

Does dapagliflozin affect the metabolic response in patients with elevated alanine aminotransferase (ALT) and Type 2 diabetes?

Association of British Clinical Diabetologists (ABCD) nationwide dapagliflozin audit

Mahender Yadagiri
ABCD Research Fellow

P Sen Gupta, JW Stephens, A Robinson, M Phylactou, A Kennedy,
J Clarke, J Wilding, IW Gallen, K A Adamson, R E J Ryder
On behalf of the ABCD nationwide dapagliflozin audit contributors

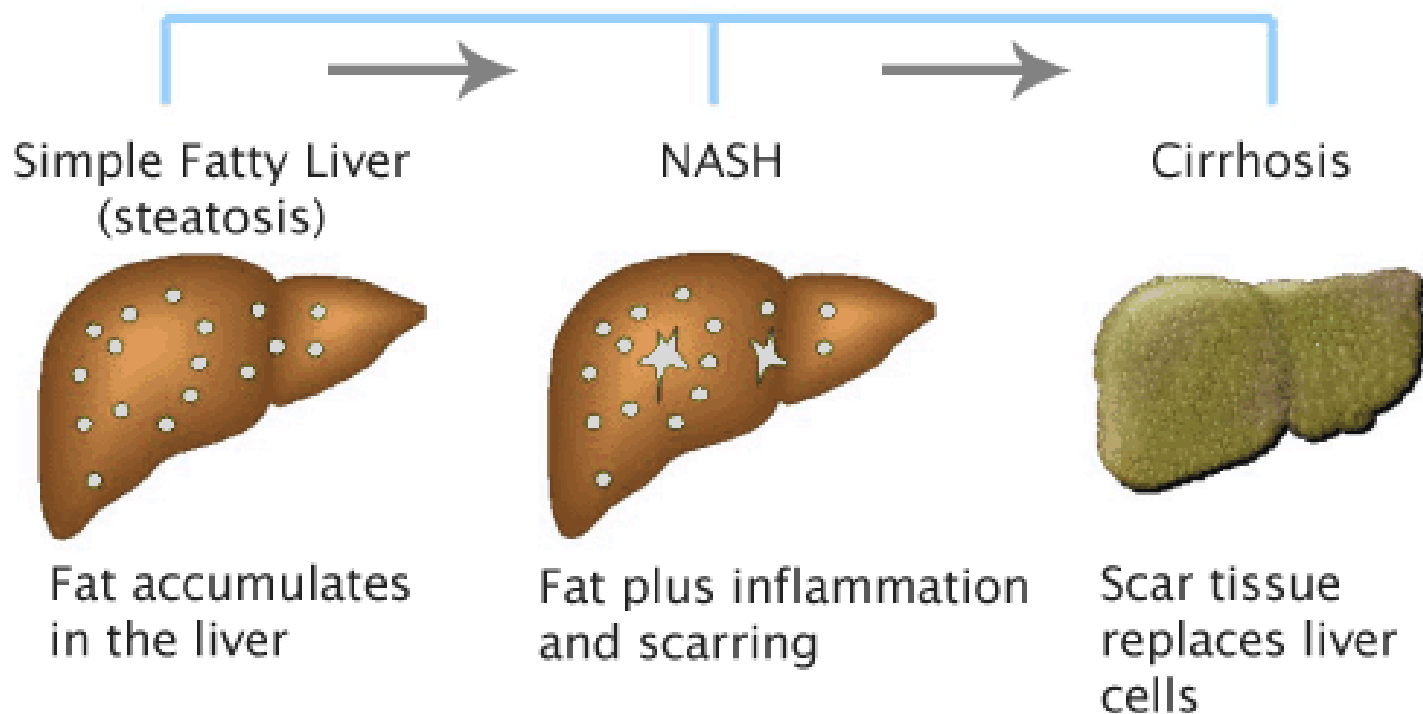
Diabetes UK Professional Conference
March 2016

