compared using student:s paired t-test.

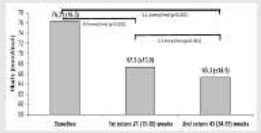
Baseline Characteristics

Data Input	Jan 2016 – March 2017
Centres	21
Contributors	40
Number of patients	690

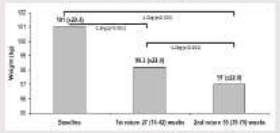
	Mean±SD
Age(years)	58.9±10.9
Duration of Diabetes(years)* *Median(range)	7.0 (2.7-12.0)
Sex(Males(%)]	60.2
Baseline HbA1c(mmol)	76.3±16.3
BMI(Kg/m^2)	34.0± 6.9
Weight(Kg)	101.3±22.2

Results

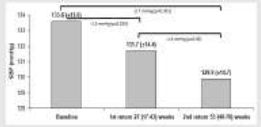
HbA1c (mmol/mol)



Weight (Kg)



SBP (mmHg)



ALT (U/L)

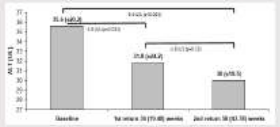


Figure: Mean (±SD) HbA1c (n=297), weight (n=242), ALT (n=177) and systolic blood pressure (n=285), baseline vs first and second return (after median (interquartile range(weeks) to clinic following commencement of canagliflozin.

•Mean Hba1c fell by 9.0±13.4 mmol/mol at first return and 11.1±14.7 mmol/mol at second return (n=297, p<0.001) with 2.1mmol/mol fall between first and second return (p=0.001).Mean weight fell by 2.8±4kg at first return and 4.0±5.4kg at second return (n=242, p<0.001) with 1.3kg fall between first and second return (p<0.001).Mean alanine aminotransferase (ALT) fell by 3.8±23.2 U/L at first return (p<0.091) and 5.6±18U/L at second return (n=177, p<0.001) with 1.8U/L fall between first and second return (p=0.25). Mean systolic blood pressure (SBP) fell by 1.9±15.4mmHg at first return (p=0.035) and 3.7±16.2mmHg at second return (n=285, p<0.001) with 1.8mmHg fall between first and second return (p=0.05). Mean diastolic blood pressure (DBP) fell by 1.0±10.1mmHg at first return (p=0.086) and 2.6±11.1mmHg at second return (n=284, p<0.001) with 1.5mmHg fall between first and second return (p=0.006).

•Median range of weeks for follow up for first and second returns (IQR) were 21 (15-30) and 44.9 (34.3-58.9) for Hba1c, 26.8 (15.5-41.6) and 54.6 (38.6-75) for weight, 30 (19-48.3) and 57.6 (42.7-77.5) for ALT, 27.3 (17.4-42.7) and 53.1 (40.4-70.3) for SBP, 27.2 (17.3-42.8) and 50 (40.3-71) for DBP.

Discussion

Canagliflozin showed statistically significant and sustained reduction in Hba1c, weight, ALT and systolic blood pressure across a wide range of real-world UK patients with type 2 diabetes. Further benefit was seen between first and second returns with statistically significant reductions in Hba1c, weight, systolic blood pressure and ALT.

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 in the analysis and the writing of this report.

Between first return to clinic and second return to clinic continued significant falls in:

- HbA1c
- Weight
- Systolic blood pressure
- Alanine aminotransferase

EASD 2018 Poster Presentation: A. Puttanna et al, on behalf of all ABCD nationwide canagliflozin audit contributors

ABCD nationwide canagliflozin audit - findings so far 2

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, [6] ABCD nationwide canagliflozin audit contributors, UK

Background

The ABCD audits new pharmacotherapies for diabetes across the UK to collect real-world data on their usage, accelerate the understanding of new agents in patients in the UK and ascertain whether experience from clinical usage matches phase 3 trial data. The ABCD nationwide canagliflozin audit was launched in January 2016 to evaluate the efficacy of canagliflozin in a real world setting of clinical use in the United Kingdom (UK).

Aims

To evaluate the metabolic outcomes and assess clinical safety of canagliflozin-treated type 2 diabetes patients in UK.

Methods

The ABCD nationwide audit of canagliflozin in real clinical use in the UK, was launched in January 2016. Anonymized data of patients treated with canagliflozin in the UK was collected by an online password protected questionnaire:

- Patient demographics
- HbA1c, weight, BMI, Systolic BP
- Diabetes medications
- Adverse events

Two year follow up data from 21 centres across the UK on 690 patients treated with canagliflozin. Male 60.2%, mean age (±SD) 58.9 ± 10.9 years, weight 101.3 ±22.2 kg, BMI 34.0 ±6.9, Hba1c 76.3 ±16.3 mmol/mol. Patients with baseline, first return and second return follow up data were included in the analysis.

ABCD members, clinicians in both primary care and secondary care, were emailed to invite them to submit clinical data on their patients treated with canagliflozin.

Those with baseline and follow-up HbA1c within a median (range) of 14.8(10.2-21.0) weeks, after commencing canagliflozin were included. Data at baseline and first follow-up were compared using student:s paired t-test.

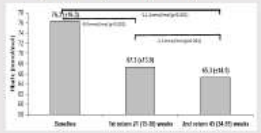
Baseline Characteristics

Data Input	Jan 2016 – March 2017
Centres	21
Contributors	40
Number of patients	690

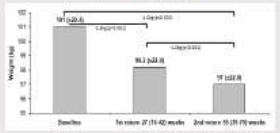
	Mean±SD
Age(years)	58.9±10.9
Duration of Diabetes(years)* *Median(range)	7.0 (2.7-12.0)
Sex(Males(%)]	60.2
Baseline HbA1c(mmol)	76.3±16.3
BMI(Kg/m^2)	34.0± 6.9
Weight(Kg)	101.3±22.2

Results

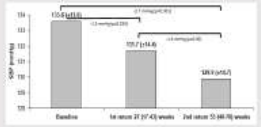
HbA1c (mmol/mol)



Weight (Kg)



SBP (mmHg)



ALT (U/L)

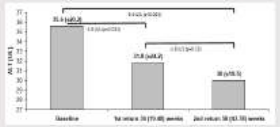


Figure: Mean (±SD) HbA1c (n=297), weight (n=242), ALT (n=177) and systolic blood pressure (n=285), baseline vs first and second return (after median (interquartile range(weeks) to clinic following commencement of canagliflozin.

•Mean Hba1c fell by 9.0±13.4 mmol/mol at first return and 11.1±14.7 mmol/mol at second return (n=297, p<0.001) with 2.1mmol/mol fall between first and second return (p=0.001).Mean weight fell by 2.8±4kg at first return and 4.0±5.4kg at second return (n=242, p<0.001) with 1.3kg fall between first and second return (p<0.001).Mean alanine aminotransferase (ALT) fell by 3.8±23.2 U/L at first return (p<0.091) and 5.6±18U/L at second return (n=177, p<0.001) with 1.8U/L fall between first and second return (p=0.25). Mean systolic blood pressure (SBP) fell by 1.9±15.4mmHg at first return (p=0.035) and 3.7±16.2mmHg at second return (n=285, p<0.001) with 1.8mmHg fall between first and second return (p=0.05). Mean diastolic blood pressure (DBP) fell by 1.0±10.1mmHg at first return (p=0.086) and 2.6±11.1mmHg at second return (n=284, p<0.001) with 1.5mmHg fall between first and second return (p=0.006).

•Median range of weeks for follow up for first and second returns (IQR) were 21 (15-30) and 44.9 (34.3-58.9) for Hba1c, 26.8 (15.5-41.6) and 54.6 (38.6-75) for weight, 30 (19-48.3) and 57.6 (42.7-77.5) for ALT, 27.3 (17.4-42.7) and 53.1 (40.4-70.3) for SBP, 27.2 (17.3-42.8) and 50 (40.3-71) for DBP.

Discussion

Canagliflozin showed statistically significant and sustained reduction in Hba1c, weight, ALT and systolic blood pressure across a wide range of real-world UK patients with type 2 diabetes. Further benefit was seen between first and second returns with statistically significant reductions in Hba1c, weight, systolic blood pressure and ALT.

Acknowledgement

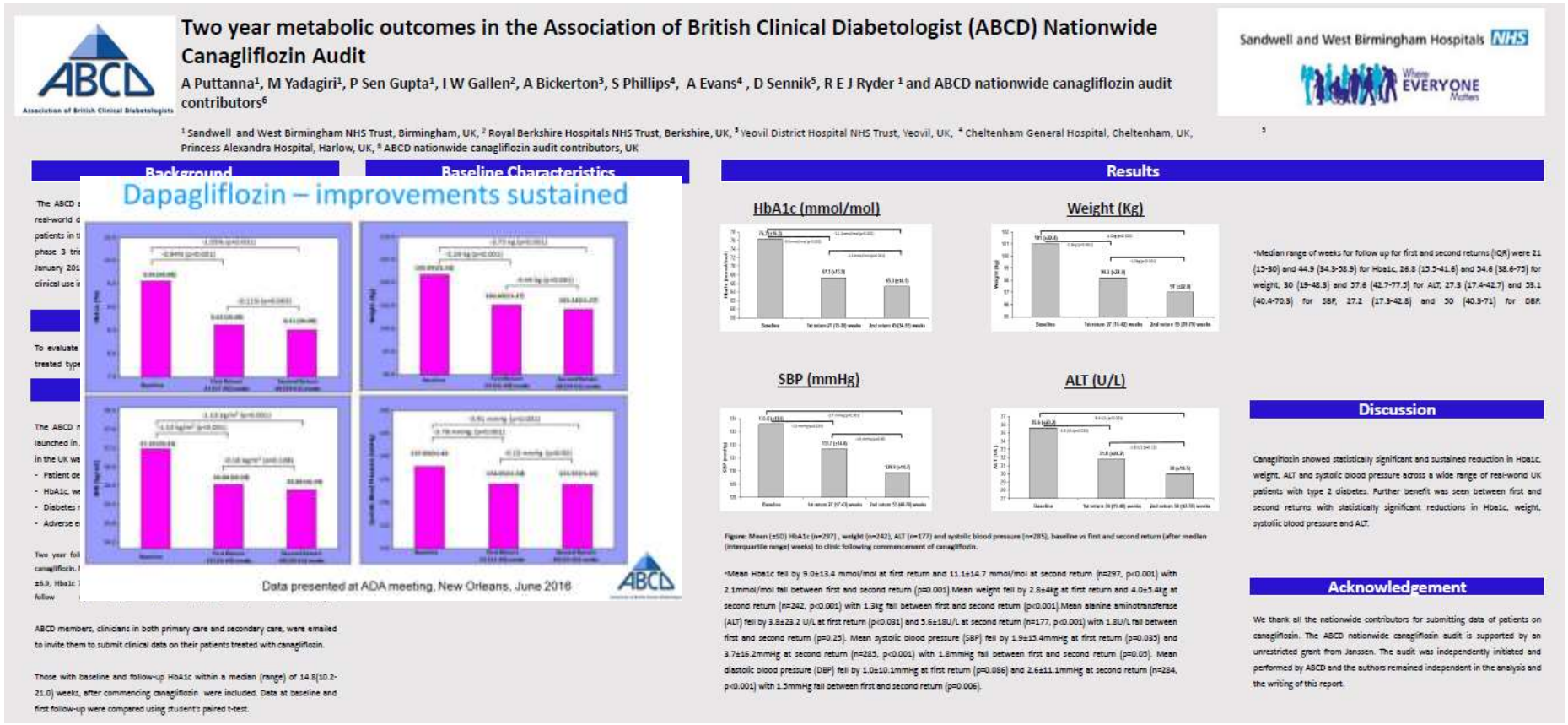
We thank all the nationwide contributors for submitting data of patients on canagliflozin. The ABCD nationwide canagliflozin audit is supported by an unrestricted grant from Janssen. The audit was independently initiated and performed by ABCD and the authors remained independent in the analysis and the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

Between first return to clinic and second return to clinic continued significant falls in:

- HbA1c
- Weight
- Systolic blood pressure
- Alanine aminotransferase

EASD 2018 Poster Presentation: A. Puttanna et al, on behalf of all ABCD nationwide canagliflozin audit contributors

ABCD nationwide canagliflozin audit - findings so far 2



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, [6] ABCD nationwide canagliflozin audit contributors, UK

Dapagliflozin – improvements sustained

Data presented at ADA meeting, New Orleans, June 2016

Results

HbA1c (mmol/mol)

Weight (Kg)

SBP (mmHg)

ALT (U/L)

Discussion

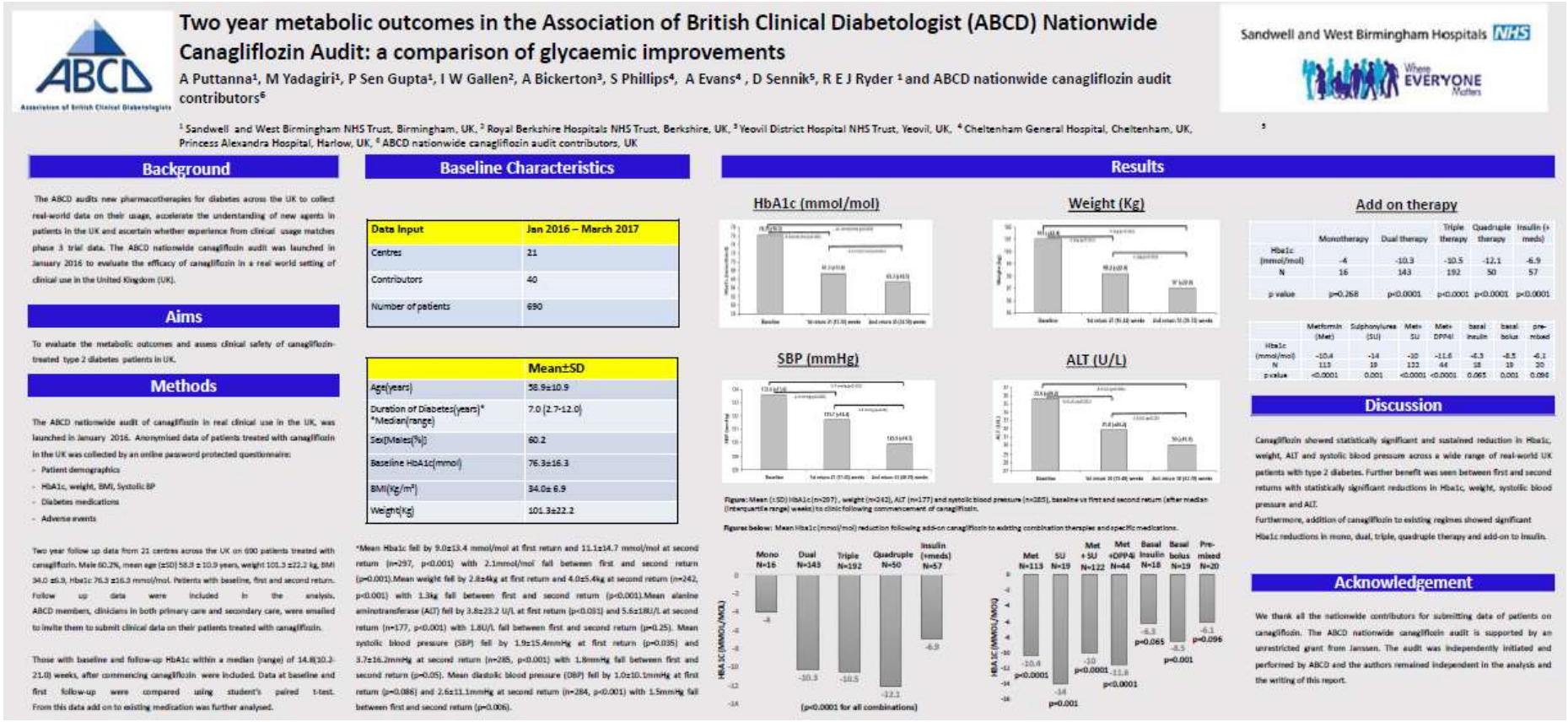
Acknowledgement

Between first return to clinic and second return to clinic continued significant falls in:

- HbA1c
- Weight
- Systolic blood pressure
- Alanine aminotransferase

EASD 2018 Poster Presentation: A. Puttanna et al, on behalf of all ABCD nationwide canagliflozin audit contributors

ABCD nationwide canagliflozin audit - findings so far 3



Two year metabolic outcomes in the Association of British Clinical Diabetologist (ABCD) Nationwide Canagliflozin Audit: a comparison of glycaemic improvements

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, [6] ABCD nationwide canagliflozin audit contributors, UK

Sandwell and West Birmingham Hospitals NHS

Where EVERYONE Matters

Background

The ABCD audits new pharmacotherapies for diabetes across the UK to collect real-world data on their usage, accelerate the understanding of new agents in patients in the UK and ascertain whether experience from clinical usage matches phase 3 trial data. The ABCD nationwide canagliflozin audit was launched in January 2016 to evaluate the efficacy of canagliflozin in a real world setting of clinical use in the United Kingdom (UK).

Aims

To evaluate the metabolic outcomes and assess clinical safety of canagliflozin-treated type 2 diabetes patients in UK.

Methods

The ABCD nationwide audit of canagliflozin in real clinical use in the UK, was launched in January 2016. Anonymised data of patients treated with canagliflozin in the UK was collected by an online password protected questionnaire:

- Patient demographics
- HbA1c, weight, BMI, Systolic BP
- Diabetes medications
- Adverse events

Two year follow up data from 21 centres across the UK on 690 patients treated with canagliflozin. Male 60.2%, mean age (±SD) 58.9 ± 10.9 years, weight 101.3 ±22.2 kg, BMI 34.0 ±6.9, Hba1c 76.3 ±16.3 mmol/mol. Patients with baseline, first and second return. Follow up data were included in the analysis. ABCD members, clinicians in both primary care and secondary care, were emailed to invite them to submit clinical data on their patients treated with canagliflozin.

Those with baseline and follow-up HbA1c within a median (range) of 14.8(10.2-21.0) weeks, after commencing canagliflozin were included. Data at baseline and first follow-up were compared using student's paired t-test. From this data add on to existing medication was further analysed.

Baseline Characteristics

Data Input	Jan 2016 – March 2017
Centres	21
Contributors	40
Number of patients	690

	Mean±SD
Age(years)	58.9±10.9
Duration of Diabetes(years)* *Median(range)	7.0 (2.7-12.0)
Sex(Males(%))	60.2
Baseline HbA1c(mmol)	76.3±16.3
BMI(Kg/m²)	34.0± 6.9
Weight(Kg)	101.3±22.2

*Mean Hba1c fell by 9.0±13.4 mmol/mol at first return and 11.1±14.7 mmol/mol at second return (n=297, p<0.001) with 2.1mmol/mol fall between first and second return (p<0.001).Mean weight fell by 2.8±4kg at first return and 4.0±5.4kg at second return (n=242, p<0.001) with 1.3kg fall between first and second return (p<0.001).Mean alanine aminotransferase (ALT) fell by 3.8±23.2 U/L at first return (p<0.05) and 5.6±18U/L at second return (n=177, p<0.001) with 1.8U/L fall between first and second return (p<0.25). Mean systolic blood pressure (SBP) fell by 1.9±15.4mmHg at first return (p<0.035) and 3.7±16.2mmHg at second return (n=285, p<0.001) with 1.8mmHg fall between first and second return (p<0.05). Mean diastolic blood pressure (DBP) fell by 1.0±10.1mmHg at first return (p=0.086) and 2.6±11.1mmHg at second return (n=284, p<0.001) with 1.5mmHg fall between first and second return (p<0.006).

Results

HbA1c (mmol/mol)

Weight (Kg)

SBP (mmHg)

ALT (U/L)

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.

Figures below: Mean Hba1c (mmol/mol) reduction following add-on canagliflozin to existing combination therapies and specific medications.

Add on therapy

	Monotherapy	Dual therapy	Triple therapy	Quadruple therapy	Insulin (+ meds)
Hba1c (mmol/mol)	-4	-10.3	-10.5	-12.1	-6.9
N	16	143	192	50	57
p value	p=0.268	p<0.0001	p<0.0001	p<0.0001	p<0.0001

	Metformin (Met)	Sulphonylurea (SU)	Met+ SU	Met+ DPP4i	basal insulin	basal bolus	pre-mixed
Hba1c (mmol/mol)	-10.4	-14	-10	-11.6	-6.3	-8.5	-6.1
N	113	19	122	44	18	19	20
p value	<0.0001	0.001	<0.0001	<0.0001	0.065	0.001	0.096

Discussion

Canagliflozin showed statistically significant and sustained reduction in Hba1c, weight, ALT and systolic blood pressure across a wide range of real-world UK patients with type 2 diabetes. Further benefit was seen between first and second returns with statistically significant reductions in Hba1c, weight, systolic blood pressure and ALT.

Furthermore, addition of canagliflozin to existing regimes showed significant Hba1c reductions in mono, dual, triple, quadruple therapy and add-on to insulin.

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 in the analysis and the writing of this report.

