Differences in response between exenatide and liraglutide in the Association of British Clinical Diabetologists (ABCD) nationwide audits

R.E.J. Ryder[1], K.Y. Thong[1], M.L. Cull[1], A.P. Mills[1], C. Walton[2]
on behalf of ABCD nationwide exenatide and liraglutide audits contributors

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

International Diabetes Federation 21st World Diabetes Congress, 6 December, Dubai, UAE

Disclosure

- The ABCD nationwide exenatide audit and nationwide liraglutide audit are supported by grants from Eli Lilly Ltd and Novo Nordisk Ltd

- The audits were independently initiated and performed by ABCD, and the authors remained independent in the analysis and writing of this report

Disclosure

- R.E.J. Ryder has received speaker fees from Eli Lilly, consultancy fees from Novo Nordisk, and educational sponsorship from Sanofi-Aventis, Takeda and GlaxoSmithKline

- K.Y. Thong has received educational sponsorship from Eli Lilly, Novo Nordisk, Sanofi-Aventis and Takeda

- C. Walton has received educational sponsorship from Boehringer-Ingelheim, Eli-Lilly, Novo Nordisk and Takeda.

Introduction

- In the LEAD-6 trial, liraglutide 1.8 mg as add-on therapy achieved greater HbA_{1c} reduction *(-1.12% vs -0.79%*) and similar weight reduction (*-3.24 kg vs -2.87 kg*) when compared with exenatide twice daily (BD)

- exenatide BD and liraglutide are both available for use in the UK *but*

- national guidelines for liraglutide only recommend the use of the 1.2 mg dose

(exenatide refers to exenatide BD in all slides)

The ABCD nationwide exenatide and liraglutide audits

- The Association of British Clinical Diabetologists (ABCD) is the national diabetes specialist society in the UK
- ABCD conducted two nationwide audits of GLP-1 RAs to evaluate their safety and efficacy in clinical practice
  - Exenatide (2007-2009) – 126 centres, 6717 patients
  - Liraglutide (2009-2011) – 77 centres, 4129 patients

ABCD
Association of British Clinical Diabetologists

The ABCD nationwide exenatide and liraglutide audits

- Diabetes centres across UK were invited to participate
- Calls for retrospective data (twice/year) on patients started on exenatide, and liraglutide
- Data anonymised and sent electronically to ABCD
- Data from routine diabetes practice