Overview

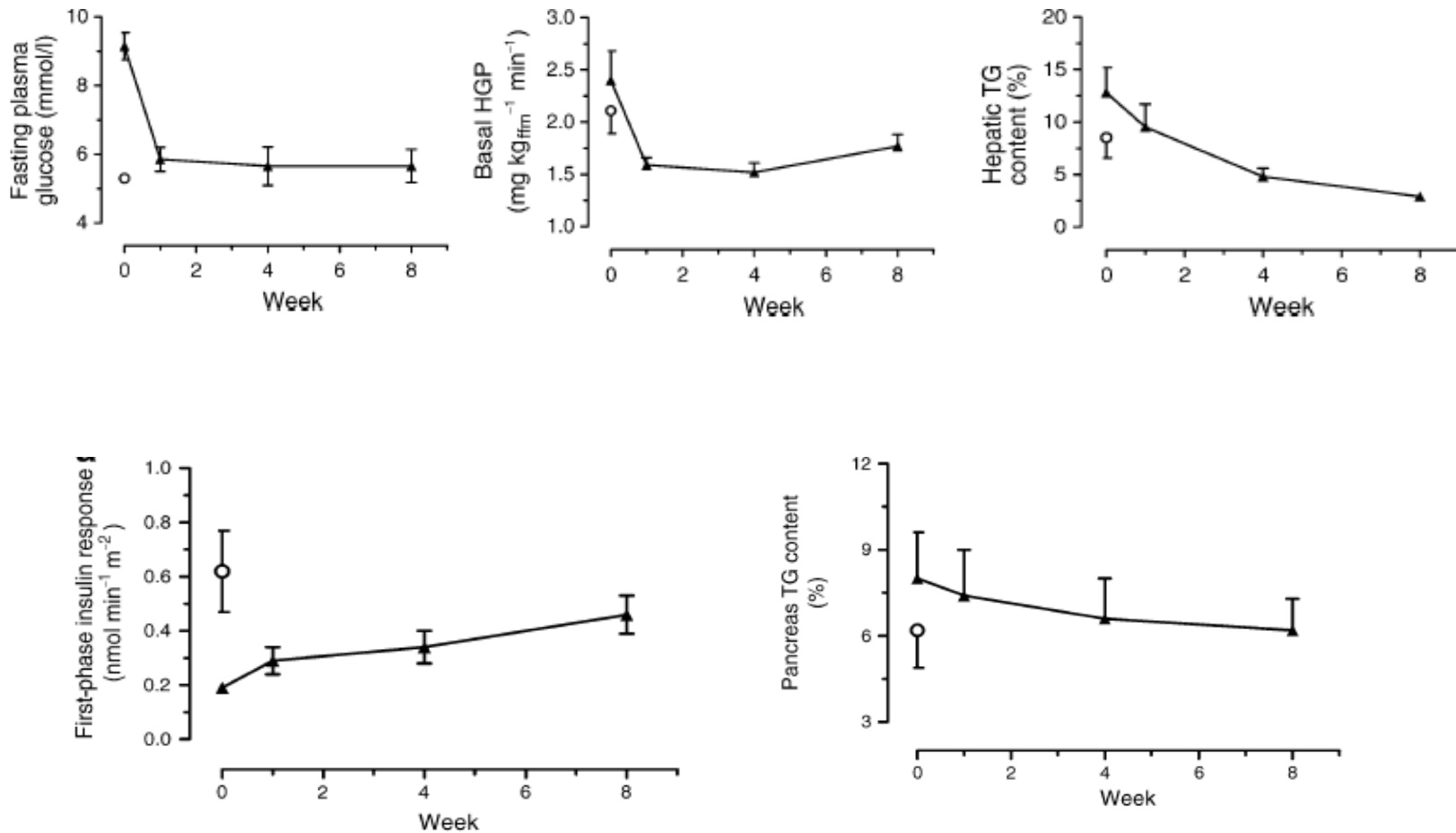
- Liver disease in T2DM
- ABCD audit - aims, methods
- Data analysis - Results
- Conclusion