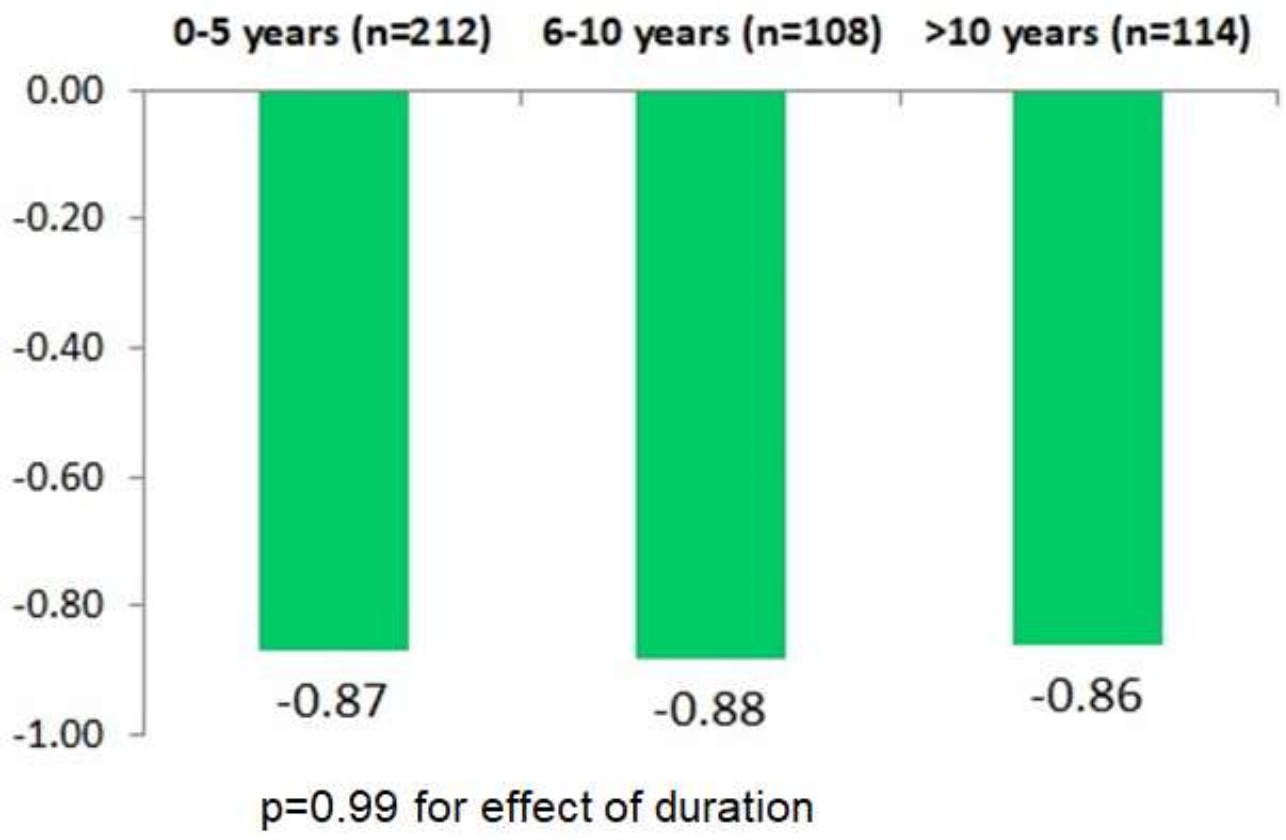
Similar falls in HbA1c when canagliflozin added to:

- One other OHA
- Two other OHAs
- Three other OHAs
- Slightly less when added to insulin+/- OHA

DUK 2019 Oral and Poster Presentation: A. Puttanna et al, on behalf of all ABCD nationwide canagliflozin audit contributors

Association of British Clinical Diabetologists

Change in HbA1c at median (IQR) 4.1 (3-6.1) months after starting canagliflozin, stratified by duration of diabetes



Similar results between the ABCD canagliflozin and dapagliflozin* audits

Figure 1: Change in HbA1c at median (IQR) 4.1 (3-6.1) months after starting canagliflozin, stratified by duration of diabetes

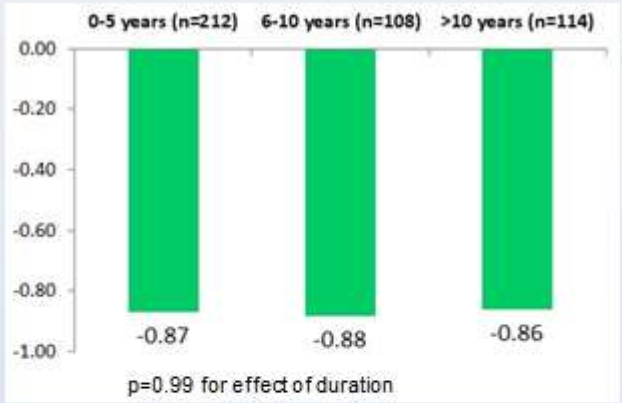
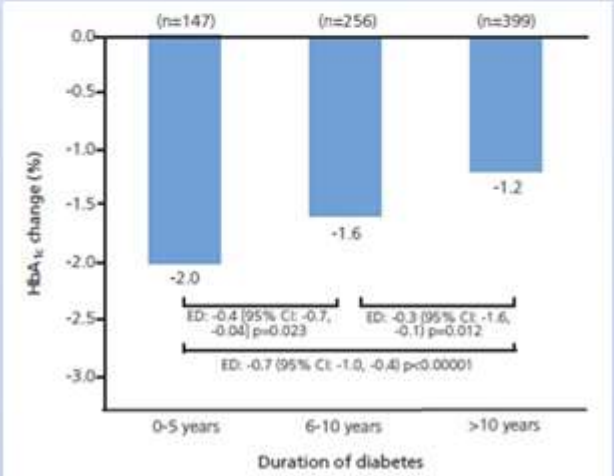
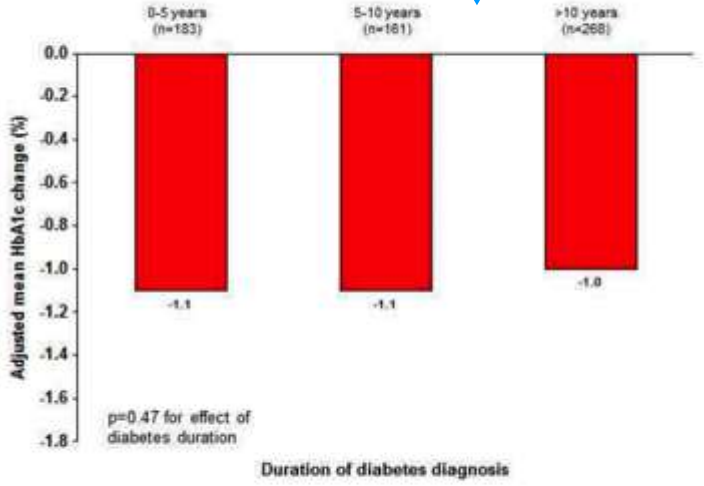


Figure 2: Change in HbA1c at 6 (3-9) months after starting liraglutide, stratified by duration of diabetes (From ABCD nationwide liraglutide audit[1] – see abstract 1038-P, ADA 2012) .



Columns show adjusted mean changes analysed by ANCOVA with baseline HbA_{1c} as a covariate. ED: estimated difference; CI: confidence interval

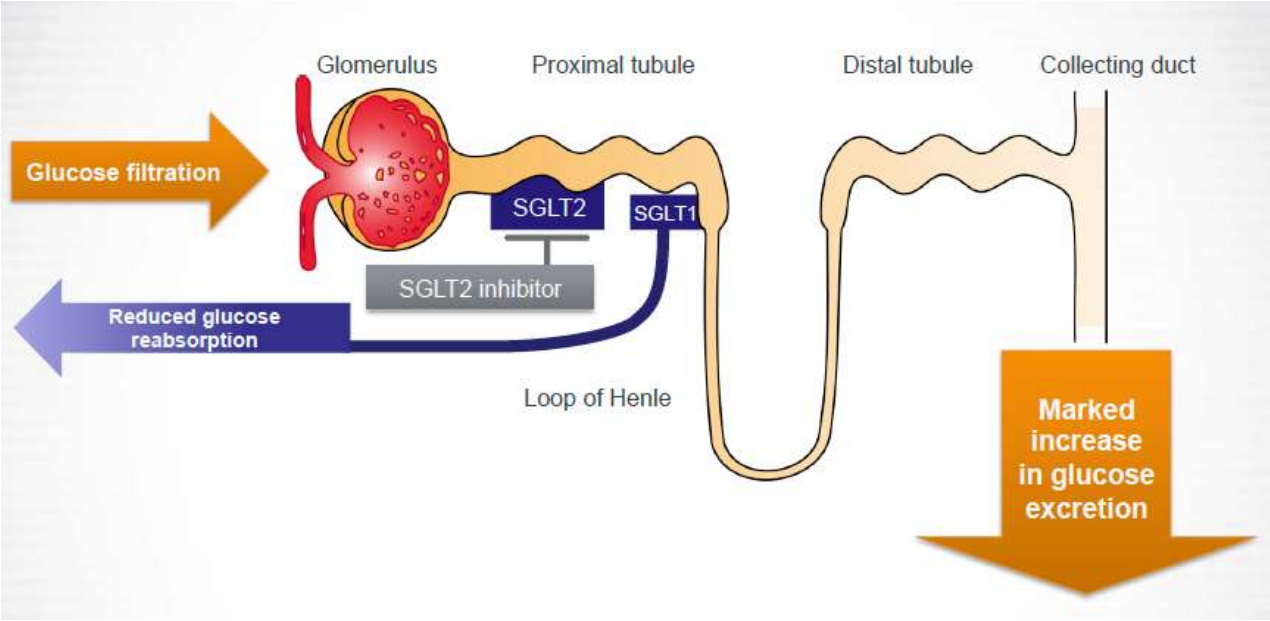


*Dapagliflozin audit data presented at ADA meeting, New Orleans, June 2016

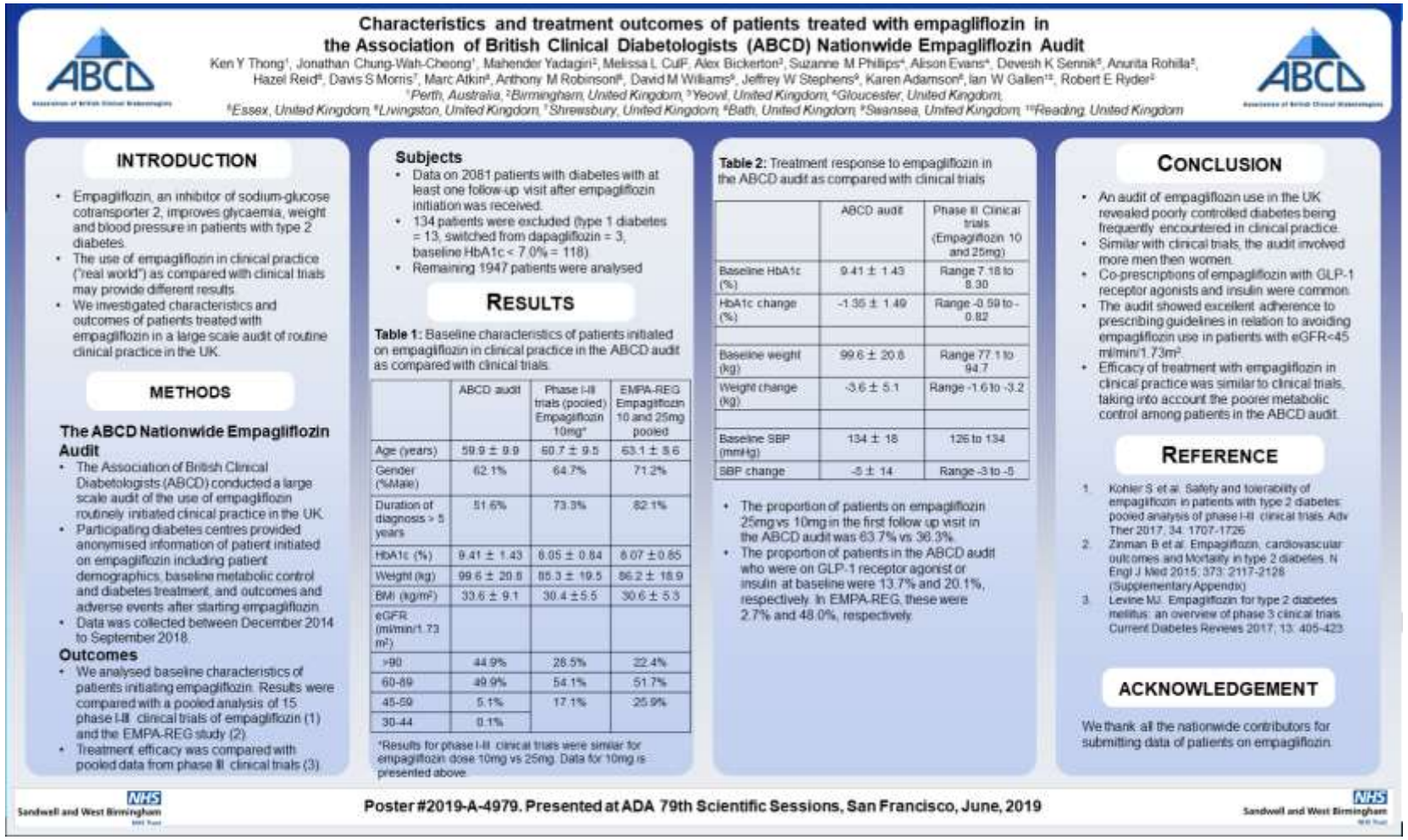
ABCD
Association of British Clinical Diabetologists

ABCD nationwide Empagliflozin audit

- Launched April 2017
- Findings so far …..



ABCD nationwide empagliflozin audit - findings so far 1



Characteristics and treatment outcomes of patients treated with empagliflozin in the Association of British Clinical Diabetologists (ABCD) Nationwide Empagliflozin Audit

Ken Y Thong[1], Jonathan Chung-Wah-Cheong[1], Mahender Yadagiri[2], Melissa L Cuff, Alex Bickerton[3], Suzanne M Phillips[4], Alison Evans[4], Devesh K Sennik[5], Anurita Rohilla[5], Hazel Reid[6], Davis S Morris[7], Marc Atkin[8], Anthony M Robinson[8], David M Williams[9], Jeffrey W Stephens[9], Karen Adamson[9], Ian W Gallen[10], Robert E Ryder[11]
[1]Perth, Australia, [2]Birmingham, United Kingdom, [3]Yeovil, United Kingdom, [4]Gloucester, United Kingdom, [5]Essex, United Kingdom, [6]Livingston, United Kingdom, [7]Shrewsbury, United Kingdom, [8]Bath, United Kingdom, [9]Swansea, United Kingdom, [10]Reading, United Kingdom

INTRODUCTION

- Empagliflozin, an inhibitor of sodium-glucose cotransporter 2, improves glycaemia, weight and blood pressure in patients with type 2 diabetes.
- The use of empagliflozin in clinical practice ("real world") as compared with clinical trials may provide different results.
- We investigated characteristics and outcomes of patients treated with empagliflozin in a large scale audit of routine clinical practice in the UK.

METHODS

The ABCD Nationwide Empagliflozin Audit

- The Association of British Clinical Diabetologists (ABCD) conducted a large scale audit of the use of empagliflozin routinely initiated clinical practice in the UK.
- Participating diabetes centres provided anonymised information of patient initiated on empagliflozin including patient demographics, baseline metabolic control and diabetes treatment, and outcomes and adverse events after starting empagliflozin.
- Data was collected between December 2014 to September 2018.

Outcomes

- We analysed baseline characteristics of patients initiating empagliflozin. Results were compared with a pooled analysis of 15 phase I-III clinical trials of empagliflozin (1) and the EMPA-REG study (2).
- Treatment efficacy was compared with pooled data from phase III clinical trials (3).

Subjects

- Data on 2081 patients with diabetes with at least one follow-up visit after empagliflozin initiation was received.
- 134 patients were excluded (type 1 diabetes = 13, switched from dapagliflozin = 3, baseline HbA1c < 7.0% = 118).
- Remaining 1947 patients were analysed

RESULTS

Table 1: Baseline characteristics of patients initiated on empagliflozin in clinical practice in the ABCD audit as compared with clinical trials.

	ABCD audit	Phase I-III trials (pooled) Empagliflozin 10mg*	EMPA-REG Empagliflozin 10 and 25mg pooled
Age (years)	59.9 ± 9.9	60.7 ± 9.5	63.1 ± 8.6
Gender (%Male)	62.1%	64.7%	71.2%
Duration of diagnosis > 5 years	51.6%	73.3%	82.1%
HbA1c (%)	9.41 ± 1.43	8.05 ± 0.84	8.07 ±0.85
Weight (kg)	99.6 ± 20.8	85.3 ± 19.5	86.2 ± 18.9
BMI (kg/m²)	33.6 ± 9.1	30.4 ±5.5	30.6 ± 5.3
eGFR (ml/min/1.73 m²)			
>90	44.9%	26.5%	22.4%
60-89	49.9%	54.1%	51.7%
45-59	5.1%	17.1%	25.9%
30-44	0.1%		

*Results for phase I-III clinical trials were similar for empagliflozin dose 10mg vs 25mg. Data for 10mg is presented above

Table 2: Treatment response to empagliflozin in the ABCD audit as compared with clinical trials

	ABCD audit	Phase III Clinical trials (Empagliflozin 10 and 25mg)
Baseline HbA1c (%)	9.41 ± 1.43	Range 7.18 to 8.30
HbA1c change (%)	-1.35 ± 1.49	Range -0.59 to -0.82
Baseline weight (kg)	99.6 ± 20.8	Range 77.1 to 94.7
Weight change (kg)	-3.6 ± 5.1	Range -1.6 to -3.2
Baseline SBP (mmHg)	134 ± 18	126 to 134
SBP change	-5 ± 14	Range -3 to -5

- The proportion of patients on empagliflozin 25mg vs 10mg in the first follow up visit in the ABCD audit was 63.7% vs 36.3%.
- The proportion of patients in the ABCD audit who were on GLP-1 receptor agonist or insulin at baseline were 13.7% and 20.1%, respectively. In EMPA-REG, these were 2.7% and 48.0%, respectively.

CONCLUSION

- An audit of empagliflozin use in the UK revealed poorly controlled diabetes being frequently encountered in clinical practice.
- Similar with clinical trials, the audit involved more men then women.
- Co-prescriptions of empagliflozin with GLP-1 receptor agonists and insulin were common.
- The audit showed excellent adherence to prescribing guidelines in relation to avoiding empagliflozin use in patients with eGFR<45 ml/min/1.73m².
- Efficacy of treatment with empagliflozin in clinical practice was similar to clinical trials, taking into account the poorer metabolic control among patients in the ABCD audit.

REFERENCE

1. Kohler S et al. Safety and tolerability of empagliflozin in patients with type 2 diabetes: pooled analysis of phase I-III clinical trials. Adv Ther 2017; 34: 1707-1726
2. Zinman B et al. Empagliflozin, cardiovascular outcomes and Mortality in type 2 diabetes. N Engl J Med 2015; 373: 2117-2128 (Supplementary Appendix)
3. Levine MJ. Empagliflozin for type 2 diabetes mellitus: an overview of phase 3 clinical trials. Current Diabetes Reviews 2017; 13: 405-423

ACKNOWLEDGEMENT

We thank all the nationwide contributors for submitting data of patients on empagliflozin.

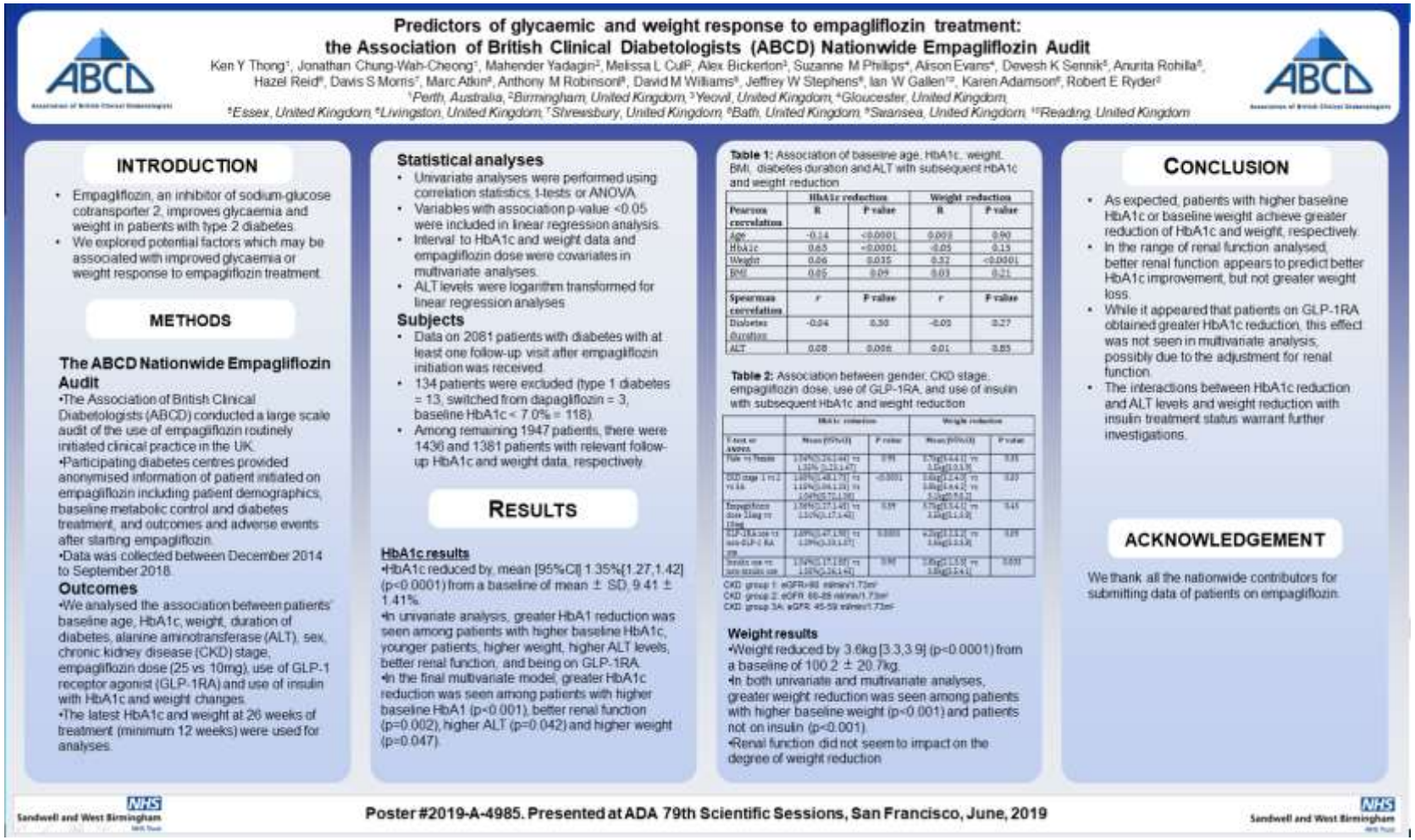
Poster #2019-A-4979. Presented at ADA 79th Scientific Sessions, San Francisco, June, 2019

By first return to clinic after starting empagliflozin

- Mean HbA1c fell by 1.35% from 9.41% to 8.06%
- Mean weight fell by 3.6 kg from 99.6 kg to 96.0 kg

ADA 2019 Poster Presentation: KY. Thong et al, on behalf of all ABCD nationwide empagliflozin audit contributors

ABCD nationwide empagliflozin audit - findings so far 2



Predictors of glycaemic and weight response to empagliflozin treatment: the Association of British Clinical Diabetologists (ABCD) Nationwide Empagliflozin Audit

Ken Y Thong[1], Jonathan Chung-Wah-Cheong[1], Mahender Yadagiri[2], Melissa L Cull[2], Alex Bickerton[3], Suzanne M Philips[4], Alison Evans[4], Devesh K Sennik[5], Anurita Rohilla[5], Hazel Reid[6], Davis S Morris[7], Marc Atkin[8], Anthony M Robinson[8], David M Williams[9], Jeffrey W Stephens[9], Ian W Gallen[10], Karen Adamson[6], Robert E Ryder[6]

[1]Perth, Australia, [2]Birmingham, United Kingdom, [3]Yeovil, United Kingdom, [4]Gloucester, United Kingdom, [5]Essex, United Kingdom, [6]Livingston, United Kingdom, [7]Shrewsbury, United Kingdom, [8]Bath, United Kingdom, [9]Swansea, United Kingdom, [10]Reading, United Kingdom

INTRODUCTION

- Empagliflozin, an inhibitor of sodium-glucose cotransporter 2, improves glycaemia and weight in patients with type 2 diabetes.
- We explored potential factors which may be associated with improved glycaemia or weight response to empagliflozin treatment.