ABCD
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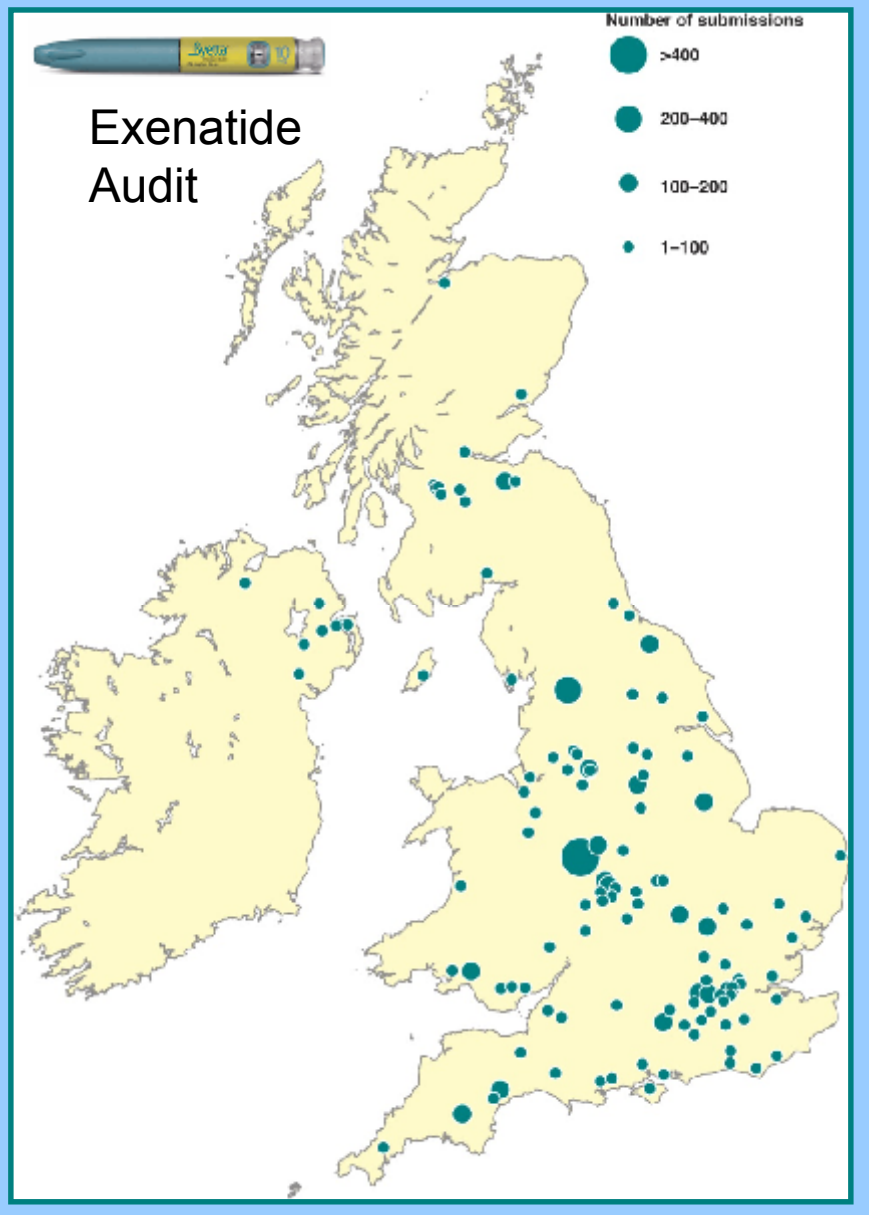
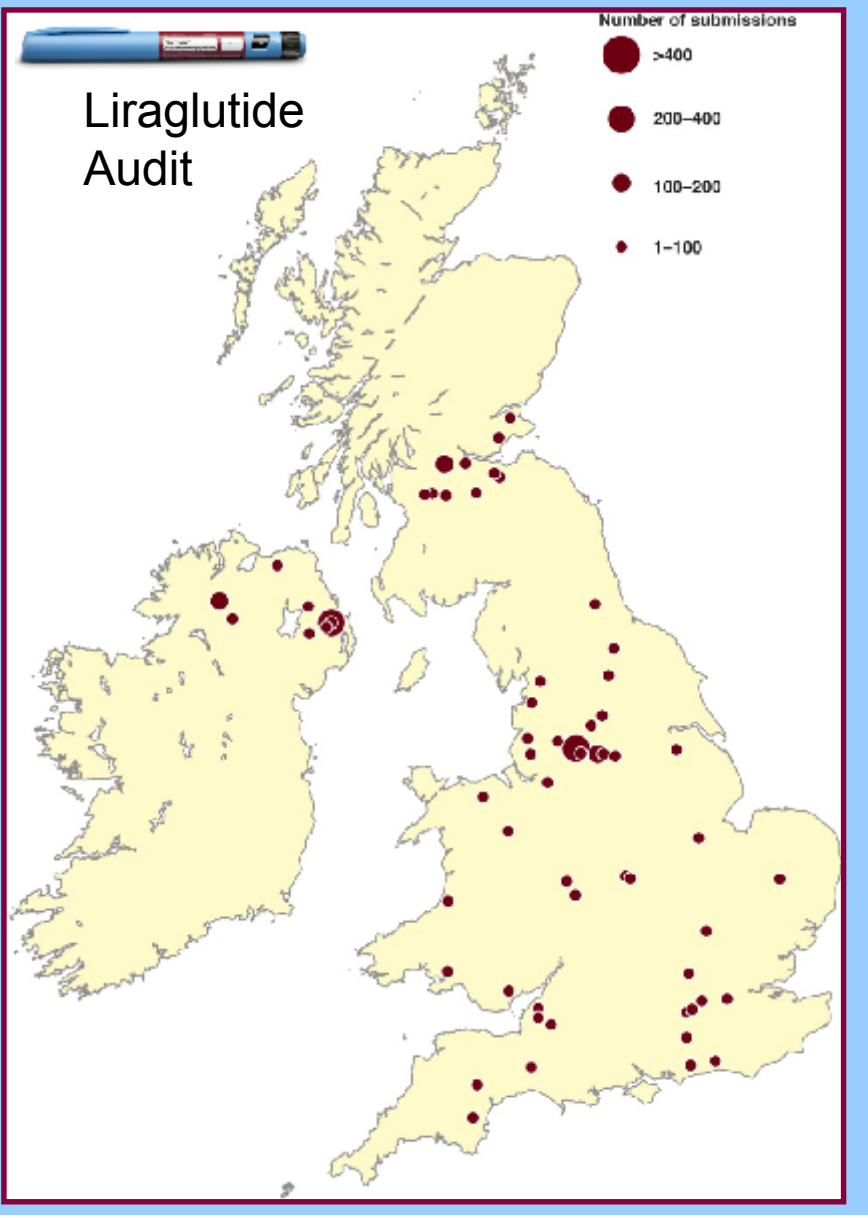