Background: Liver Disease in T2DM

Non-alcoholic Fatty Liver Disease and Cirrhosis



Background: Fatty liver and insulin resistance in T2DM



Lim EL, Taylor R et al Diabetologia 2011; 54: 2506-2514

Background: ALT and fatty liver

- ALT => Marker of fatty liver
- ALT tends to be elevated in fatty liver disease and tends to fall when liver fat reduces

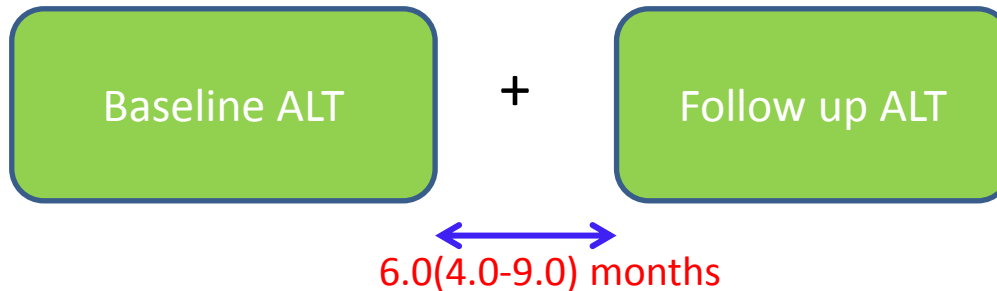
Aims

To evaluate the effect of :

- Dapagliflozin on metabolic response to patients with elevated alanine aminotransferase(ALT) and
- Baseline ALT on metabolic response to dapagliflozin.