METHODS

The ABCD Nationwide Empagliflozin Audit

•The Association of British Clinical Diabetologists (ABCD) conducted a large scale audit of the use of empagliflozin routinely initiated clinical practice in the UK.
•Participating diabetes centres provided anonymised information of patient initiated on empagliflozin including patient demographics, baseline metabolic control and diabetes treatment, and outcomes and adverse events after starting empagliflozin.
•Data was collected between December 2014 to September 2018.

Outcomes

•We analysed the association between patients' baseline age, HbA1c, weight, duration of diabetes, alanine aminotransferase (ALT), sex, chronic kidney disease (CKD) stage, empagliflozin dose (25 vs 10mg), use of GLP-1 receptor agonist (GLP-1RA) and use of insulin with HbA1c and weight changes.
•The latest HbA1c and weight at 26 weeks of treatment (minimum 12 weeks) were used for analyses.

Statistical analyses

- Univariate analyses were performed using correlation statistics, t-tests or ANOVA.
- Variables with association p-value <0.05 were included in linear regression analysis.
- Interval to HbA1c and weight data and empagliflozin dose were covariates in multivariate analyses.
- ALT levels were logarithm transformed for linear regression analyses.

Subjects

- Data on 2081 patients with diabetes with at least one follow-up visit after empagliflozin initiation was received.
- 134 patients were excluded (type 1 diabetes = 13, switched from dapagliflozin = 3, baseline HbA1c < 7.0% = 118).
- Among remaining 1947 patients, there were 1436 and 1381 patients with relevant follow-up HbA1c and weight data, respectively.

RESULTS

HbA1c results

•HbA1c reduced by, mean [95%CI] 1.35%[1.27,1.42] (p<0.0001) from a baseline of mean ± SD, 9.41 ± 1.41%.
•In univariate analysis, greater HbA1 reduction was seen among patients with higher baseline HbA1c, younger patients, higher weight, higher ALT levels, better renal function, and being on GLP-1RA.
•In the final multivariate model, greater HbA1c reduction was seen among patients with higher baseline HbA1 (p<0.001), better renal function (p=0.002), higher ALT (p=0.042) and higher weight (p=0.047).

Table 1: Association of baseline age, HbA1c, weight, BMI, diabetes duration and ALT with subsequent HbA1c and weight reduction

	HbA1c reduction		Weight reduction	
Pearson correlation	**R**	**P value**	**R**	**P value**
Age	-0.14	<0.0001	0.003	0.90
HbA1c	0.65	<0.0001	-0.05	0.13
Weight	0.06	0.015	0.32	<0.0001
BMI	0.05	0.04	0.03	0.21
Spearman correlation	**r**	**P value**	**r**	**P value**
Diabetes duration	-0.04	0.30	-0.05	0.27
ALT	0.08	0.006	0.01	0.85

Table 2: Association between gender, CKD stage, empagliflozin dose, use of GLP-1RA, and use of insulin with subsequent HbA1c and weight reduction

	HbA1c reduction		Weight reduction	
T-test or ANOVA	Mean [95%CI]	P value	Mean [95%CI]	P value
Male vs Female	1.34% [1.25,1.44] vs 1.33% [1.23,1.47]	0.91	3.7kg [3.4,4.1] vs 3.2kg [3.0,3.3]	0.05
CKD stage 1 vs 2 vs 3A	1.08% [0.98,1.21] vs 1.19% [1.09,1.29] vs 1.56% [1.37,1.76]	<0.0001	3.6kg [3.2,4.3] vs 3.8kg [3.4,4.2] vs 3.2kg [2.9,3.5]	0.20
Empagliflozin dose 25mg vs 10mg	1.36% [1.27,1.45] vs 1.30% [1.17,1.45]	0.39	3.7kg [3.5,4.1] vs 3.4kg [3.1,3.8]	0.45
GLP-1RA use vs non-GLP-1 RA use	1.49% [1.41,1.58] vs 1.29% [1.20,1.37]	0.0003	4.2kg [3.8,4.7] vs 3.4kg [3.2,3.6]	0.05
Insulin use vs non-insulin use	1.54% [1.47,1.62] vs 1.16% [1.06,1.26]	0.90	3.8kg [3.5,4.1] vs 3.6kg [3.3,4.1]	0.69

CKD group 1: eGFR>90 ml/min/1.73m²
CKD group 2: eGFR 60-89 ml/min/1.73m²
CKD group 3A: eGFR 45-59 ml/min/1.73m²

Weight results

•Weight reduced by 3.6kg [3.3,3.9] (p<0.0001) from a baseline of 100.2 ± 20.7kg.
•In both univariate and multivariate analyses, greater weight reduction was seen among patients with higher baseline weight (p<0.001) and patients not on insulin (p<0.001).
•Renal function did not seem to impact on the degree of weight reduction.

CONCLUSION

- As expected, patients with higher baseline HbA1c or baseline weight achieve greater reduction of HbA1c and weight, respectively.
- In the range of renal function analysed, better renal function appears to predict better HbA1c improvement, but not greater weight loss.
- While it appeared that patients on GLP-1RA obtained greater HbA1c reduction, this effect was not seen in multivariate analysis, possibly due to the adjustment for renal function.
- The interactions between HbA1c reduction and ALT levels and weight reduction with insulin treatment status warrant further investigations.

ACKNOWLEDGEMENT

We thank all the nationwide contributors for submitting data of patients on empagliflozin.

Sandwell and West Birmingham NHS

Poster #2019-A-4985. Presented at ADA 79th Scientific Sessions, San Francisco, June, 2019

Sandwell and West Birmingham NHS

- The higher baseline HbA1c or weight achieve greater the reduction of HbA1c or weight
- Better renal function predicts better HbA1c improvement, but not greater weight loss

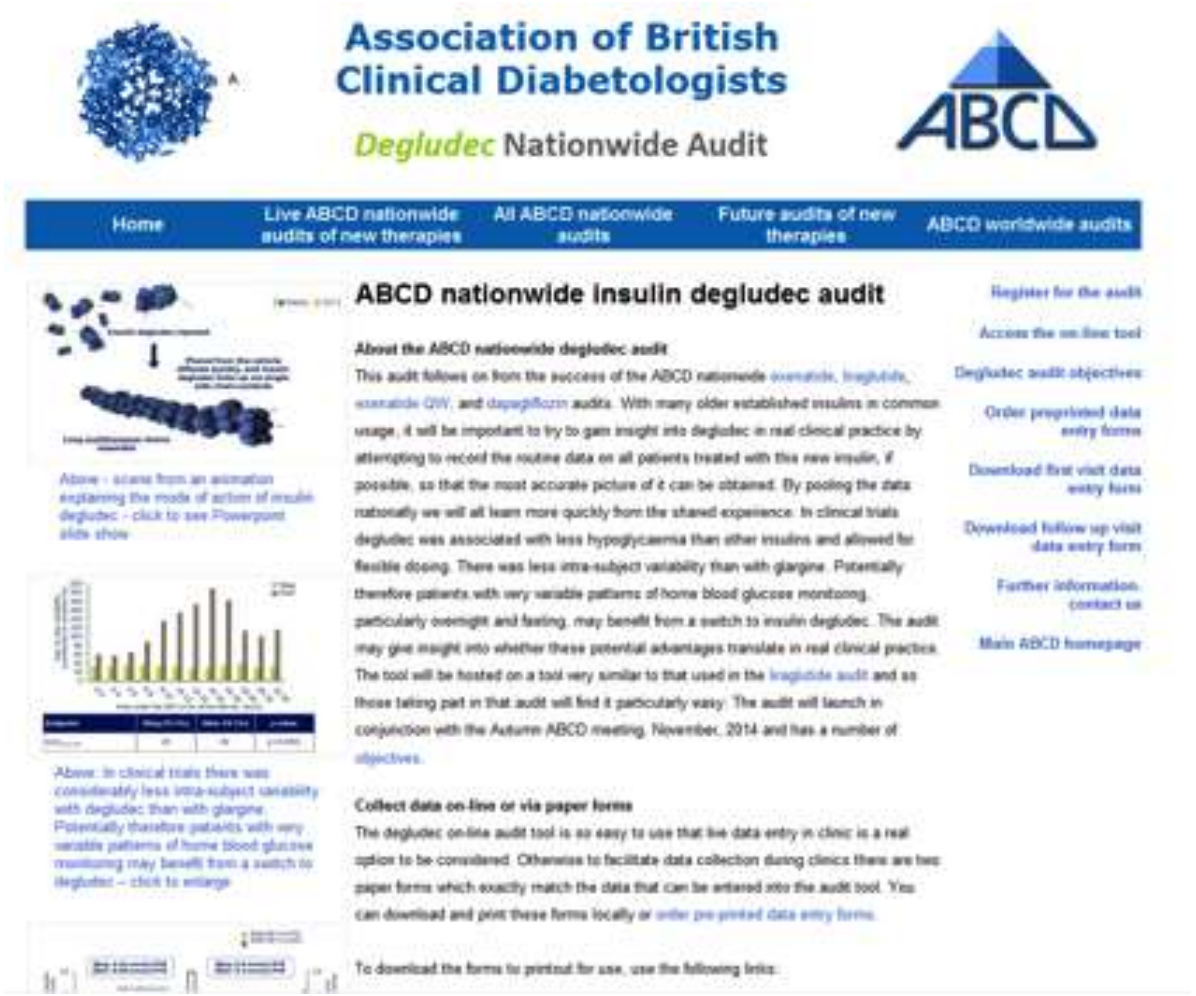
ADA 2019 Poster Presentation: KY. Thong et al, on behalf of all ABCD nationwide empagliflozin audit contributors

ABCD
Association of British Clinical Diabetologists

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD nationwide degludec audit – findings so far



Association of British Clinical Diabetologists

Degludec Nationwide Audit

ABCD

Home | Live ABCD nationwide audits of new therapies | All ABCD nationwide audits | Future audits of new therapies | ABCD worldwide audits

ABCD nationwide insulin degludec audit

Above - scans from an animation explaining the mode of action of insulin degludec - click to see Powerpoint slide show

Above: In clinical trials there was considerably less intra-subject variability with degludec than with glargine. Potentially therefore patients with very variable patterns of home blood glucose monitoring may benefit from a switch to degludec – click to enlarge

About the ABCD nationwide degludec audit

This audit follows on from the success of the ABCD nationwide exenatide, liraglutide, exenatide QW, and dapagliflozin audits. With many older established insulins in common usage, it will be important to try to gain insight into degludec in real clinical practice by attempting to record the routine data on all patients treated with this new insulin, if possible, so that the most accurate picture of it can be obtained. By pooling the data nationally we will all learn more quickly from the shared experience. In clinical trials degludec was associated with less hypoglycaemia than other insulins and allowed for flexible dosing. There was less intra-subject variability than with glargine. Potentially therefore patients with very variable patterns of home blood glucose monitoring, particularly overnight and fasting, may benefit from a switch to insulin degludec. The audit may give insight into whether these potential advantages translate in real clinical practice. The tool will be hosted on a tool very similar to that used in the liraglutide audit and so those taking part in that audit will find it particularly easy. The audit will launch in conjunction with the Autumn ABCD meeting, November, 2014 and has a number of objectives.

Collect data on-line or via paper forms

The degludec on-line audit tool is so easy to use that live data entry in clinic is a real option to be considered. Otherwise to facilitate data collection during clinics there are two paper forms which exactly match the data that can be entered into the audit tool. You can download and print these forms locally or order pre-printed data entry forms.

To download the forms to printout for use, use the following links:

Register for the audit

Access the on-line tool

Degludec audit objectives

Order preprinted data entry forms

Download first visit data entry form

Download follow up visit data entry form

Further information, contact us

Main ABCD homepage

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

Degludec audit - reasons for switching to degludec from another basal insulin

RATIONALE FOR STARTING DEGLUDEC? (Please tick all that apply)

Problems with hypoglycaemia	◉ Yes	○ No
Poor compliance, e.g. need flexible injection timing	○ Yes	◉ No
Need of more than 80 IU/day	○ Yes	◉ No
Needs OD basal insulin	○ Yes	◉ No
Considering going into a pump	○ Yes	◉ No
To fit in with variably timed visit by third party to administer (eg district nurse, relative...)	○ Yes	◉ No
Intrasubject variability of glucoses with current basal insulin	○ Yes	◉ No
Intra variability in absorption	○ Yes	◉ No

Screenshot from the ABCD degludec nationwide audit on-line form

ABCD
Association of British Clinical Diabetologists

Effect of insulin degludec on hypoglycaemia

Change in frequency of hypoglycaemia where reason for switching to insulin degludec was hypoglycaemia

		Reduced	Same	Increased	P value
T1DM	Minor	31	16	0	p < .000001
	Severe	16	13	1	P < 0.01
	Nocturnal	22	12	0	P < .00001
T2DM	Minor	12	12	2	p < .05
	Severe	2	12	0	ns
	Nocturnal	7	12	1	ns

Data presented at EASD meeting, Lisbon, September 2017

Effect of insulin degludec on hypoglycaemia

Change in frequency of hypoglycaemia where reason for switching to insulin degludec was hypoglycaemia

		Reduced	Same	Increased	P value
T1DM	Minor	31	16	0	p < .000001
	Severe	16	13	1	P < 0.01
	Nocturnal	22	12	0	P < .00001
T2DM	Minor	12	12	2	p < .05
	Severe	2	12	0	ns
	Nocturnal	7	12	1	ns

Data presented at EASD meeting, Lisbon, September 2017

Effect of insulin degludec on hypoglycaemia

Change in frequency of hypoglycaemia where reason for switching to insulin degludec was hypoglycaemia

		Reduced	Same	Increased	P value
T1DM	Minor	31	16	0	p < .000001
	Severe	16	13	1	P < 0.01
	Nocturnal	22	12	0	P < .00001
T2DM	Minor	12	12	2	p < .05
	Severe	2	12	0	ns
	Nocturnal	7	12	1	ns

Data presented at EASD meeting, Lisbon, September 2017

Effect of insulin degludec on HbA1c

Change in HbA1c (mmol/mol) after switching to insulin degludec from another basal insulin

Type of diabetes	T1D		T2D	
Reason for degludec	Hypoglycaemia	Other	Hypoglycaemia	Other
n	100	41	40	100
HbA1c before degludec	68.2 ± 20.4	87.4 ± 24.4	64.1 ± 18.4	87.9 ± 23.0
HbA1c after degludec	69.5 +22.2	80.2 ± 22.5	61.6 ± 18.5	76.1 ±22.4
Change in HbA1c	**+1.0 ± 1.3 (ns)**	**-7.2 ± 1.9 * (p < .001)**	**-2.34 ± 1.8 (ns)**	**-11.8 ± 2.4 * (p < .00001)**

Data presented at EASD meeting, Lisbon, September 2017

Effect of insulin degludec on HbA1c

Change in HbA1c (mmol/mol) after switching to insulin degludec from another basal insulin

Type of diabetes	T1D		T2D	
Reason for degludec	Hypoglycaemia	Other	Hypoglycaemia	Other
n	100	41	40	100
HbA1c before degludec	68.2 ± 20.4	87.4 ± 24.4	64.1 ± 18.4	87.9 ± 23.0
HbA1c after degludec	69.5 +22.2	80.2 ± 22.5	61.6 ± 18.5	76.1 ±22.4
Change in HbA1c	**+1.0 ± 1.3 (ns)**	**-7.2 ± 1.9 * (p < .001)**	**-2.34 ± 1.8 (ns)**	**-11.8 ± 2.4 * (p < .00001)**

Data presented at EASD meeting, Lisbon, September 2017

Effect of insulin degludec on weight

Change in weight (kg) after switching to insulin degludec from another basal insulin

Type of diabetes	T1D		T2D	
Reason for degludec	Hypoglycaemia	Other	Hypoglycaemia	Other
n	83	52	37	74
Weight before degludec	74.5 ± 14.4	79.4 ± 20.5	87.9 ± 16.3	105.5 ± 28.1
Weight after degludec	74.3 ± 14.0	80.5 ±20.6	85.6 ± 15.1	104.8 ± 27.1
Change in weight	**-0.2 ± 0.6 (ns)**	**+1.1 ± 0.5 * (p < .05)**	**-2.4 ± 1.8 * (P < 0.05)**	**-0.7 ± 0.7 (ns)**

Data presented at EASD meeting, Lisbon, September 2017

Effect of insulin degludec on weight

Change in weight (kg) after switching to insulin degludec from another basal insulin

Type of diabetes	T1D		T2D	
Reason for degludec	Hypoglycaemia	Other	Hypoglycaemia	Other
n	83	52	37	74
Weight before degludec	74.5 ± 14.4	79.4 ± 20.5	87.9 ± 16.3	105.5 ± 28.1
Weight after degludec	74.3 ± 14.0	80.5 ±20.6	85.6 ± 15.1	104.8 ± 27.1
Change in weight	**-0.2 ± 0.6 (ns)**	**+1.1 ± 0.5 * (p < .05)**	**-2.4 ± 1.8 * (P < 0.05)**	**-0.7 ± 0.7 (ns)**

Data presented at EASD meeting, Lisbon, September 2017

Effect of insulin degludec on weight

Change in weight (kg) after switching to insulin degludec from another basal insulin

Type of diabetes	T1D		T2D	
Reason for degludec	Hypoglycaemia	Other	Hypoglycaemia	Other
n	83	52	37	74
Weight before degludec	74.5 ± 14.4	79.4 ± 20.5	87.9 ± 16.3	105.5 ± 28.1
Weight after degludec	74.3 ± 14.0	80.5 ±20.6	85.6 ± 15.1	104.8 ± 27.1
Change in weight	**-0.2 ± 0.6 (ns)**	**+1.1 ± 0.5 * (p < .05)**	**-2.4 ± 1.8 * (P < 0.05)**	**-0.7 ± 0.7 (ns)**

Data presented at EASD meeting, Lisbon, September 2017

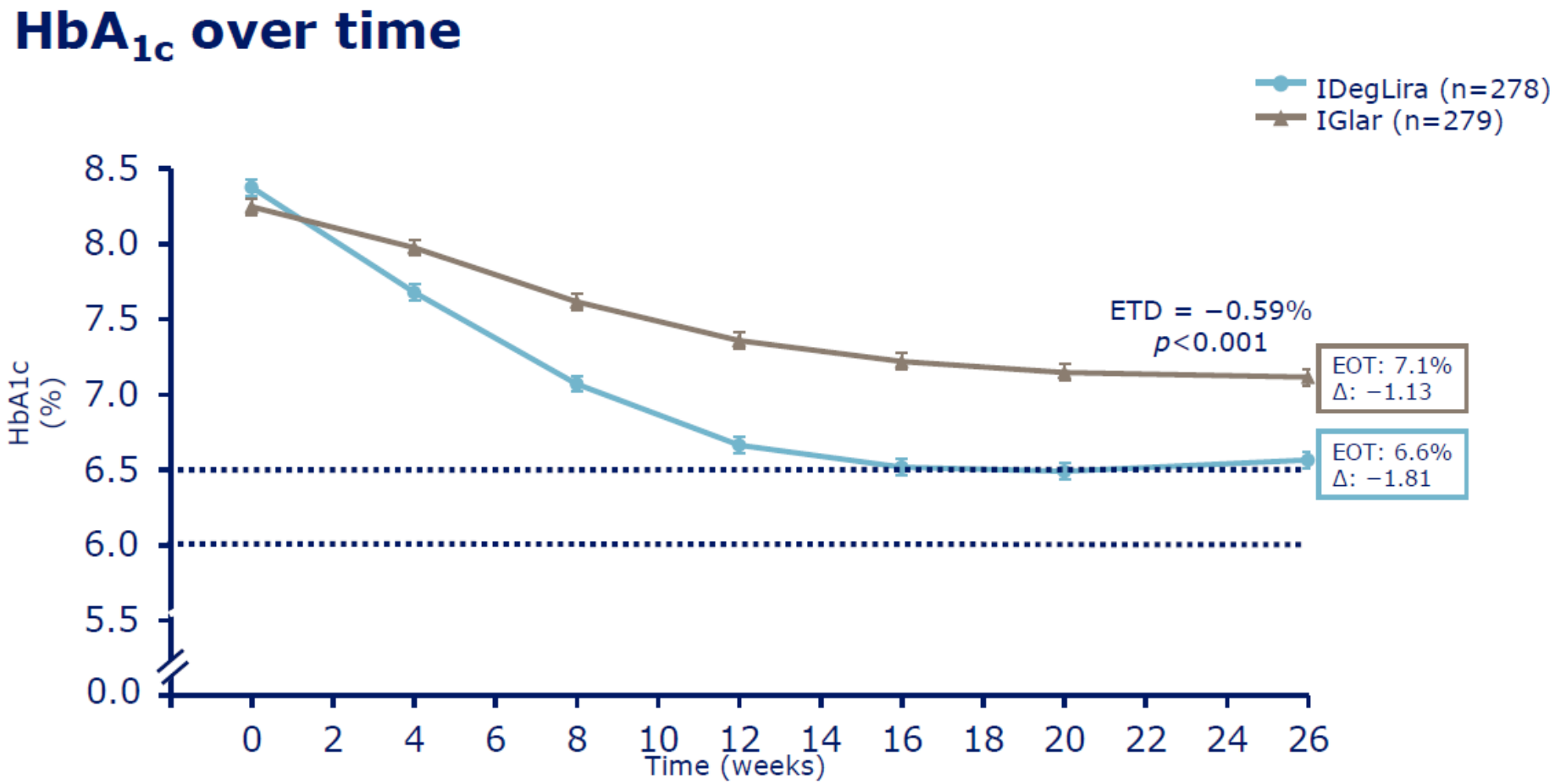
ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD nationwide and worldwide audit programme

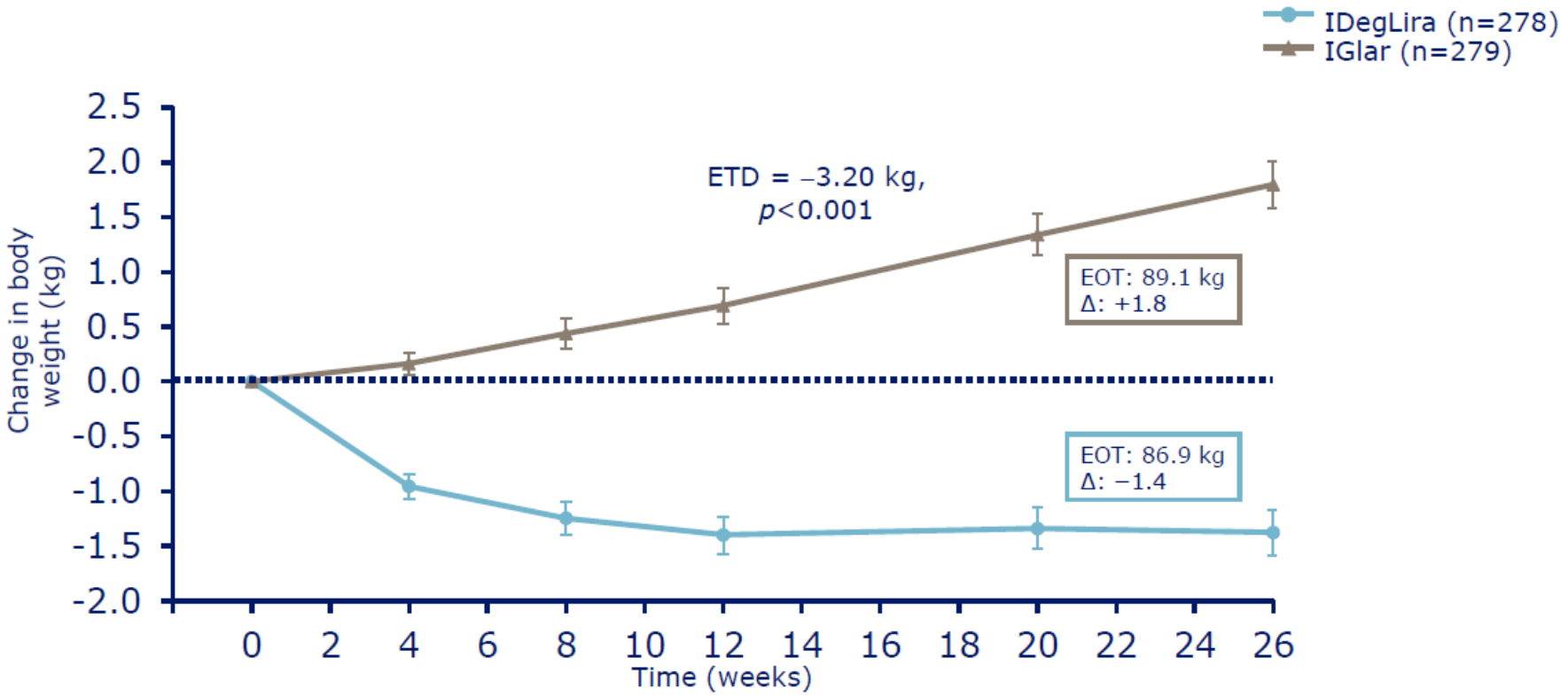
- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

Treat to Target – IDegLira Vs Glargine



Treat to Target – IDegLira Vs Glargine

Change in body weight over time



IDegLira is not licensed for weight loss. Change in bodyweight from baseline was a secondary endpoint in DUAL V, a 26 week study.