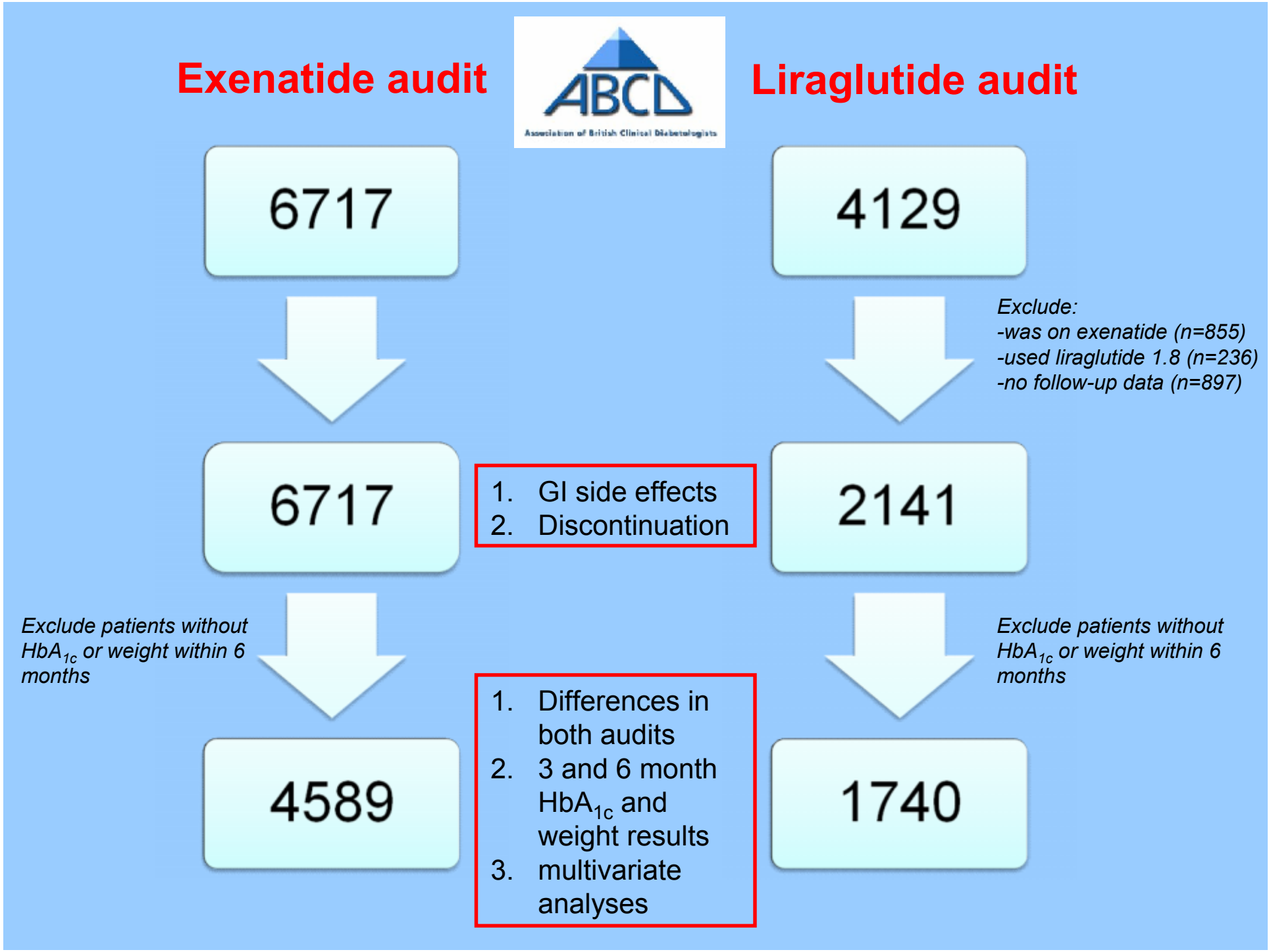
Nationwide contribution to exenatide and liraglutide national audit