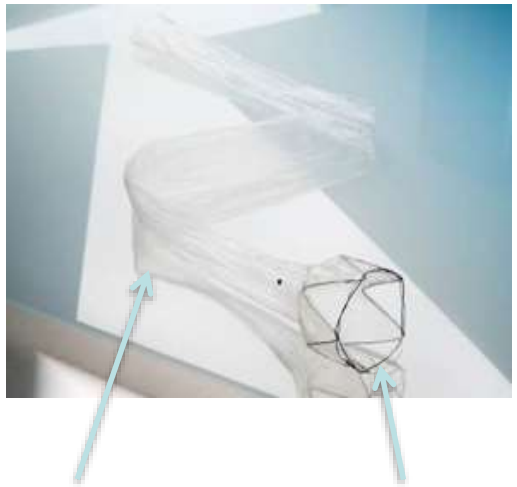
ABCD nationwide and worldwide audit programme

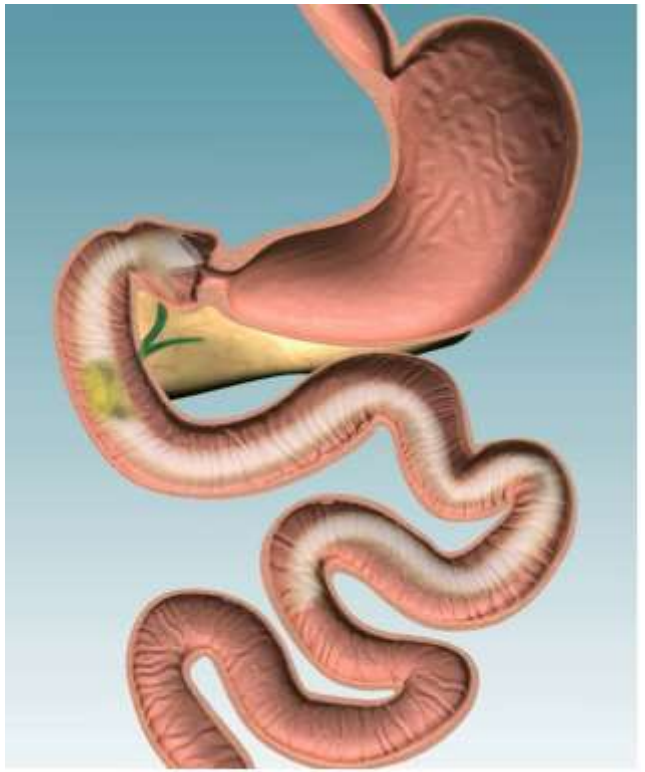
- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

Endobarrier – implantable duodenal-jejunal liner

- 60 cm impermeable sleeve
- Minimally invasive

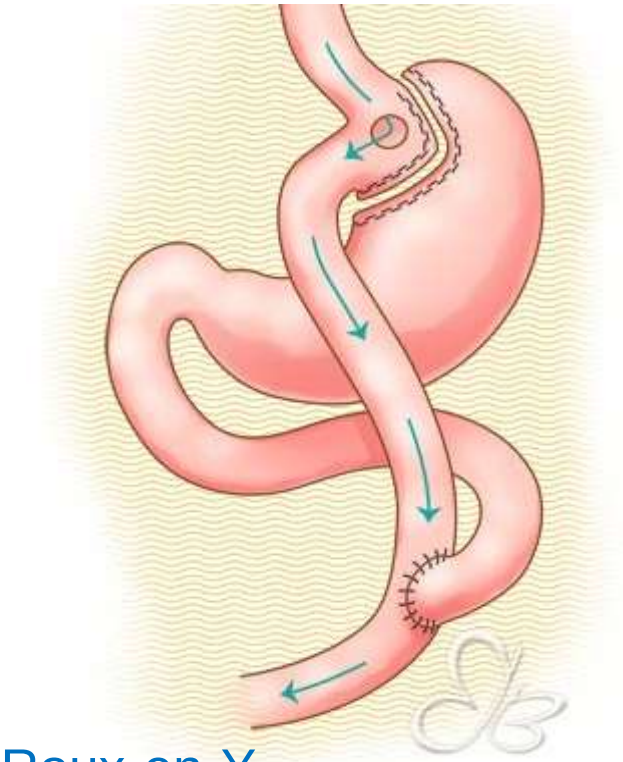
Endobarrier – implantable duodenal-jejunal liner





- 60 cm impermeable sleeve
- Minimally invasive

Endobarrier – implantable duodenal-jejunal liner

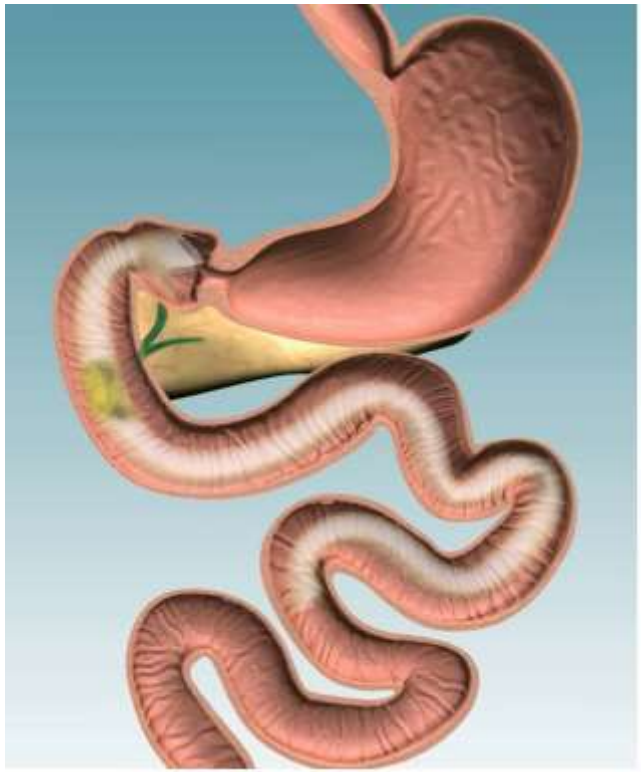


Roux-en-Y gastric bypass surgery

Fluoropolymer wall

Nitinol Anchor

- 60 cm impermeable sleeve
- Minimally invasive



Print this Page for Your Records Close Window

Control/Tracking Number: A-19-2265-EASD
Activity: Abstract
Current Date/Time: 4/1/2019 1:55:16 PM

Duodenal jejunal bypass liner (DJBL) fo
registry in 871 patient

851 patients

28 Centres, 8 Countries, 4 Continents

Autho

de Jonge[7], J. Greve[7], L. Kow[8], J. Bessell[9], H. Sourij[10],

[1]Freibur, Germany, [3]Epworth Hospital, Richmond, Australia, [4]Sourasky Medical, Tel Aviv, Israel, [5]Oswaldc ess Alexandra Hospital, Woolloongabba, Australia, [7]MUMC, Maastricht, Netherlands, [8]ABC, Adelaide, Australia, [9]AOS, Ad Medical University, Graz, Austria, [11]Clinical and Experimental Medicine, Prague, Czech Republic, [12]City Hospital, Birmingham, UK.

Duodenal jejunal bypass liner (DJBL) for treatment of type 2 diabetes and obesity – the risk benefit ratio from the worldwide EndoBarrier (EB) registry

K. Laubner[1], J. Seufert[1], J. Aberle[2], H. Frydenberg[3], L. Munro[3], S. Fishman[4], R. Cohen[5], G. Holtmann[6], C. de Jonge[7], J. Greve[7], L. Kow[8], J. Bessell[9], H. Sourij[10], M. Benes[11], R.E.J. Ryder[12]

[1]Freiburg, Germany, [2]Hamburg, Germany, [3]Richmond, Australia, [4]Tel Aviv, Israel, [5]São Paulo, Brazil [6]Brisbane, Australia, [7]Maastricht, Netherlands, [8]ABC, Adelaide, Australia, [9]AOS,Adelaide, Australia, [10]Graz, Austria, [11]Prague, Czech Republic, [12]Birmingham, UK

BACKGROUND

EndoBarrier® (GI Dynamics, Boston, USA), also known as the duodenal–jejunal bypass liner, is a 60 cm long impermeable fluoropolymer sleeve which is implanted by endoscopy into the first part of the small intestine where it remains for about 1 year (Figure 1). It is held in place by a nitinol anchor, such that food passes through it without coming into contact with the small intestine, thereby interfering with the normal digestive processes that occur in this region[1]. The endoscopic insertion and removal of EndoBarrier are day case procedures, performed in less than an hour under general anaesthesia or heavy sedation. This form of reversible bariatric procedure has been shown to reduce weight and improve glycaemic control in patients with diabetes and obesity[1,2].

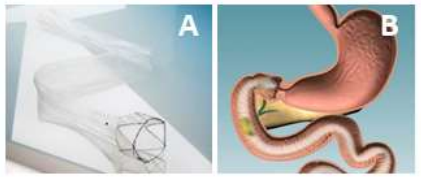


Fig. 1A. Photograph of Endobarrier with crown anchor in foreground and tubing posteriorly; **1B** shows the device implanted in the proximal intestine with ingested food (yellow) passing within the device.

AIM

Nevertheless uncertainty exists about risks versus benefits of EndoBarrier. In view of this, during 2017, an independent, secure, on-line registry was established under the auspices of the Association of British Clinical Diabetologists (ABCD), for the collection of safety and efficacy data of EndoBarrier treated patients worldwide.

METHOD

We invited EndoBarrier users from centres worldwide to register to enter the before and after data from their EndoBarrier treated patients into the registry.

REFERENCES

1. Ryder REJ et al. Br J Diabetes 2018;18:14-17
2. Jirapinyo P et al. Diabetes Care 2018;41(5):1106-1115
3. See http://gidynamics.com/2016/06/23/final-efficacy-and-safety-results-of-u-s-endo-trial-announced-at-ada/

RESULTS

As of April 2019, data had been entered on 871 EndoBarrier treated patients from 28 centres in 8 countries: Australia, Austria, Brazil, Czech Republic, Germany, Israel, Netherlands and United Kingdom. The demographics of these patients are shown in Table 1.

Table 1: Baseline demographics of the 871 patients

Parameter	n=871
Age (years)	52.1±10.5
Sex (% male)	53.8
BMI (kg/m²)	41.6±9.2
Diabetes (%)	84.2

EndoBarrier led to many benefits, including: in those with both baseline and explant data, mean ± SD weight fell by 14.5 ± 10.3 kg from 125.3 ± 26.7 to 110.8 ± 26.4 kg (n = 265 p<0.001), HbA1c by 1.4 ± 1.6%, from 8.7 ± 1.8 to 7.2 ± 1.2% (n = 195, p<0.001), systolic BP fell from 138.5 ± 18.1 to 130.0 ± 17.2 mmHg (n = 149, <0.001) and cholesterol fell from 4.8 ± 1.2 to 4.3 ± 1.0 mmol/L (n = 332, <0.001) (Table 2).

Table 2: Changes in weight, HbA1c, systolic BP and cholesterol

Parameter	n	Baseline	EndoBarrier Explant	Difference	P-value
Weight (kg)	662	121.6±25.8	107.9±2644	-13.7±9.8	<0.001
HbA1c (mmol/mol)	501	8.2±1.8	7.0±1.2	-1.2±1.4	<0.001
Systolic BP (mmHg)	298	137.9±18.2	130.5±16.8	-7.4±20.1	<0.001
Cholesterol (mmol/L)	332	4.8±1.2	4.3±1.0	0.55±0.98	<0.001

Table 3: HbA1c response according to baseline HbA1c

HbA1c Range (%)	n	Baseline	At Removal	Difference	P value
All HbA1c	501	8.2±1.8	7.0±1.2	-1.2±1.4	<0.001
All HbA1c ≥ 7	377	8.9±1.5	7.4±1.1	-1.6±1.5	<0.001
All HbA1c ≥ 8	262	9.6±1.4	7.6±1.1	-1.9±1.5	<0.001
All HbA1c ≥ 9	143	10.5±1.2	7.8±1.2	-2.7±1.5	<0.001
HbA1c ≥ 10	86	11.2±1.0	7.9±1.3	-3.3±1.5	<0.001

Fall in HbA1c

The fall in HbAc1 found in the whole group was affected by the fact that over 15% of the patients did not have diabetes, and many of those with diabetes the glycaemic control was good. Analysis of the data according to baseline HbA1c is shown in Table 3 and this data clearly shows that the higher the baseline HbA1c the greater the impact of EndoBarrier treatment.

Serious Adverse (Events

There were 37 (4.2%) serious adverse events and 105 (12.5%) less serious adverse events (Table 4). All SAE patients made a full recovery and most derived significant benefit despite the setback. Some serious adverse events could have been avoided if patients had adhered to guidelines.

Table 4. Serious adverse events in 871 EndoBarrier treated patients (GI = gastrointestinal).

Serous Adverse Event	n	%
Early removal because of GI bleed	22	2.5
Liver abscess (early removal = 7/10; found at time of routine explant = 3/10)	10	1.1
Early removal because of pancreatitis	2	0.2
Early removal because of cholecystitis	1	0.1
Abdominal abscess due to small perforation of bowel in relation to Endobarrier	1	0.1
Liver abscess after prolonged implant (nearly 2 years EndoBarrier treatment; lost 37 kg)	1	0.1
Total	**37**	**4.2**
Less serious adverse event	**n**	**%**
Early removal because of GI symptoms	33	3.8
Precautionary hospitalisation because of transient GI symptoms - removal not required	31	3.6
Early removal because of GI symptoms - EndoBarrier had migrated	18	2.1
Early removal because of liner obstruction	7	0.8
Minor GI bleeding. EndoBarrier not removed	5	0.6
Precautionary hospitalisation because of transient GI problems at time of removal	4	0.5
Hospitalisation because difficult removal - needed two attempts	3	0.3
Transient obstruction of device cleared at endoscopy - device not removed	3	0.3
Precautionary early removal because of asymptomatic EndoBarrier migration	1	0.1
Total	**105**	**12.5**

SUMMARY AND CONCLUSION

In this analysis from the worldwide EndoBarrier registry, the mean weight loss during the period of EndoBarrier implantation was 13.7 kg with associated improvements in glycaemic control, blood pressure and cholesterol. The higher the baseline HbA1c the greater the fall in HbA1c with a mean fall of 3.3% with those with a baseline HbA1c ≥ 10%. The rate of serious adverse events was 4,2% with the majority of these (2.5%) being gastrointestinal bleeds.

The rate of early removal for hepatic abscess (1.1%) was noticeably less than that the 3.5% rate found in the US pivotal trial[3]. All patients with a serious adverse event made a full recovery and most experienced considerable benefit from the treatment despite the adverse event. The effects of EndoBarrier therapy on glycaemic control, weight and blood pressure are likely to reduce the complications of diabetes. This international data from the EndoBarrier worldwide registry suggests that the likely benefits of EndoBarrier treatment, outweigh the risks.

Presented at EASD 55th Annual Meeting, Barcelona, September 16-20, 2019

EASD 2019 Poster Presentation: K. Laubner et al,

Table 1: Baseline demographics of the 871 patients

Parameter	n=871
Age (years)	52.1±10.5
Sex (% male)	53.8
BMI (kg/m^2)	41.6±9.2
Diabetes (%)	84.2

Table 2: Changes in weight, HbA1c, systolic BP and cholesterol

Parameter	n	Baseline	EndoBarrier Explant	Difference	P-value
Weight (kg)	662	121.6±25.8	107.9±2644	-13.7±9.8	<0.001
HbA1c (mmol/mol)	501	8.2±1.8	7.0±1.2	-1.2±1.4	<0.001
Systolic BP (mmHg)	298	137.9±18.2	130.5±16.8	-7.4±20.1	<0.001
Cholesterol (mmol/L)	332	4.8±1.2	4.3±1.0	0.55±0.98	<0.001

EASD 2019 Poster Presentation: K. Laubner et al,

Table 1. Impact of EndoBarrier on HbA1c depending on baseline HbA1c.
Conclusion – the higher the baseline HbA1c the greater the impact. Values are mean±SD

HbA1c (%)	n	Baseline	At removal	Difference	P value
All HbA1c	501	8.2±1.8	7.0±1.2	1.2±1.4	<0.001
≥ 7	377	8.9±1.5 to	7.4±1.1	1.6±1.5	<0.001
≥ 8	262	9.6±1.4	7.6±1.1	1.9 ±1.5	<0.001
≥ 9	143	10.5±1.2	7.8±1.2	2.7±1.5	<0.001
≥ 10	86	11.2±1.0	7.9±1.3	3.3±1.5	<0.001

Table 1. Impact of EndoBarrier on HbA1c depending on baseline HbA1c.
Conclusion – the higher the baseline HbA1c the greater the impact. Values are mean±SD

HbA1c (%)	n	Baseline	At removal	Difference	P value
All HbA1c	501	8.2±1.8	7.0±1.2	1.2±1.4	<0.001
≥ 7	377	8.9±1.5 to	7.4±1.1	1.6±1.5	<0.001
≥ 8	262	9.6±1.4	7.6±1.1	1.9 ±1.5	<0.001
≥ 9	143	10.5±1.2	7.8±1.2	2.7±1.5	<0.001
≥ 10	86	11.2±1.0	7.9±1.3	3.3±1.5	<0.001

Table 1. Impact of EndoBarrier on HbA1c depending on baseline HbA1c.
Conclusion – the higher the baseline HbA1c the greater the impact. Values are mean±SD

HbA1c (%)	n	Baseline	At removal	Difference	P value
All HbA1c	501	8.2±1.8	7.0±1.2	1.2±1.4	<0.001
≥ 7	377	8.9±1.5 to	7.4±1.1	1.6±1.5	<0.001
≥ 8	262	9.6±1.4	7.6±1.1	1.9 ±1.5	<0.001
≥ 9	143	10.5±1.2	7.8±1.2	2.7±1.5	<0.001
≥ 10	86	11.2±1.0	7.9±1.3	3.3±1.5	<0.001

MedTech

FDA puts hold on pivotal GI Dynamics trial for obesity device due to bacterial infection

by Stacy Lawrence | Mar 6, 2015 10:27am

The U.S. Food and Drug Administration has placed a hold on enrollment in the ongoing U.S. pivotal trial for the EndoBarrier. The device is a gastric liner from GI Dynamics that is intended to inhibit the absorption of nutrients, thereby providing weight loss and addressing obesity and Type 2 diabetes.

The FDA hold was due to four cases of bacterial infection of the liver, or hepatic abscess, in the 325 trial subject population. This is a known adverse event related to use of the EndoBarrier--but it presented at higher rates than expected in the trial. The company had set relative thresholds for an anticipated incident rate of hepatic abscess in the trial; the incident with the fourth patient exceeded that and triggered an analysis.

On a conference call, GI Dynamics' President and CEO Michael Dale said the infections are "likely related to the anchoring system interacting with the duodenum."

The EndoBarrier is a flexible, tube-shaped liner that is inserted endoscopically and placed at the beginning of the small intestine for up to one year. After that, it's removed during another endoscopic procedure.

Of the more than 2,900 commercial EndoBarrier units shipped outside the U.S. since 2009, about 1% of these have been implicated in hepatic abscess cases. Enrolled patients in the trial will continue to be the subject of data collection in the trial that's been put on hold. Patients presenting with bacterial infection due to the EndoBarrier typically have the device removed and are treated with antibiotics to resolve the infection.

The company said it has implemented "several risk mitigation strategies" in the pivotal trial and is working with the FDA toward resuming enrollment.

Dale said the company is "expeditiously working to submit additional risk/benefit information as requested by the FDA to resume the trial as quickly as possible."

Already a penny stock, GI Dynamics shares were cut in half on the trial hold news to $0.15.

- here is the release

The EndoBarrier in the intestine--Courtesy of GI Dynamics

March 2015

Hepatic abscess rate 3.5%

Table 1: Serious adverse events in 871 EndoBarrier treated patients (GI = gastrointestinal).

Serous Adverse Event	n	%
Early removal because of GI bleed	22	2.5
Liver abscess (early removal = 7/10; found at time of routine explant = 3/10)	10	1.1
Early removal because of pancreatitis	2	0.2
Early removal because of cholecystitis	1	0.1
Abdominal abscess due to small perforation of bowel in relation to Endobarrier	1	0.1
Liver abscess after prolonged implant (nearly 2 years EndoBarrier treatment; lost 37 kg)	1	0.1
Total	**37**	**4.2**
Less serious adverse event	**n**	**%**
Early removal because of GI symptoms	33	3.8
Precautionary hospitalisation because of transient GI symptoms - removal not required	31	3.6
Early removal because of GI symptoms - EndoBarrier had migrated	18	2.1
Early removal because of liner obstruction	7	0.8
Minor GI bleeding. EndoBarrier not removed	5	0.6
Precautionary hospitalisation because of transient GI problems at time of removal	4	0.5
Hospitalisation because difficult removal - needed two attempts	3	0.3
Transient obstruction of device cleared at endoscopy - device not removed	3	0.3
Precautionary early removal because of asymptomatic EndoBarrier migration	1	0.1
Total	**105**	**12.5**

Table 1: Serious adverse events in 871 EndoBarrier treated patients (GI = gastrointestinal).

Serous Adverse Event	n	%
Early removal because of GI bleed	22	2.5
Liver abscess (early removal = 7/10; found at time of routine explant = 3/10)	10	1.1
Early removal because of pancreatitis	2	0.2
Early removal because of cholecystitis	1	0.1
Abdominal abscess due to small perforation of bowel in relation to Endobarrier	1	0.1
Liver abscess after prolonged implant (nearly 2 years EndoBarrier treatment; lost 37 kg)	1	0.1
Total	**37**	**4.2**
Less serious adverse event	**n**	**%**
Early removal because of GI symptoms	33	3.8
Precautionary hospitalisation because of transient GI symptoms - removal not required	31	3.6
Early removal because of GI symptoms - EndoBarrier had migrated	18	2.1
Early removal because of liner obstruction	7	0.8
Minor GI bleeding. EndoBarrier not removed	5	0.6
Precautionary hospitalisation because of transient GI problems at time of removal	4	0.5
Hospitalisation because difficult removal - needed two attempts	3	0.3
Transient obstruction of device cleared at endoscopy - device not removed	3	0.3
Precautionary early removal because of asymptomatic EndoBarrier migration	1	0.1
Total	**105**	**12.5**

GI Dynamics wins FDA nod for pivotal US EndoBarrier trial

AUGUST 13, 2018 BY FINK DENSFORD — LEAVE A COMMENT

GI Dynamics (ASX:GID) said today it won FDA investigational device exemption approval to launch a pivotal trial of its EndoBarrier device designed for treating patients with type 2 diabetes and obesity, pending Institutional Review Board approval.

The EndoBarrier device is a plastic gut sleeve designed to prevent the absorption of nutrients from food as it exits the stomach and enters the intestinal tract to treat type 2 diabetes and obesity, the Lexington, Mass.-based company said.

The approval is a boon for the company, which has faced a number of hurdles with its device over the past few years, including shutting down an initial FDA-approved study, being pulled off the shelves in Australia and losing its CE Mark approval in the European Union.

"It's the first good news and a positive sign of all of the hard work the team has been putting in over the last two years. This is the first sign that the results are starting to turn around, so we're very excited about it," CEO Scott Schorer, who took over the company in March 2016, told **MassDevice.com** in an interview.

August 2018

GI Dynamics' 2nd Chance at an EndoBarrier Pivotal Trial

The company has had significant struggles with the EndoBarrier in the past, but a nod from FDA and the IRB to begin a new pivotal trial might be step back in the right direction for the technology.

By Omar Ford
February 14, 2019 in *Regulatory and Compliance*

GI Dynamics' fortunes might be changing, as the embattled device maker has crossed the last hurdle in its bid for the approval of a new pivotal trial to evaluate its obesity and diabetes treatment device, the EndoBarrier.

The company recently announced it had received Institutional Review Board approval to launch a pivotal trial of the EndoBarrier. GI Dynamics has struggled significantly with the device in the past (more on that later), but until recently it has had some success.

In August of 2018, FDA gave a nod to the EndoBarrier's pivotal trial. The last step was for the firm to

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD FreeStyle Libre Audit

Association of British Clinical Diabetologists

ABCD FreeStyle Libre Audit

The ABCD FSL Audit aims to explore the impact of the FSL on:

- HbA1c
- Hypoglycaemia awareness
- Resource utilisation: hospital admissions
- User satisfaction
- Diabetes related distress
- Discontinuation rate and causes

ABCD
Association of British Clinical Diabetologists

ABCD FreeStyle Libre Audit

- As of May 29, 2019 there are 296 users registered to the audit at 156 sites in 114 centres contributing data on 6644 patients.

Association of British Clinical Diabetologists

ABCD FreeStyle Libre Audit

- **Hypoglycaemia**
  - Mean GOLD score reduced from 2.85 to 2.46 (P<0.0001)
  - FSL use was associated with reversal of impaired awareness of hypoglycaemia (IAH):
  - 33% had IAH at baseline; 23% at follow up
  - Hypoglycaemia related admissions reduced from 2.71% to 0.5%
  - 79% (966/1234) reported that with use of FSL they were able to reduce the proportion of time in hypoglycaemia
  - 31% (372/1200) reported a reduced rate of hypoglycaemia
  - 39% (380/968) reported reduced nocturnal hypoglycaemia

ABCD
Association of British Clinical Diabetologists

ABCD FreeStyle Libre Audit

- **Diabetes Distress**
  - Diabetes Distress Scores improved from 3 (2-4) at baseline to 2 (1-3) at follow-up P<0.0001

- **HbA1c**
  - Change in HbA1c: -0.6% (6 mmol/mol) (P<0.0001)

The audit continues in particular to gather longer term results

Association of British Clinical Diabetologists

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD NATIONWIDE AUDIT OF TESTOSTERONE DEFICIENCY IN MEN WITH TYPE 2 DIABETES

Questionnaire developed – audit tool being built

Lead – Professor Hugh Jones, Barnsley

TESTOSTERONE DEFICIENCY IN MEN WITH TYPE 2 DIABETES

- Asking about erectile dysfunction should be part of routine annual review in all men with diabetes
- If present should measure testosterone and, if low, repeat with SHBG, LH, FSH

ABCD
Association of British Clinical Diabetologists

TESTOSTERONE DEFICIENCY IN MEN WITH TYPE 2 DIABETES

- High prevalence - 40% of men with type 2 diabetes have symptomatic testosterone deficiency
- Testosterone deficiency is associated with an adverse effect on cardiovascular risk factors, osteoporosis, reduced muscular strength (including frailty), anaemia and psychological well-being
- Testosterone deficiency is also associated with an increased mortality in type 2 diabetes and independently in cardiovascular disease
- Testosterone replacement has been shown to improve insulin resistance, lower HbA1c and cholesterol as well as reduce body weight and mortality

ABCD
Association of British Clinical Diabetologists

New ABCD audit imminent

The ABCD Nationwide Testosterone Deficiency audit is an independent audit supported by an unrestricted grant from Besins Healthcare

ABCD NATIONWIDE AUDIT OF TESTOSTERONE DEFICIENCY IN MEN WITH TYPE 2 DIABETES

ABCD
Association of British Clinical Diabetologists

FIRST VISIT DATA COLLECTION FORM

Date / (dd/mm/yyyy) /

Clinician | Clinician's email | Centre ID

PATIENT IDENTIFICATION

AFFIX PATIENT LABEL

FORENAME

SURNAME

DoB / / (dd/mm/yyyy)

NHS Number

Etnicity	☐ Afro-Carribean	☐ Asian
	☐ Oriental	☐ White
Marital Status	☐ Married/Civil	☐ Single
	☐ Separated/Divorced	☐ Widowed

DIAGNOSIS OF HYPOGONADISM MUST COMPRISE BOTH SYMPTOMS AND LOW TESTOSTERONE

PURPOSE OF THE AUDIT - 1

Testosterone replacement therapy is being used more commonly in men with hypogonadism and T2D

- TO DETERMINE THE CLINICAL BENEFITS OF TESTOSTERONE REPLACEMENT THERAPY

  Effect on symptoms of testosterone deficiency

  (a) Sexual (b) Physical (c) Psychological

  Glycaemic control, Lipid profile, body weight and change in diabetes medication.

  Effect of Testosterone therapy on Diabetes Distress

  and to assess normalisation of testosterone levels on treatment

ABCD
Association of British Clinical Diabetologists

PURPOSE OF THE AUDIT - 2

- TO DETERMINE THE SAFETY OF TESTOSTERONE REPLACEMENT THERAPY
  - To determine how frequently hypoglycaemia is reported after initiation of testosterone therapy
  - Secondary polycythaemia – haematocrit >0.54
  - Cardiovascular events
  - Rate and cause of hospitalisation

An audit that is not yet on the list

ABCD Nationwide Audit of Open Artificial Pancreas Systems

ABCD research fellow – Dr Tom Crabtree

Dr Emma Wilmot lead - Derby

Please be active in the current ABCD audits

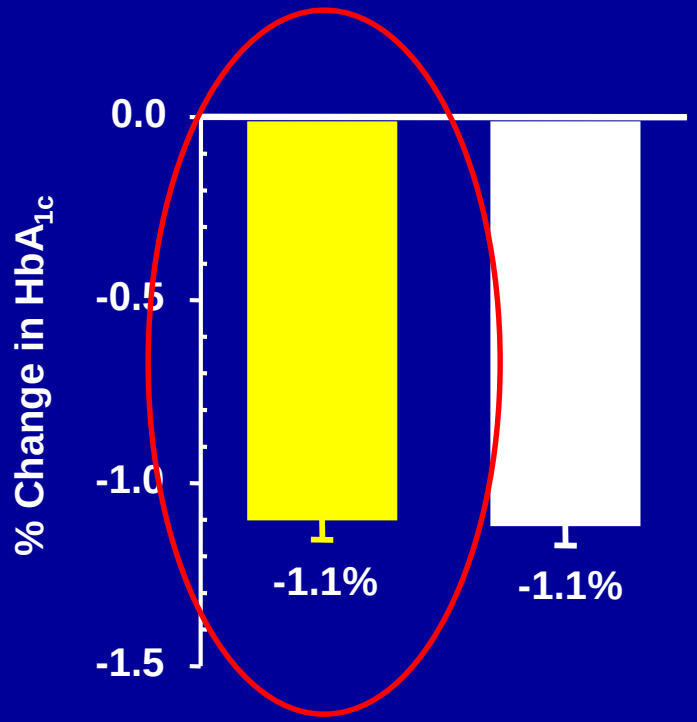
Especially:

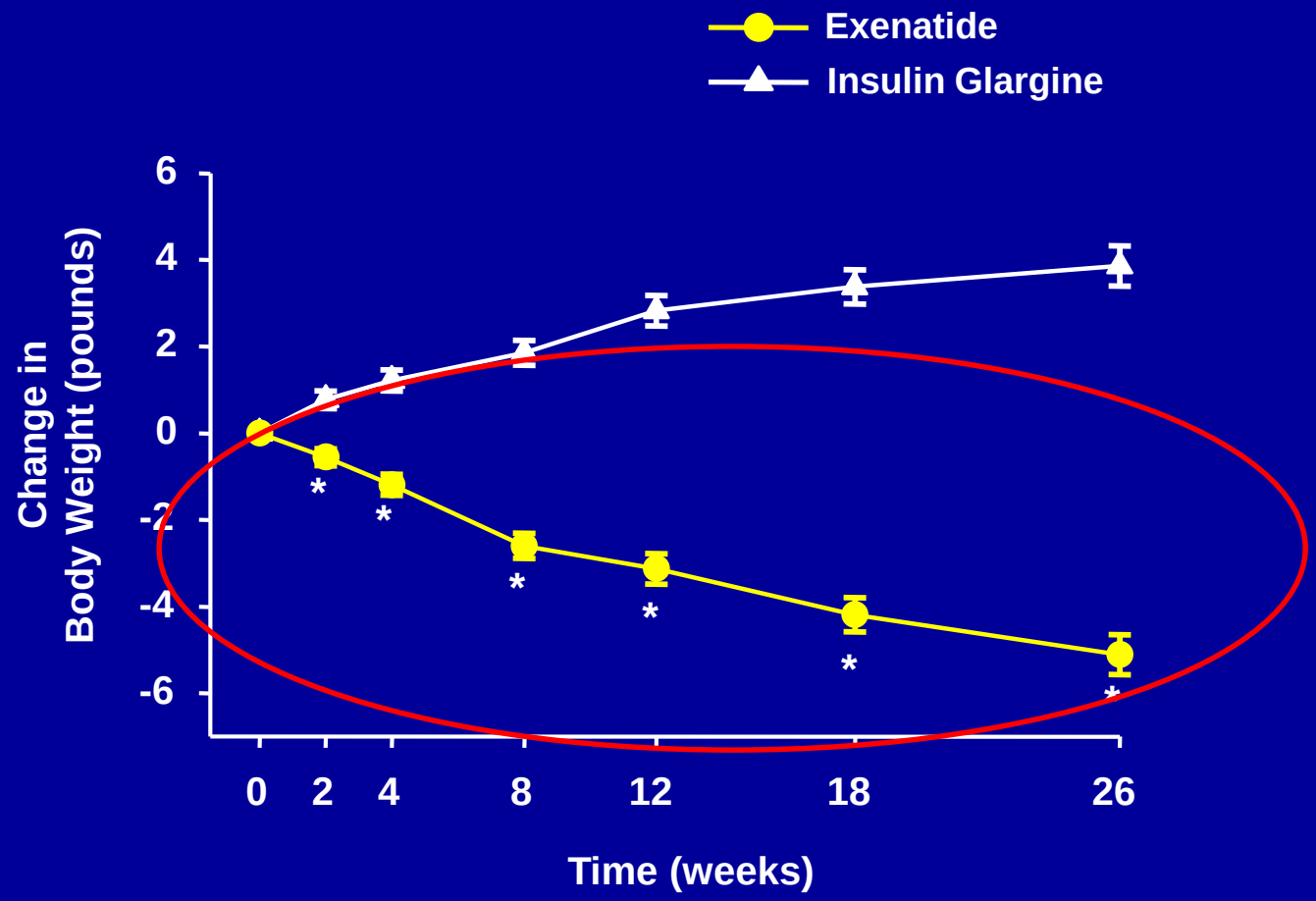
- FreeStyle Libre
- Semaglutide
- Testosterone – when it starts
- Open APS – start making a note of your patients ready to contact them – they are very enthusiastic and want to help!

https://abcd.care/abcd-audits-n3
http://www.diabetologists-abcd.org.uk/n3/n3.htm

ABCD
Association of British Clinical Diabetologists

Using insulin in type 2 diabetes (HbA1c down but weight up)





Heine RJ, et al. *Ann Intern Med.* 2005;143:559-569.

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

GLP-1 receptor agonists

Association of British Clinical Diabetologists

ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutideaudit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit

ABCD Nationwide Semaglutide Audit

Dr Bob Ryder
ABCD-DPC, London
October 29, 2019

Association of British Clinical Diabetologists

Semaglutide

- Semaglutide now accepted onto most formularies and can be readily prescribed
- Semaglutide is considerably more effective at reducing HbA1c and Weight than other GLP1-receptor agonists. It is the same price or cheaper

Previous ABCD GLP1 RA Nationwide Audits

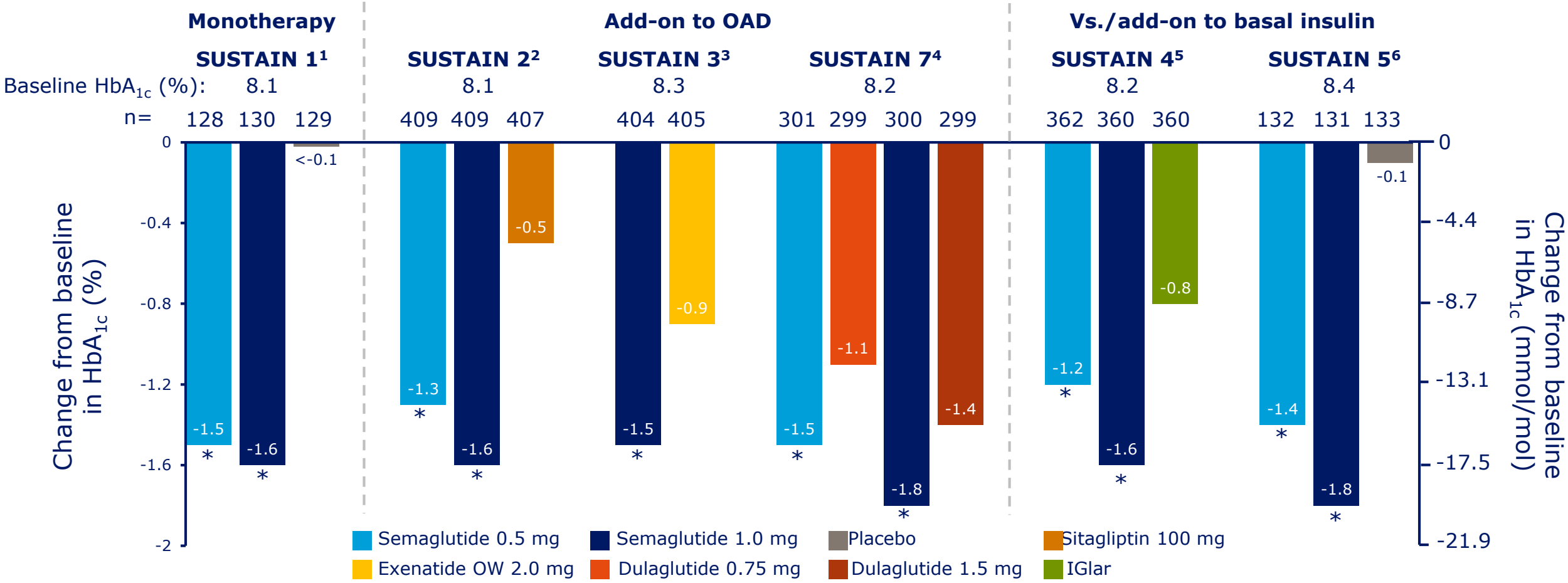
- Combined trials v real world

	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

ABCD
Association of British Clinical Diabetologists

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}

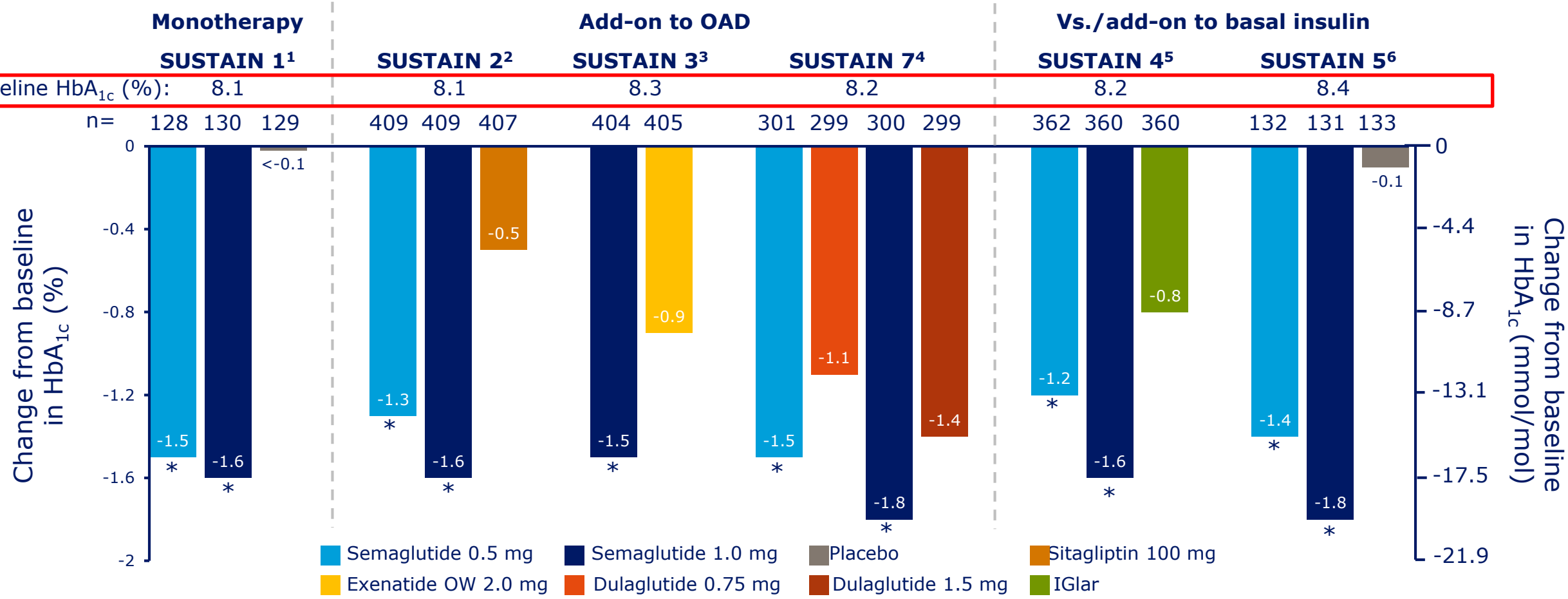


*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}



*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

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]

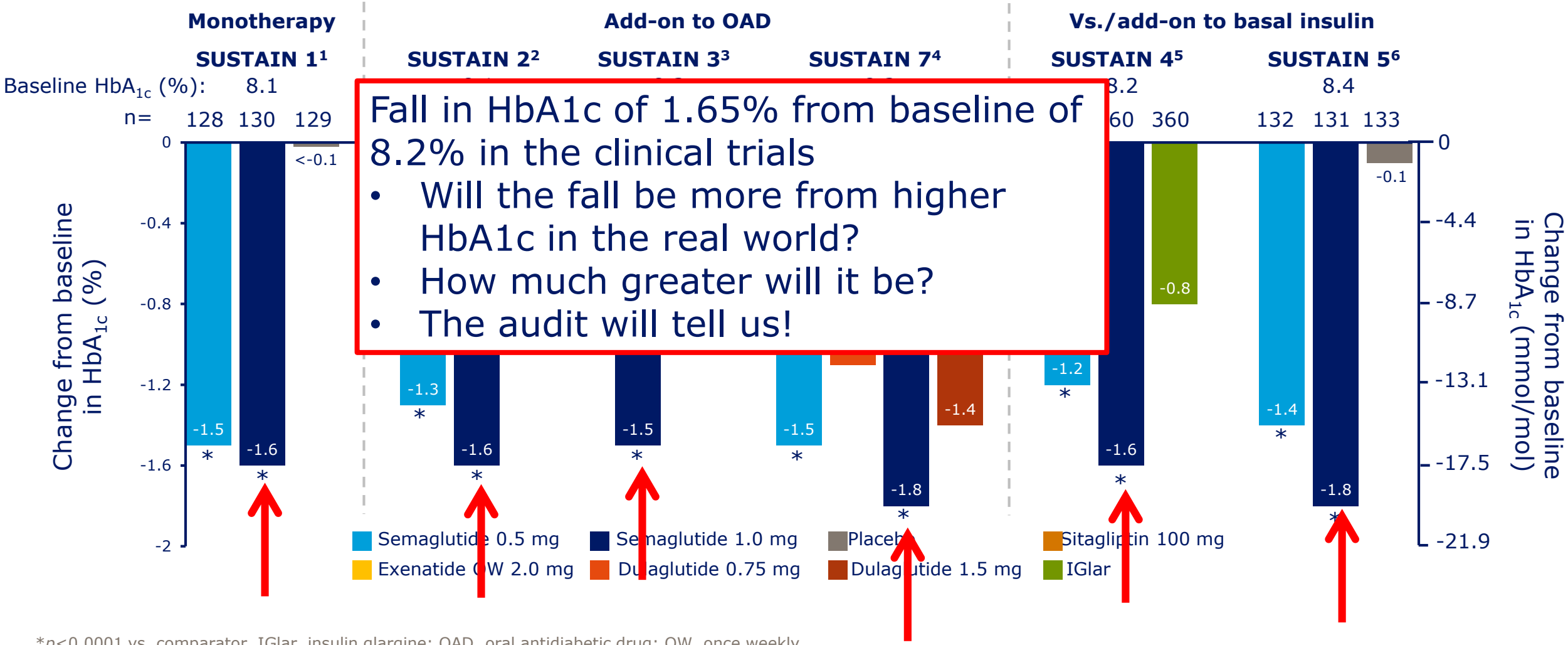
Results show patients are more likely to achieve ≥1% HbA_{1c} reduction when baseline HbA_{1c} is higher and conversely more likely to achieve target HbA_{1c} of 7% if baseline HbA_{1c} is lower.