Aims

- To assess the treatment response achieved by the nationwide use of exenatide, and subsequently liraglutide, based on the two audits
- To explore whether differences in patient characteristics and diabetes treatment practice influenced treatment outcomes
- Data shown is ***NOT*** from a head-to head clinical trial


Exenatide audit
Liraglutide audit
6717
4129
Exclude:
-was on exenatide (n=855)
-used liraglutide 1.8 (n=236)
-no follow-up data (n=897)
6717
1. GI side effects
2. Discontinuation
2141
Exclude patients without HbA1c or weight within 6 months
Exclude patients without HbA1c or weight within 6 months
4589
1. Differences in both audits
2. 3 and 6 month HbA1c and weight results
3. multivariate analyses
1740

Results

Rates of gastrointestinal (GI) side effects and GLP-1 RA Discontinuation

	Exenatide Audit (n=6717)	Liraglutide Audit (n=2141)	P value
Duration of follow-up (weeks)	26 (14-41)	24 (14-40)	0.002
All reported GI side effects	23.7%	21.8%	
Discontinuation before 6 months	14.7%	13.0%	0.053
Lack of efficacy	3.7%	3.2%	
GI side effects	7.2%	5.1%	
Non GI side effects	0.8%	0.8%	
All other reasons	2.9%	3.9%	

Duration of follow up expressed as median(inter-quartile range)

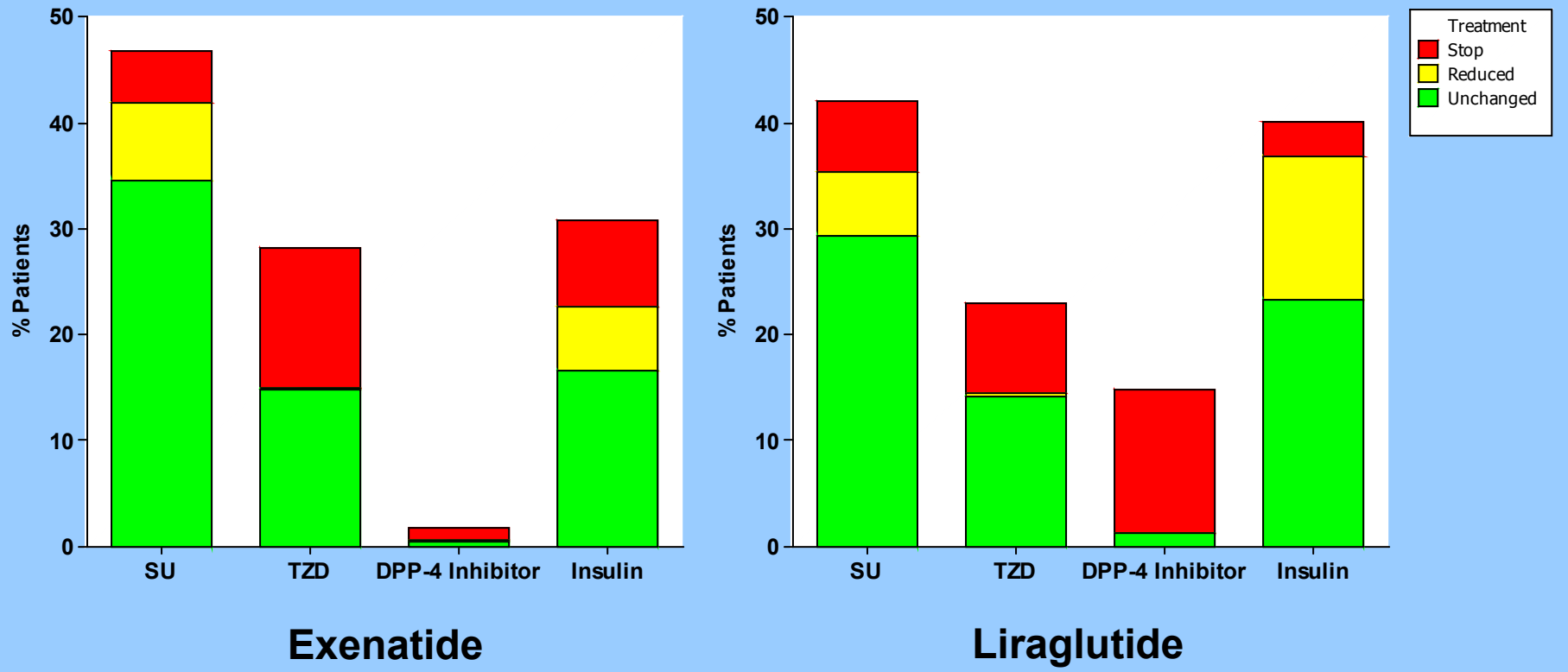
Baseline characteristics of patients with HbA_{1c} or Weight data within 6 months after starting GLP-1 RA