Association of British Clinical Diabetologists

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

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}



Fall in HbA1c of 1.65% from baseline of 8.2% in the clinical trials

- Will the fall be more from higher HbA1c in the real world?
- How much greater will it be?
- The audit will tell us!

*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

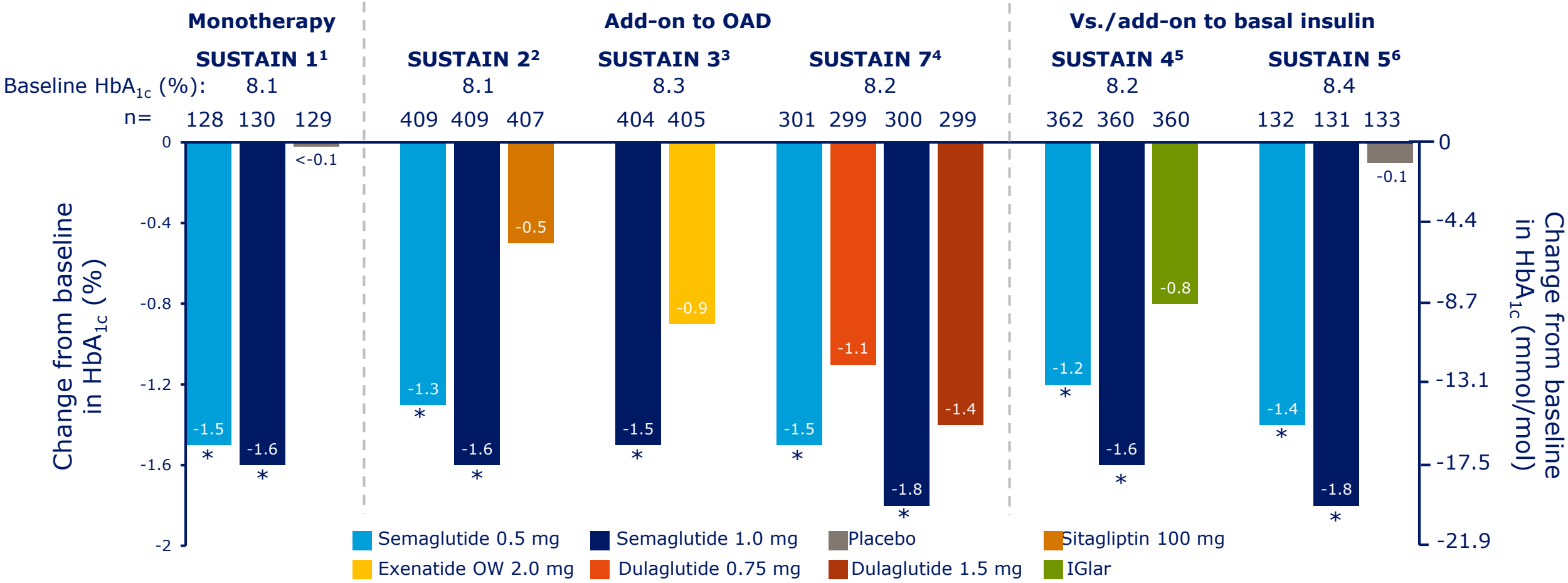
1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

Switching to semaglutide from another GLP-1RA

Association of British Clinical Diabetologists

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}

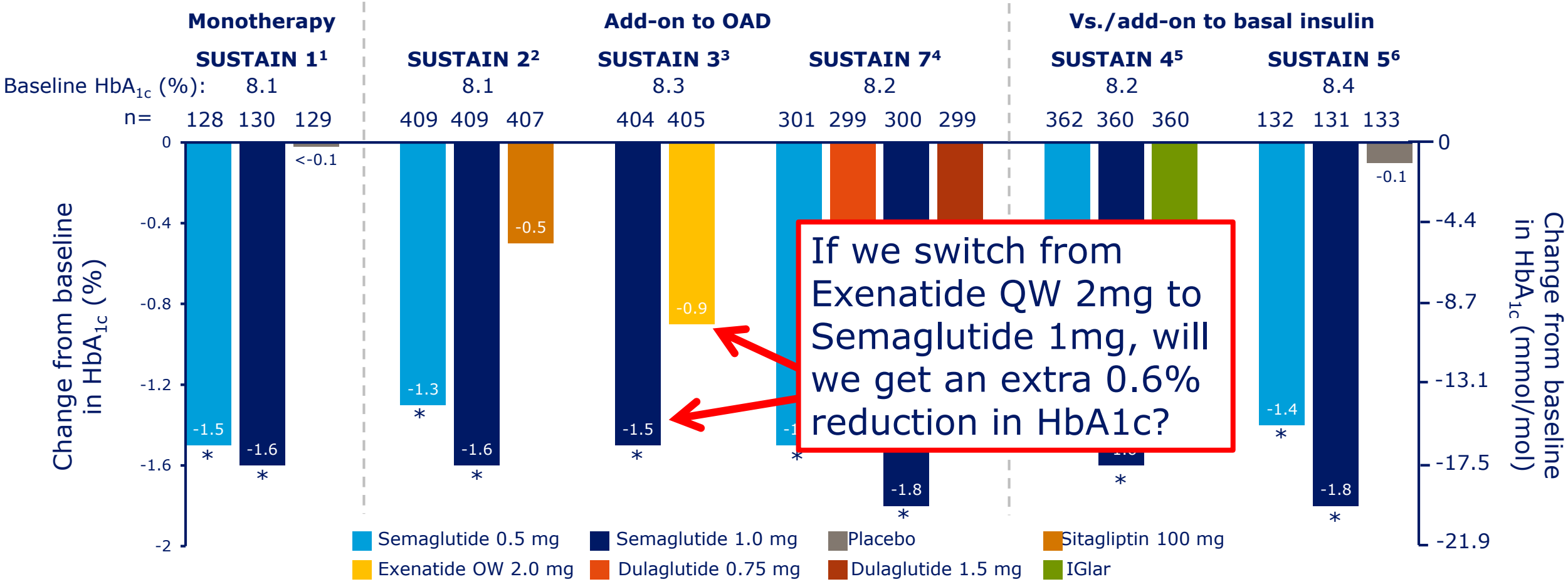


*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}

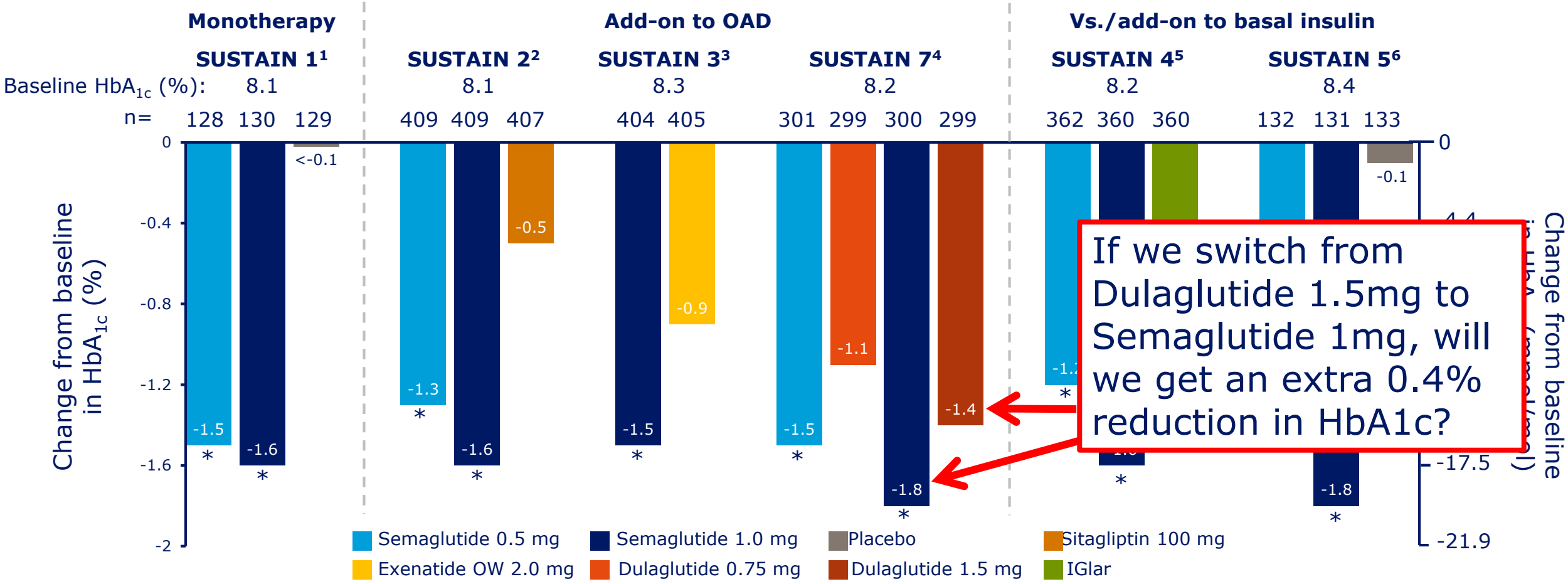


*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}

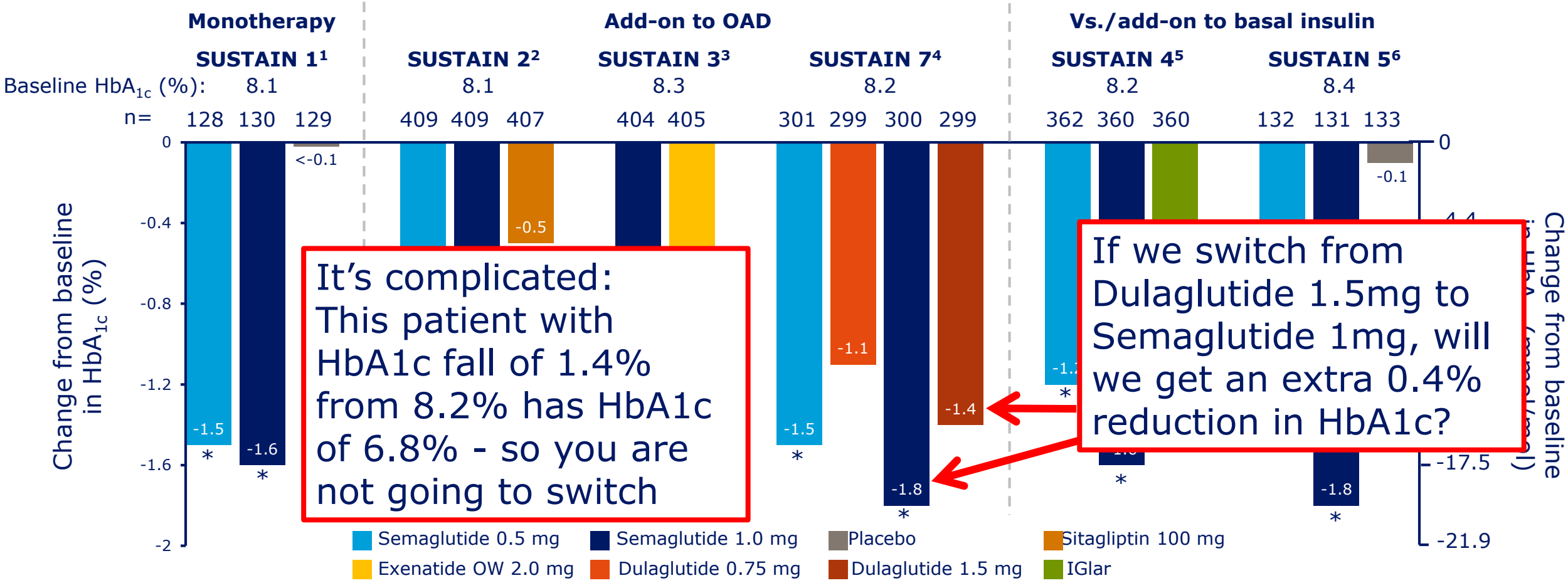


*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}



It's complicated: This patient with HbA1c fall of 1.4% from 8.2% has HbA1c of 6.8% - so you are not going to switch

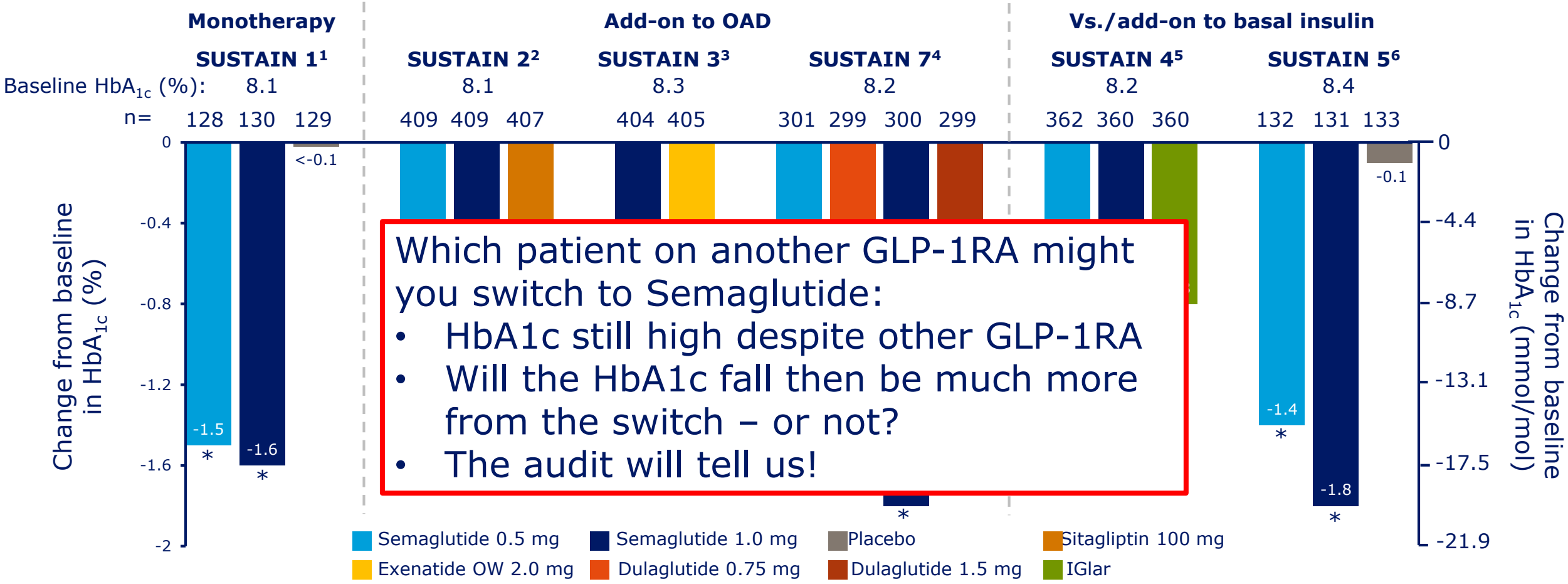
If we switch from Dulaglutide 1.5mg to Semaglutide 1mg, will we get an extra 0.4% reduction in HbA1c?

*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

HbA_{1c} changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA_{1c}



*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

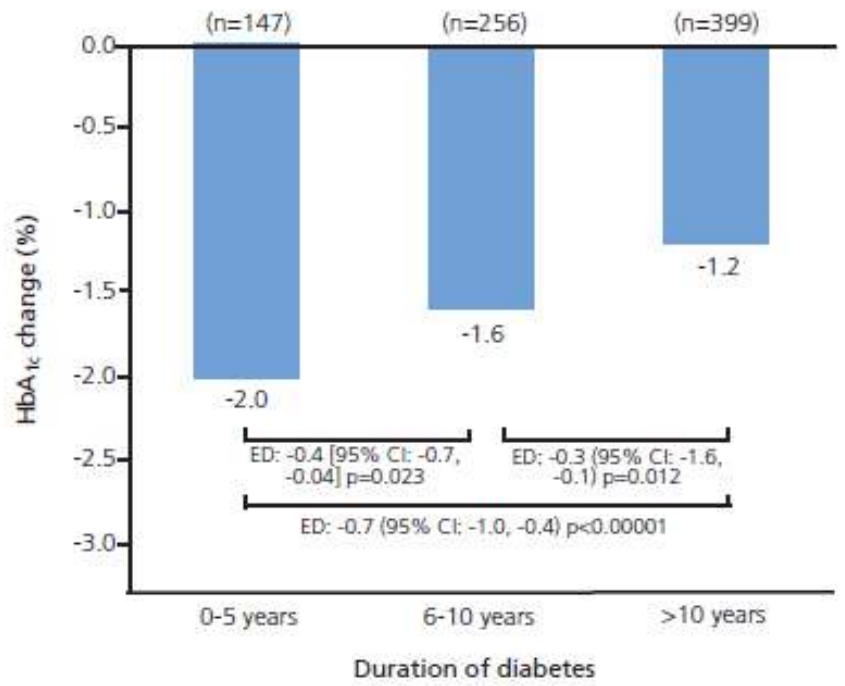
1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

Duration of diabetes

Association of British Clinical Diabetologists

ABCD liraglutide audit - HbA1c changes according to duration of diabetes

Figure 2. Mean HbA_{1c} changes after 26 weeks of liraglutide treatment, stratified according to duration of diabetes



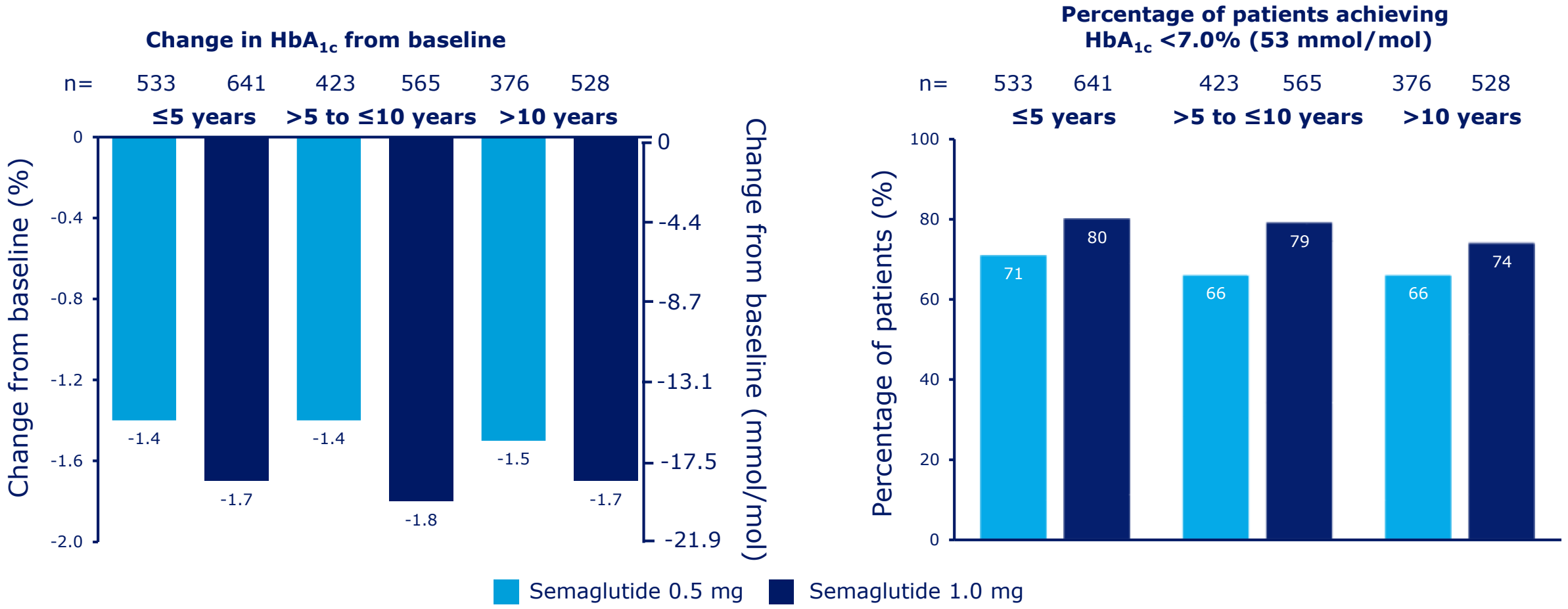
Columns show adjusted mean changes analysed by ANCOVA with baseline HbA_{1c} as a covariate. ED: estimated difference; CI: confidence interval

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

ABCD
Association of British Clinical Diabetologists

Differences in glycaemic control by baseline diabetes duration

SUSTAIN 1–5 and 7



Data presented are estimated change from baseline to week 30 or week 40 based on a meta-analysis of data from the six trials. n, number of subjects in the full analysis set

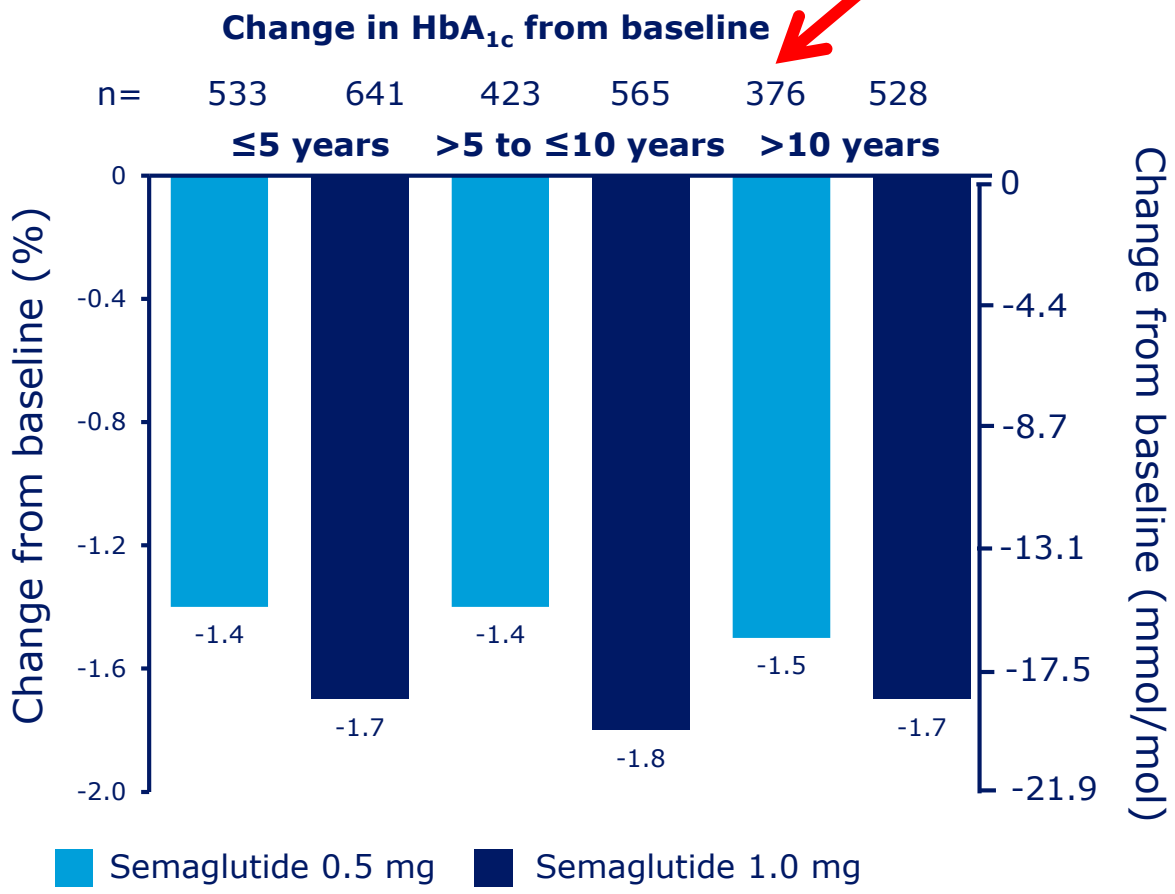
Adapted from: Rosenstock *et al. Diabetes* 2018; 67(Suppl. 1):A287 (abstract and poster 1081-P)

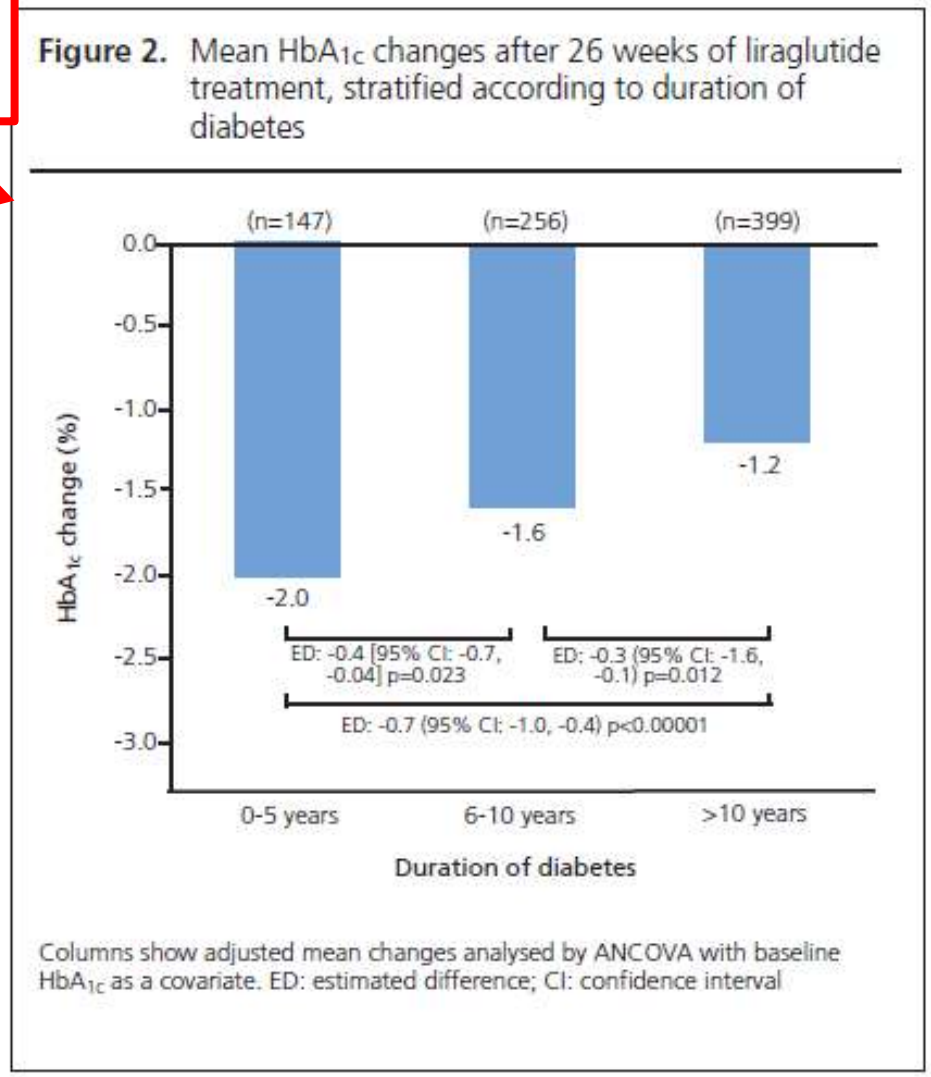
Differences in glycaemic control by baseline diabetes duration

SUSTAIN 1–5 ar

Semaglutide in clinical trials

Liraglutide in ABCD audit



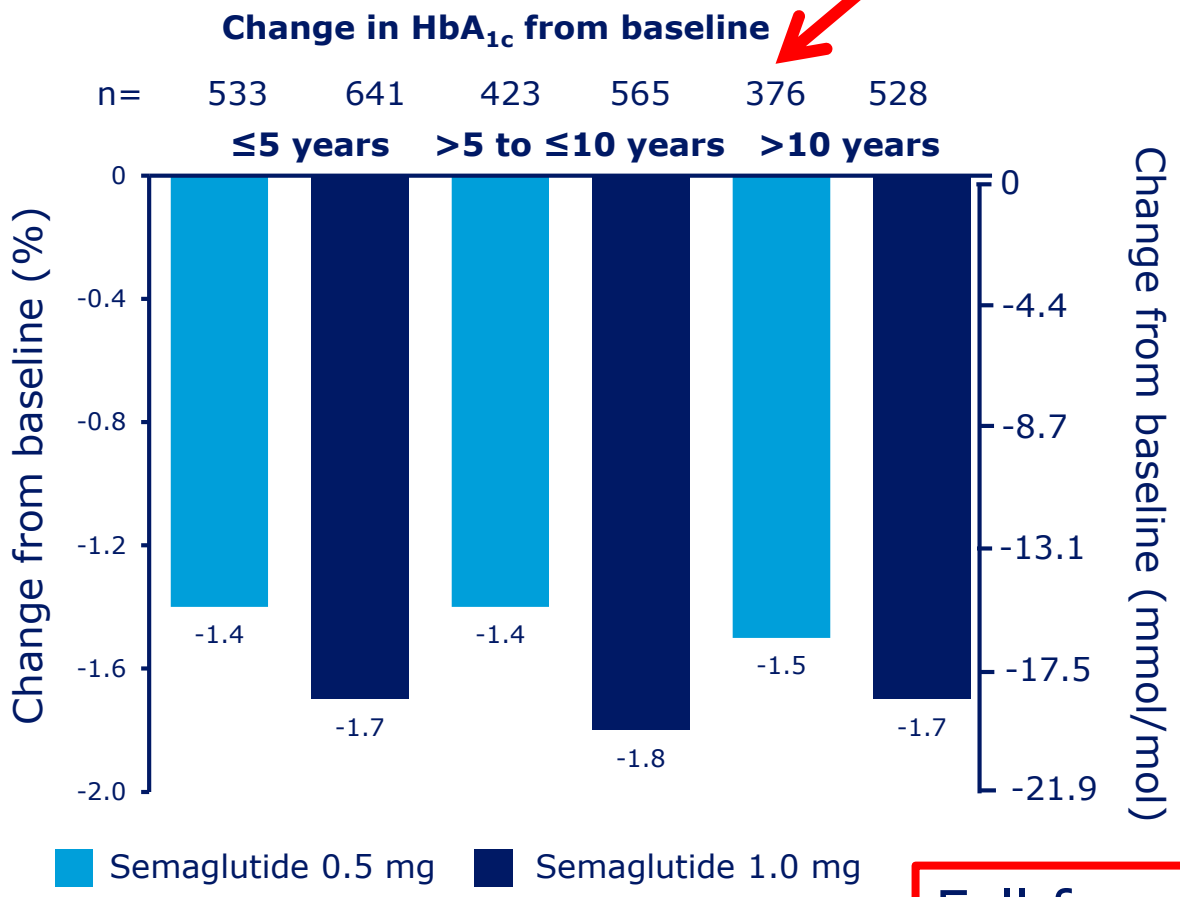


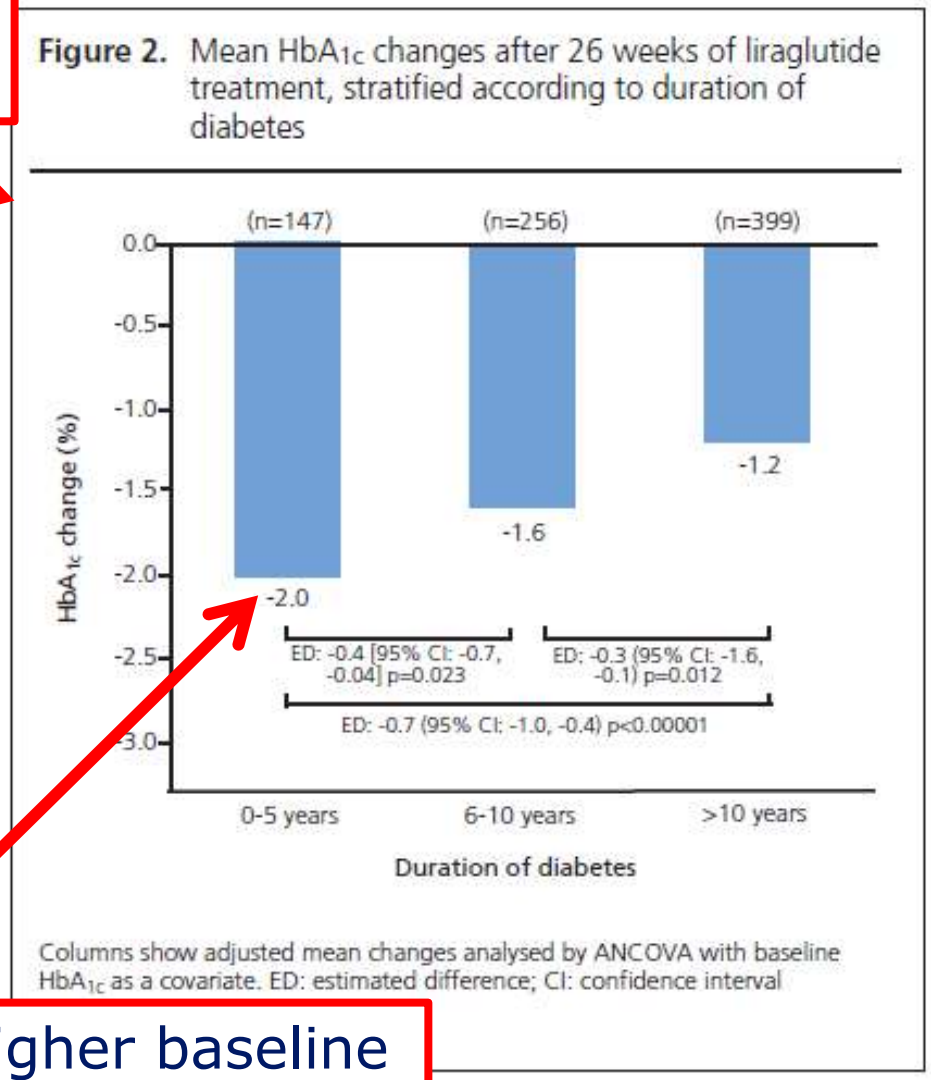
Differences in glycaemic control by baseline diabetes duration

SUSTAIN 1–5 ar

Semaglutide in clinical trials

Liraglutide in ABCD audit





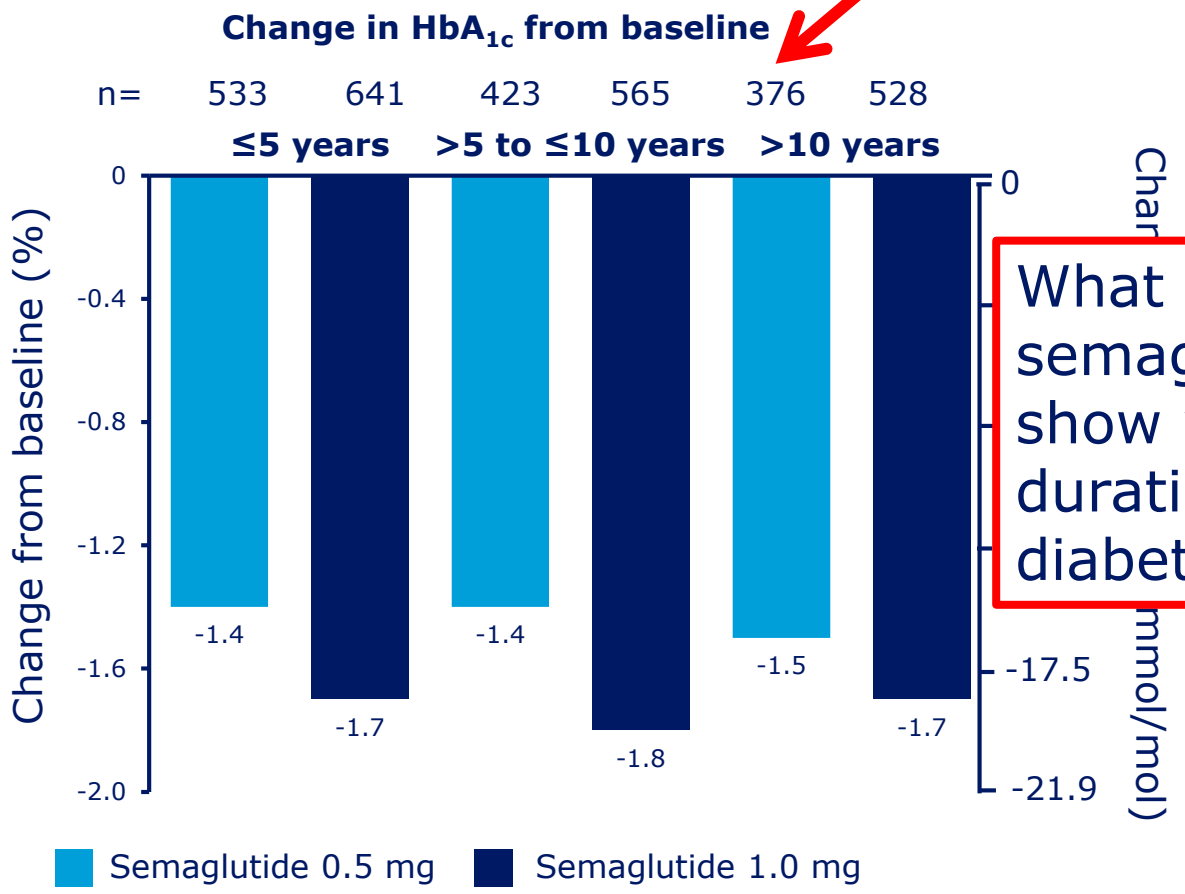
Fall from much higher baseline in audit compared to trial

Differences in glycaemic control by baseline diabetes duration

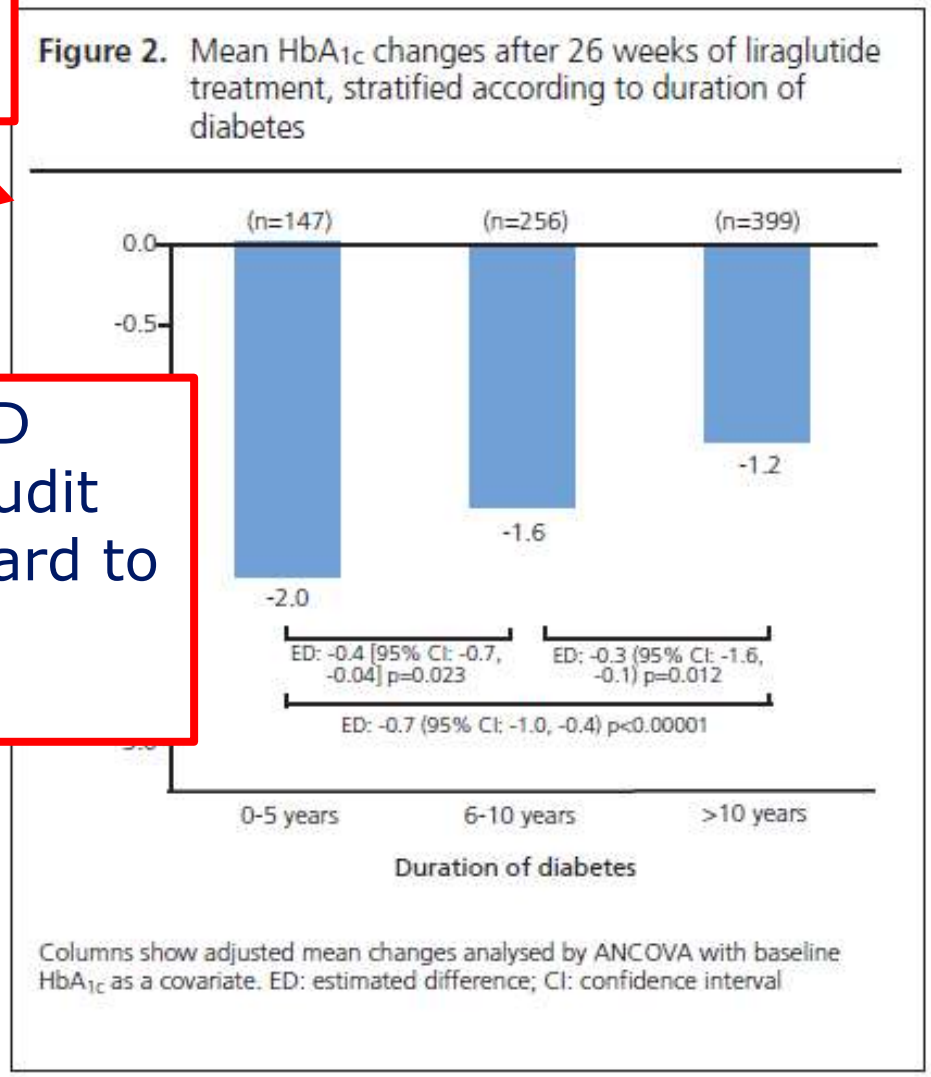
SUSTAIN 1–5 ar

Semaglutide in clinical trials

Liraglutide in ABCD audit



What will ABCD semaglutide audit show with regard to duration of diabetes?

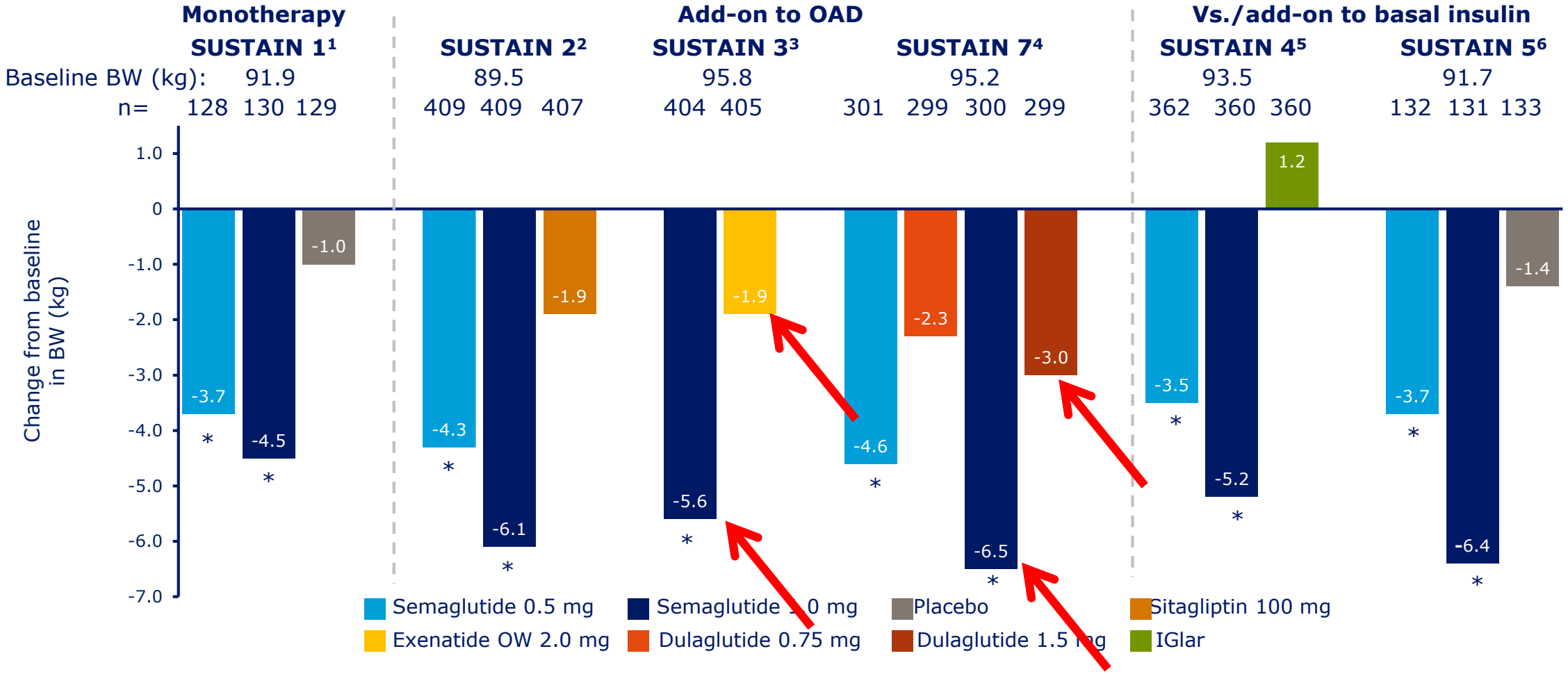


What about weight?