	n	Exenatide Audit (n total=4589)	n	Liraglutide Audit (n total=1740)	p value
Gender (%Male)	4402	55.8	1737	53.6	0.112
Ethnicity (%Caucasian)	3335	92.3	1515	92.4	0.917
Age (yrs)	4330	54.9 (10.6)	1732	55.7 (11.1)	0.009
Diabetes duration (yrs)	3582	9 (5-13)	1563	9 (5-13)	0.890
HbA_{1c} (%)	4297	9.49 (1.69)	1602	9.36 (1.71)	0.009
Weight (kg)	4121	113.8 (23.0)	1611	111.2 (22.1)	<0.001
BMI (kg/m^2)	2423	39.9 (7.9)	1660	39.2 (7.5)	0.007
On insulin (%)	4589	31.0	1740	41.8	<0.001
Insulin Dose (U/day)	1199	113 (102)	709	112 (99)	0.998*
Insulin Dose (U/kg/day)	1076	1.0 (0.9)	651	1.0 (0.8)	0.551

Results quoted as mean (SD) and median diabetes duration (inter-quartile range)

**log comparison*

Changes to baseline diabetes treatment at GLP-1 RA initiation



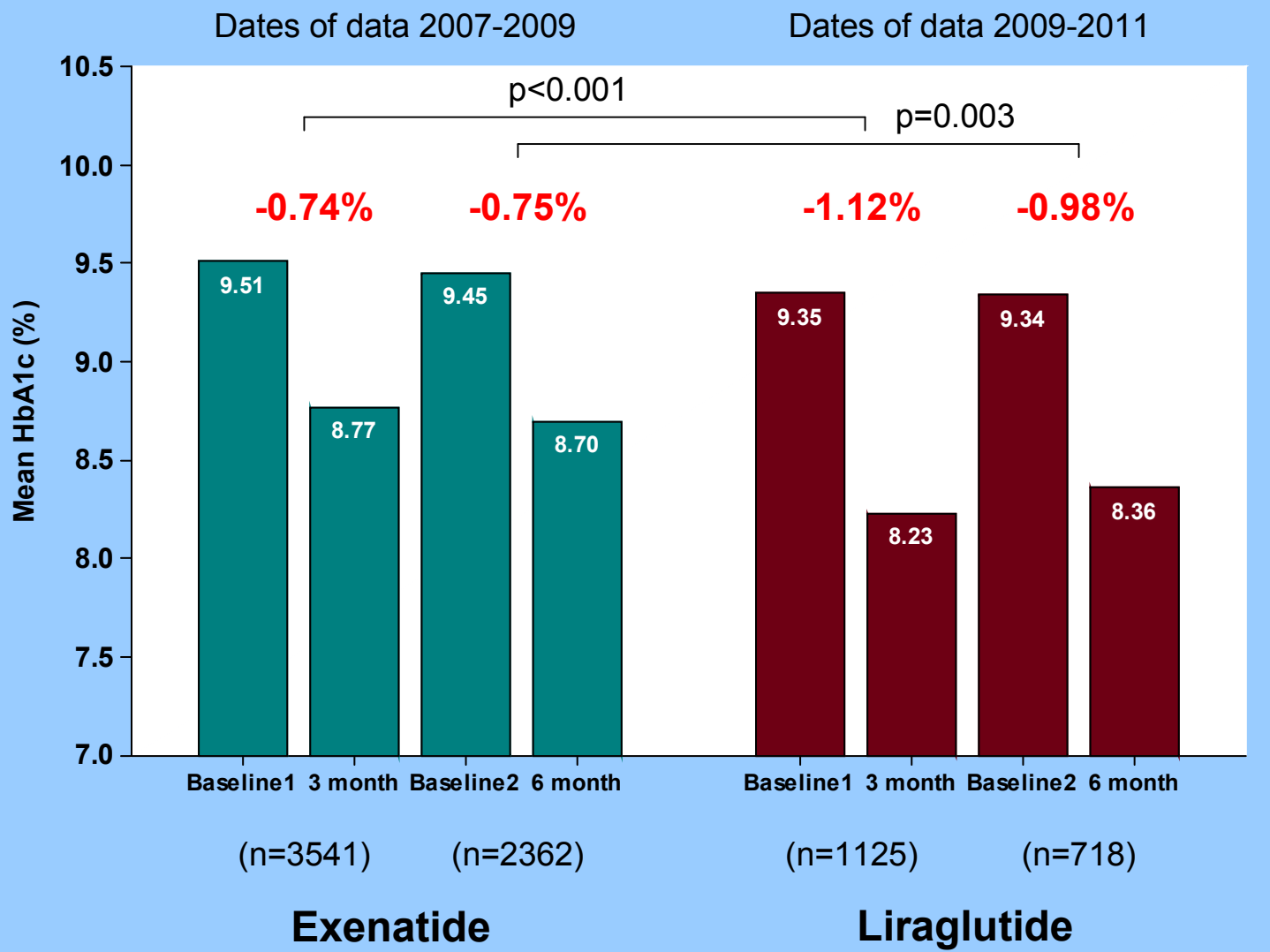
Median (IQR) %insulin dose reduction: Exenatide: 20%(0-100%) vs Liraglutide: 0%(0-38%) ($p<0.001$)

Patients with an increase in dose or unknown dose change omitted for clarity

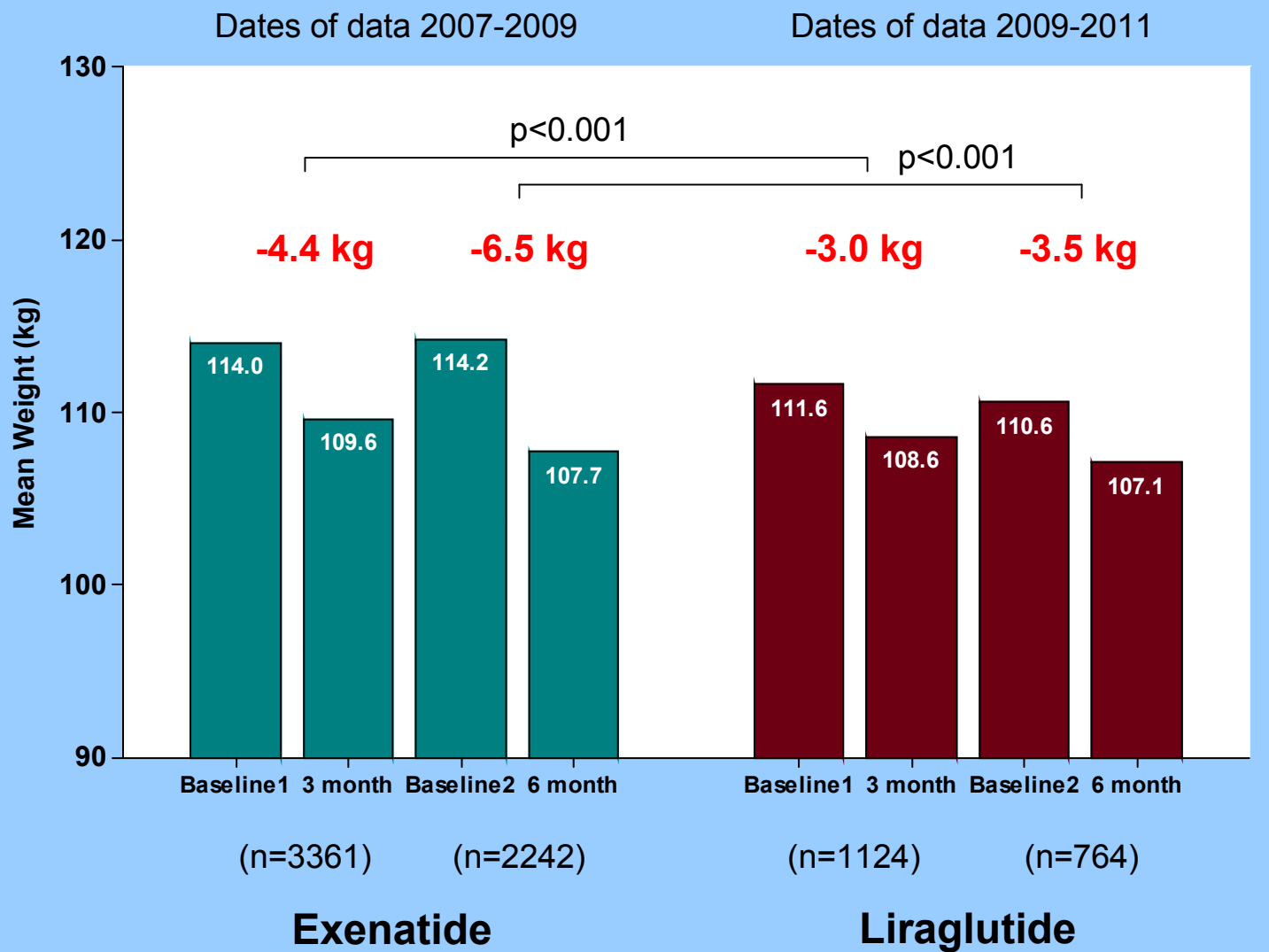
Characteristics and differences in both audits