Association of British Clinical Diabetologists

Body weight in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN BODY WEIGHT

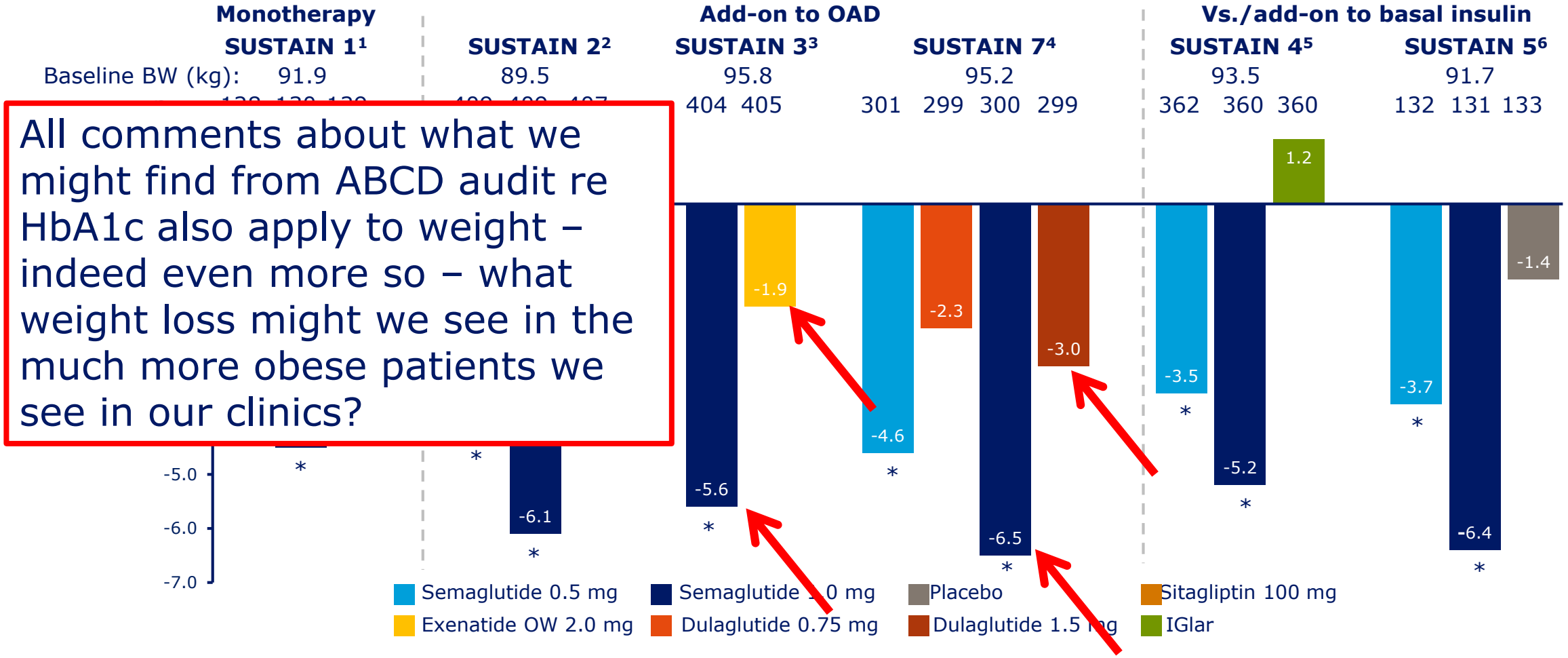


*p<0.0001 vs. comparator. Change from baseline in BW was a secondary endpoint. BW, body weight; IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

Body weight in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN BODY WEIGHT



All comments about what we might find from ABCD audit re HbA1c also apply to weight – indeed even more so – what weight loss might we see in the much more obese patients we see in our clinics?

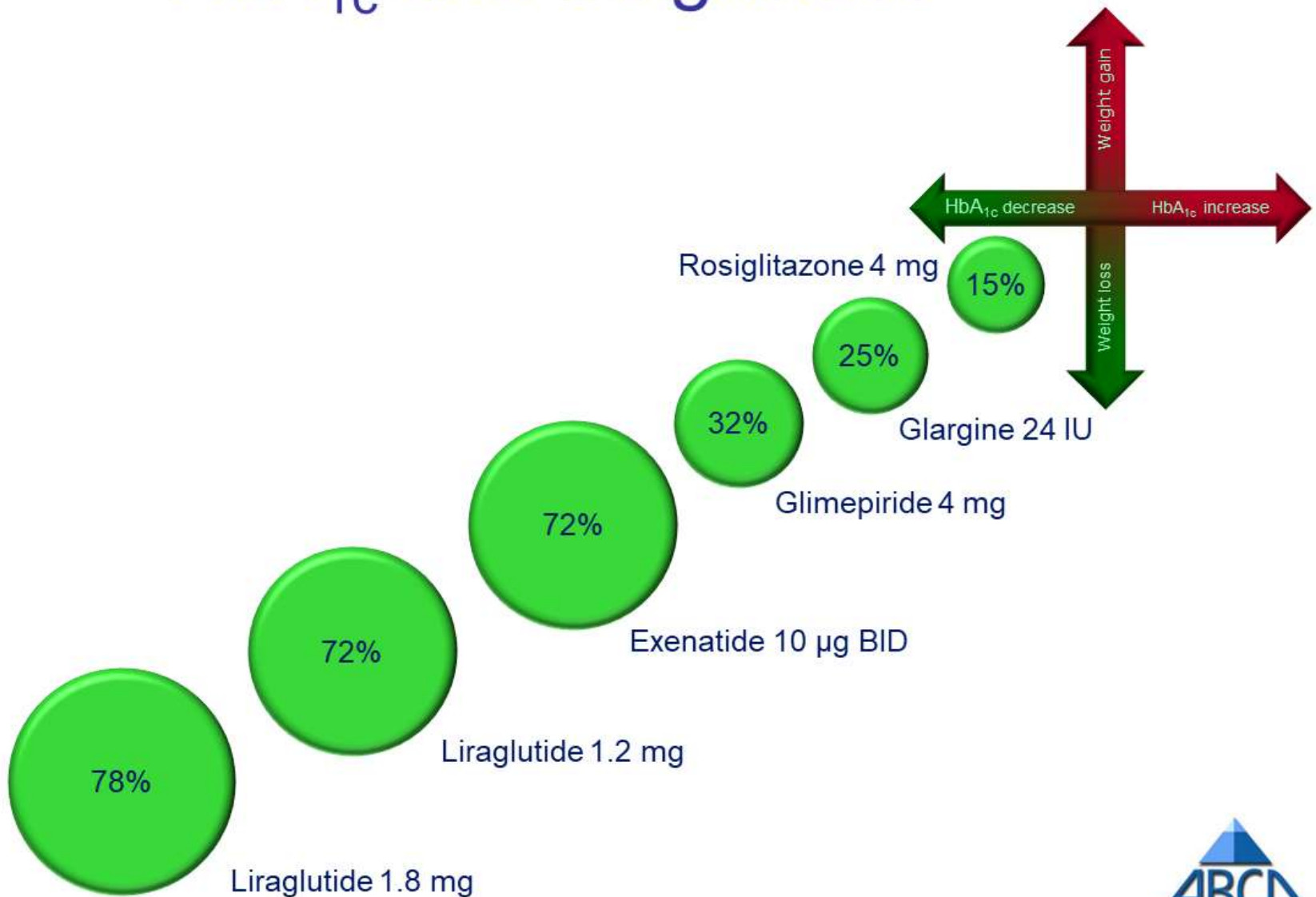
*$p<0.0001$ vs. comparator. Change from baseline in BW was a secondary endpoint. BW, body weight; IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

1. Sorli *et al. Lancet Diabetes Endocrinol* 2017;5:251–60; 2. Ahrén *et al. Lancet Diabetes Endocrinol* 2017;5:341–54; 3. Ahmann *et al. Diabetes Care* 2018;41:258–66; 4. Pratley *et al. Lancet Diabetes Endocrinol* 2018;6:275–86; 5. Aroda *et al. Lancet Diabetes Endocrinol* 2017;5:355–66; 6. Rodbard *et al. J Clin Endocrinol Metab* 2018;103:2291–301

Losing weight AND HbA1c

Association of British Clinical Diabetologists

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

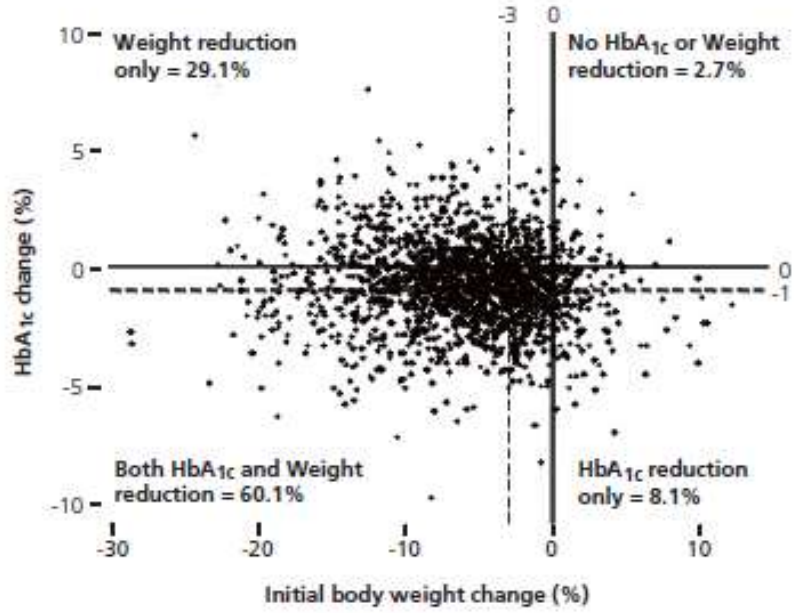


Data on file, Novo Nordisk

ABCD
Association of British Clinical Diabetologists

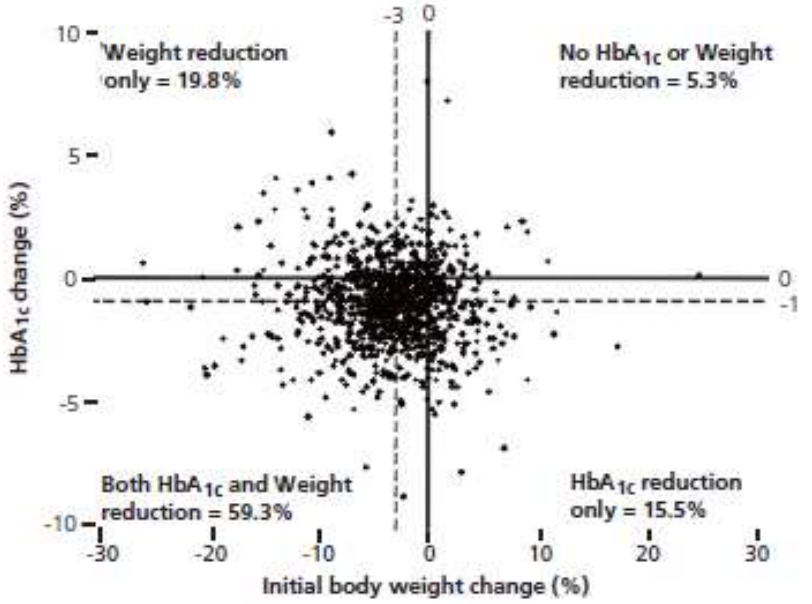
Patients improving weight AND HbA1c in previous audits

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.

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

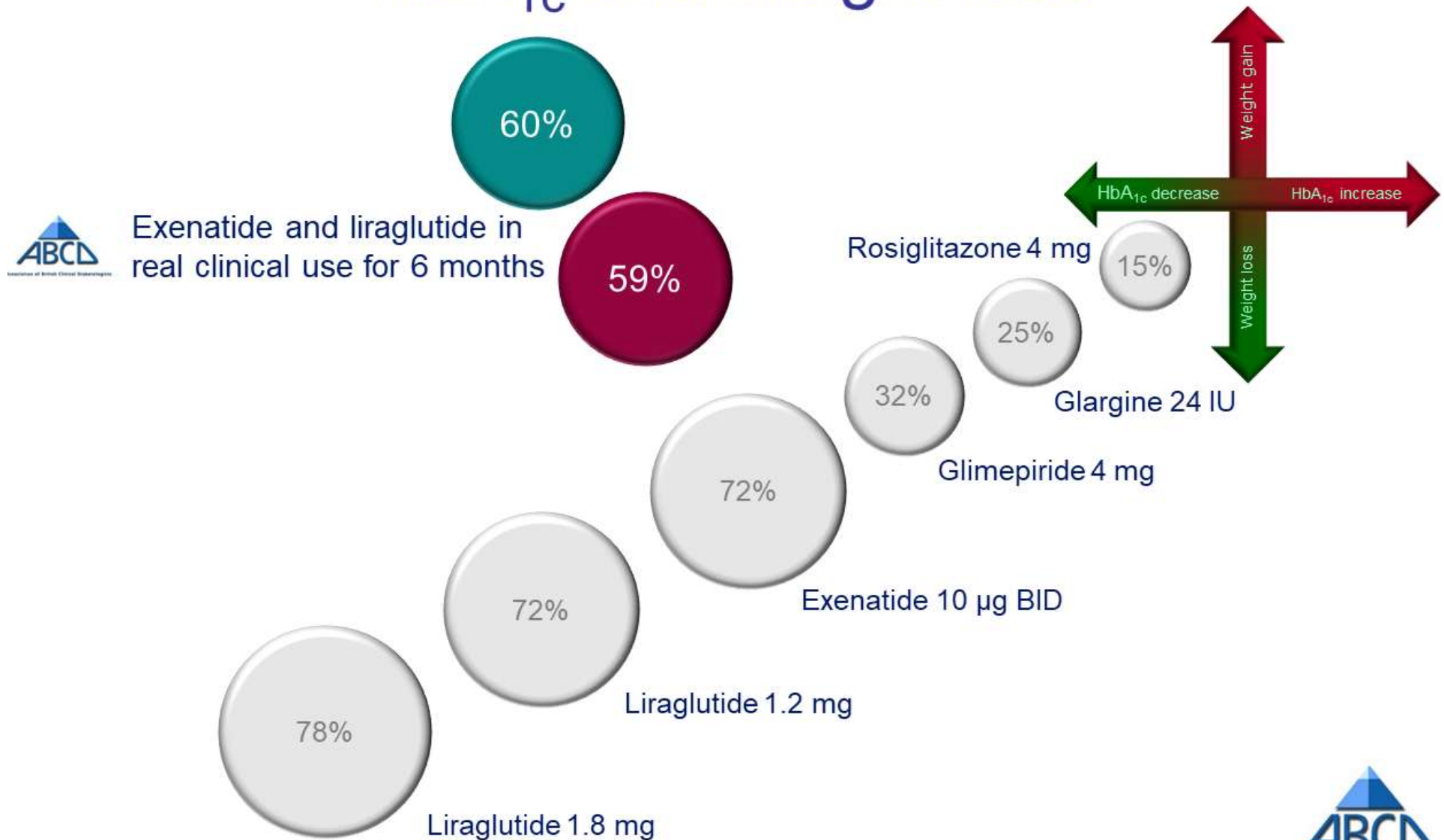


Dotted line indicates criteria of ≥1% HbA_{1c} reduction and ≥3% IBW reduction require by NICE for continuation of therapy – while 59.3% of patients achieved both HbA_{1c} and weight reduction, only 25.0% achieved this to the criteria level set by NICE.

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

ABCD
Association of British Clinical Diabetologists

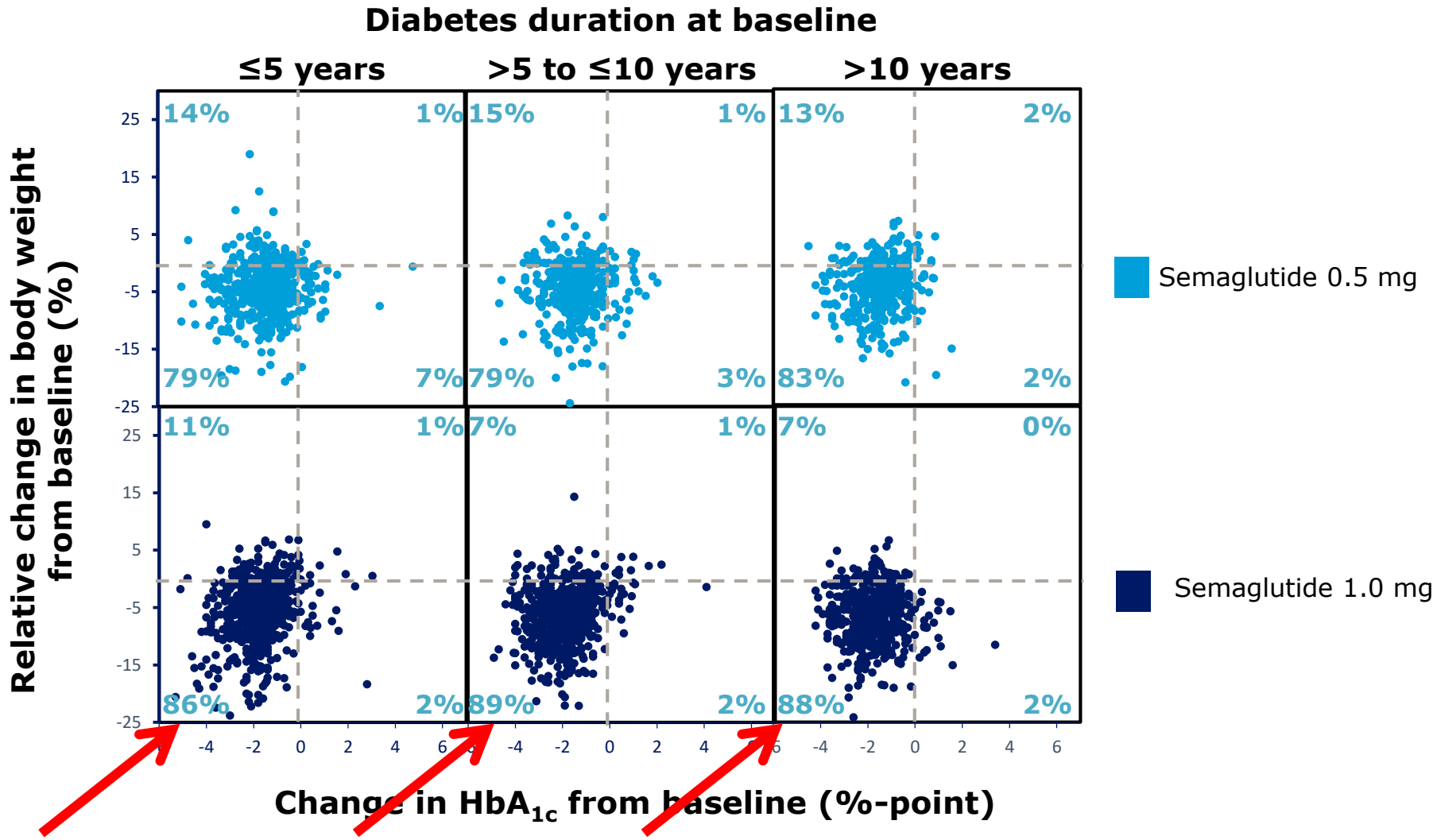
Percentage of subjects achieving fall in HbA_{1c} and weight loss



Data on file, Novo Nordisk

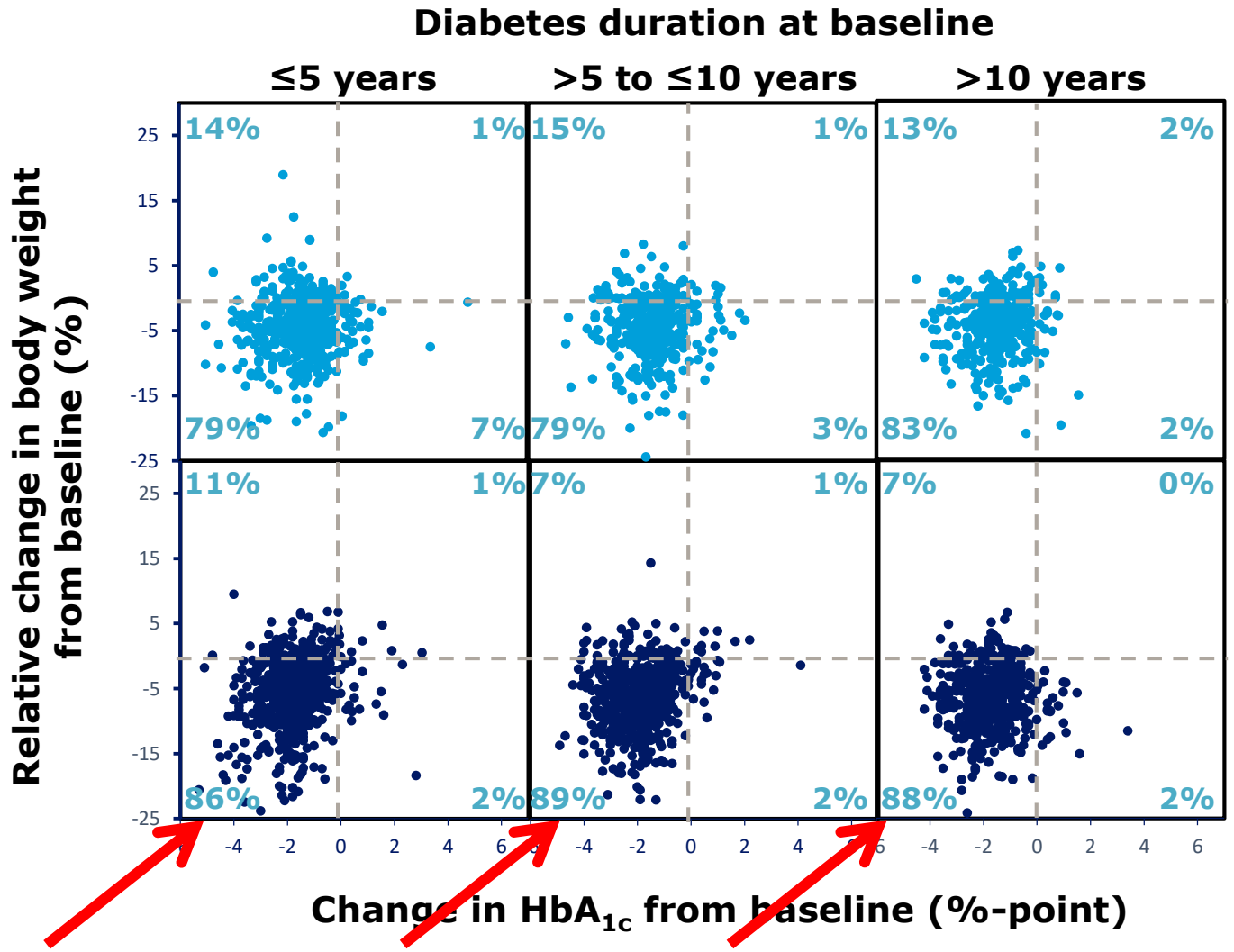
Association of British Clinical Diabetologists

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.

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



Semaglutide 0.5 mg

Semaglutide 1.0 mg

What percentage will lose both weight and HbA1c in the semaglutide audit?

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 Nationwide Semaglutide Audit

- As you start to use semaglutide please enter ALL your patients into the nationwide audit
- The audit tool allows you easily to analyse your own data – good audit exercise for SpR, CMT or medical student
- All contributors listed in publications – top contributors co-authors

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

ABCD
Association of British Clinical Diabetologists