- Audits had poorly controlled and very obese patients
  - patients referred to secondary care
  - impact of national guidelines
- Overall trend of less diabetes treatment reduction at GLP-1 initiation in subsequent liraglutide audit

HbA_{1c} results at 3 and 6 months: exenatide and liraglutide



Weight results at 3 and 6 months: exenatide and liraglutide



Effect of treatment group (exenatide vs liraglutide) on 3 month HbA_{1c} reduction

	T value	p value
Baseline HbA_{1c}	30.0	<0.001
Insulin use	-12.7	<0.001
Exenatide vs Liraglutide	-9.0	<0.001
TZD reduction	-6.4	<0.001
Baseline Weight	-4.1	<0.001
DPP-4 inhibitor reduction	-4.1	<0.001

Stepwise regression analysis of 3 month HbA_{1c} reduction inputting variables that were significantly different between patients on exenatide vs liraglutide – 3482 patients

Effect of treatment group (exenatide vs liraglutide) on 3 month Weight reduction

	T value	p value
Baseline Weight	12.9	<0.001
Insulin dose reduction	8.8	<0.001
Baseline HbA_{1c}	-7.0	<0.001
Exenatide vs Liraglutide	6.1	<0.001
Age	5.8	<0.001
TZD reduction	4.4	<0.001

Stepwise regression analysis of 3 month Weight reduction inputting variables that were significantly different between patients on exenatide vs liraglutide – 3482 patients

Conclusions

- In patients tolerating treatment, exenatide and liraglutide are both effective in improving diabetes control and reducing weight in real-life clinical practice

- There was a trend towards less diabetes treatment reduction, in particular insulin, in the liraglutide audit. This contributed to better HbA_{1c} reduction but less weight reduction as compared with the exenatide audit

- Results from the two audits raise the possibility of a difference in glycaemic and weight reduction efficacy between liraglutide and exenatide but this finding can only be ascertained in a head-to-head clinical trial

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.

ABCD nationwide prospective 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, Cull ML, Mills AP. Statistician: Blann A.*

Addenbrookes Hospital: Simmons D, Bejinariu E. **Altnagelvin Area Hospital:** Lindsay J, O'Kane M, Black N, Moles K, Williams L, Caskey H, McDaid A-M, King L, McIlvor E, Hamilton L, Early R, Morahan S, Giff K, Johnston S. **Basildon University Hospital:** Mulcahy M, Krishnan L. **Belfast City Hospital:** Henry RW, Nugent A, McMullan P. **Benhsam General Hospital:** Narayanan KR. **Birmingham Community Healthcare NHS Trust:** Muralidhara K, Shahid S, Thomas A, Cunningham B, Haughton K. **Bristol General Hospital:** Croxson S. **Bristol Royal Infirmary:** Richards G, Pople J-A, John H, Jones L. **Bronglais Hospital:** Kotonya C, Phillips L, Saunders H, Powell P. **Cape Hill Medical Centre (GP):** Gardner G, Chitnis J, Merali A, Maan P. **Causeway Hospital:** Kassim SB, Ryan MF, Diong KL, Hutchinson K, Glass M, Spiers K, Woodend J, Davidson E. **Chorley Hospital:** Rajbhandari SM, Acharya S. Whittaker J, Caunce K. **City Hospital, Birmingham:** Ryder REJ, Basu A, De P, Lee BC, Thong KY, Blann A, Mills AP, Cull ML, Burbridge W, Irwin S, Cutler J, Zzizinger A, Mehrali T, Guthrie S, Bedi T, Stevenson-Mort J. **Dewsbury Hospital:** Bissell J. **East Lancashire Hospital NHS Trust:** Ramtoola S, Ali A, Jones G, Wilkinson R, Littley M, Mishra M, Glew M, Jostel A, Demssie Y. **East Surrey Hospital, Redhill:** Sennik D, Prajapati C, Chinnasamy E. **Forth Valley Hospital:** Buchanan L, Mackintosh L. **Friarage Hospital, Northallerton:** Owen K, Kamaruddin MS, Leek C. **Furness General Hospital:** Banerjee M, Obale O. **Huddersfield Royal Infirmary:** Moisey R. **Hull Royal Infirmary:** Sugunendran S, Sathyapalan T, Walton C. **King's College Hospital, London:** Vitello S, Hunt K. **Lagan Valley Hospital, Lisburn:** Au S. **Leicester General Hospital:** Tarigopula G, Kong M-F, Gregory R, Jackson S. **Leicester Royal Infirmary:** Htike ZZ. **Monklands Hospital, Airdrie:** Sandeep TC, White A. **New Cross Hospital, Wolverhampton:** Singh BM, Khalid Y, Nayak AU, Katreddy V. **Newham University Hospital, London:** Gelding S, Menon R, Balakumar Y. **Ninewells, Dundee:** George P. **North Tees & Hartlepool Trust:** Robinson M, Dobson M, Presgrave M, Mehaffy J, Roper N, Pye S, Macleod J, Worrall E, Sinclair J, Anthony S, Jones S. **Pendyffryn Medical Group (GP):** Morrison CL. **Pennine Acute Hospitals Trust:** Smith G. **Pilgrim Hospital, Boston:** Jacob K, Htwe N. **Pinderfields General, Wakefield:** D'Costa R. **Pontefract General Infirmary:** Bissell J. **Queen Elizabeth II Hospital & Lister Hospital, Welwyn Garden City:** Winocour PH, Darzy K, Qureshi SA, Ford M, Barker L, O' Donnell L. **Royal Blackburn Hospital:** Ramtoola S, Ali A, Jones G, Wilkinson R, Littley M, Mishra M, Glew M, Jostel A, Demssie Y. **Royal Devon & Exeter:** Lockett H. **Royal Infirmary of Edinburgh:** McLaren J. **Royal United Hospitals, Bath:** Allen K, Higgs E, Robinson A, Ward A, Ward A, Hall B, Hillier N, Catchpole S, Wylie S. **Royal Sussex County Hospital, Brighton:** Burberry A. **Royal Victoria Hospital, Belfast:** Cooke B, Hunter S, Mcerlean U. **Sandwell Hospital, West Bromwich:** Davies P, Rock K. **Singleton Hospital, Swansea:** Udiawar M. **Smethwick Health Centre:** Harrington J. **Southern General Hospital, Glasgow:** Semple C, Struthers S, Kennon B. **St George's Hoapital, London:** Ahmed FW, Bano G, Patel N, Flanagan A, Wilson Z, O'Brien J, Firth P. **St John's Hospital, Livingston:** Teoh WL, Adamson K. **St Stephens Gate Medical Practice (Norfolk PCT) (SSGMP):** Haylock C. **Stirling Royal Infirmary:** Kelly C, Mackenzie A, Ryan L, Dewar L. **Stobhill Hopsital:** Smith C, Gordon D. **Sunderland Royal:** Nayar R, Carey P, Aspray T. **Torbay Hospital, Torquay:** Paisey R, Smith J, Lissett K, Dyer R, Dimitropoulos I, Weekes C. **Trafford General Hospital:** Snell A, Stephens WP, George A, Hopewell L. **Tyrone County Hospital:** Helmy A, Hameed A, McGirr B, Patterson H, Monaghan S, Bradley P, Evan H. **Ulster Hospital, Belfast:** Harper R, Carr S, McDonald P, Harding J, McIlwaine W, McLaughlin D, Whitehead H. **Victoria Hospital, Kirkcaldy:** Duncan C, Chalmers J. **Western General Hospital, Edinburgh:** Zammitt N. **Westmoreland General Hosptital:** Banerjee M, Obale O. **Wharfedale Hospital:** Amery C. **Wrexham Maelor:** Dixon AN. **Yeovil District Hospital:** Bickerton AST, Pramodh S, Crocker M.