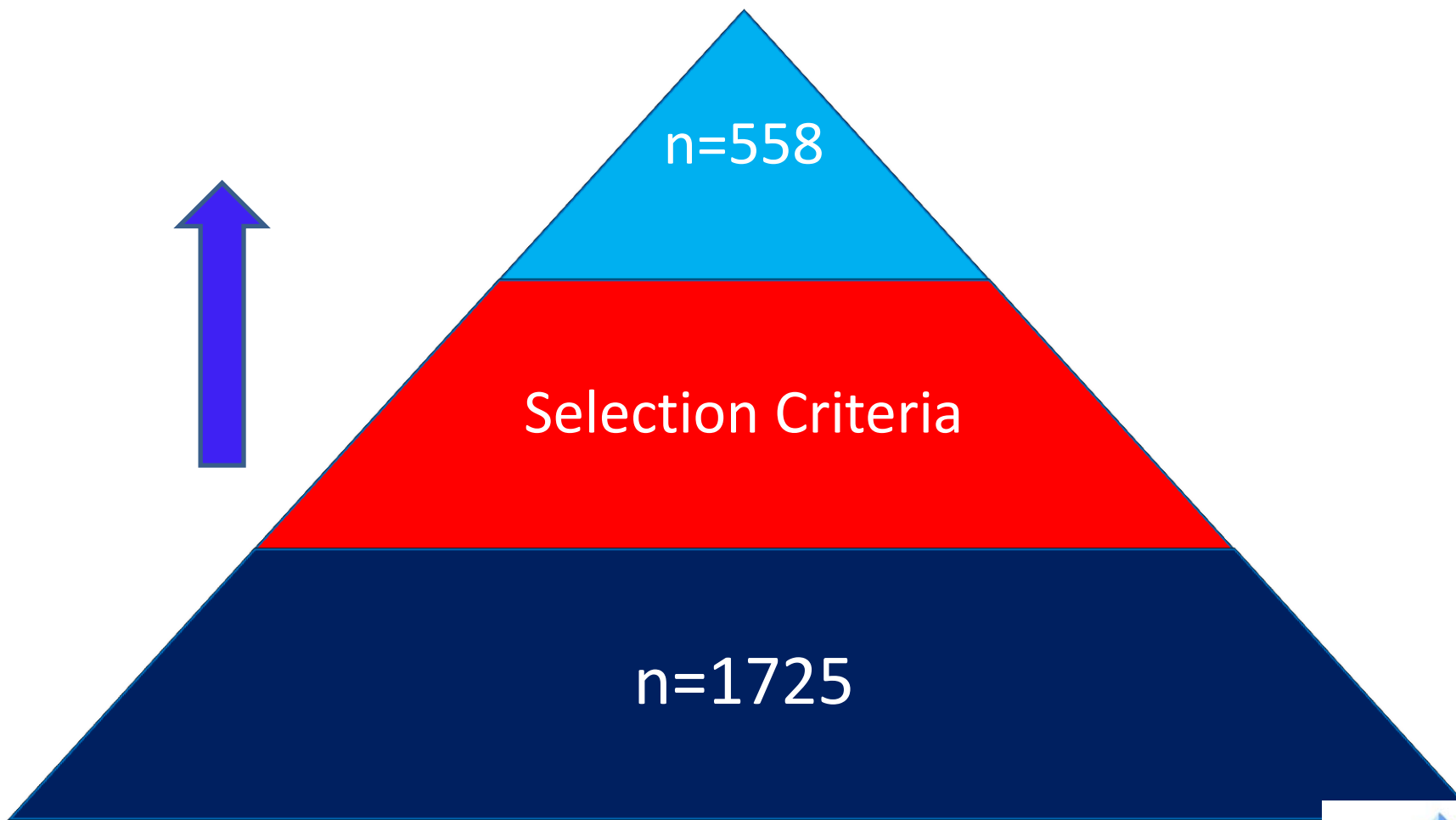
Methods

- Data from ABCD Dapagliflozin Audit (2014-2015)
- Selection criteria :



- Patients categorised into 3 groups depending on baseline ALT:
 - ALT < 30U/l
 - ALT 30-50U/l
 - ALT ≥ 50 U/l
- **Descriptive analysis**
- **Wilcoxon signed rank test**
- **Spearman's correlation**

Methods



Results: Baseline Characteristics

n(%)	ALT<30U/l n=250 (44.8)	ALT 30-50U/l n=209 (37.1)	ALT>50U/l n=101(18.1)	P value
Males(%)	49.2	65.2	66.3	<0.001
Age(yrs)	58.9±10.1	57.1±10.3	55.9±8.5	<0.001
Diabetes of Duration(yrs)	12.0(7.0-17.0)	9.0(3.0-15.0)	6.0(4.0-12.5)	<0.01
HbA1c(mmol)	79.2±16.9	78.1±17.5	79.2±16.7	<0.001
HbA1c(%)	9.4±1.5	9.3±1.3	9.4±1.3	<0.001
BMI(Kg/m ²)	35.8±8.4	36.2±9.9	35.7±6.7	<0.01
Weight(Kg)	99.2±21.9	103.3±24.1	103.1±19.6	<0.01
ALT(U/l)*	21.0(17.0-25.0)	37.0(33.0-41.0)	63.0(57.0-73.5)	n/a

Results: Baseline Characteristics

n(%)	ALT<30U/l n=250 (44.8)	ALT 30-50U/l n=209 (37.1)	ALT>50U/l n=101(18.1)	P value
Males(%)	49.2	65.2	66.3	<0.001
Age(yrs)	58.9±10.1	57.1±10.3	55.9±8.5	<0.001
Diabetes of Duration(yrs)	12.0(7.0-17.0)	9.0(3.0-15.0)	6.0(4.0-12.5)	<0.01
HbA1c(mmol)	79.2±16.9	78.1±17.5	79.2±16.7	<0.001
HbA1c(%)	9.4±1.5	9.3±1.3	9.4±1.3	<0.001
BMI(Kg/m ²)	35.8±8.4	36.2±9.9	35.7±6.7	<0.01
Weight(Kg)	99.2±21.9	103.3±24.1	103.1±19.6	<0.01
ALT(U/l)*	21.0(17.0-25.0)	37.0(33.0-41.0)	63.0(57.0-73.5)	n/a

Results: Baseline Characteristics

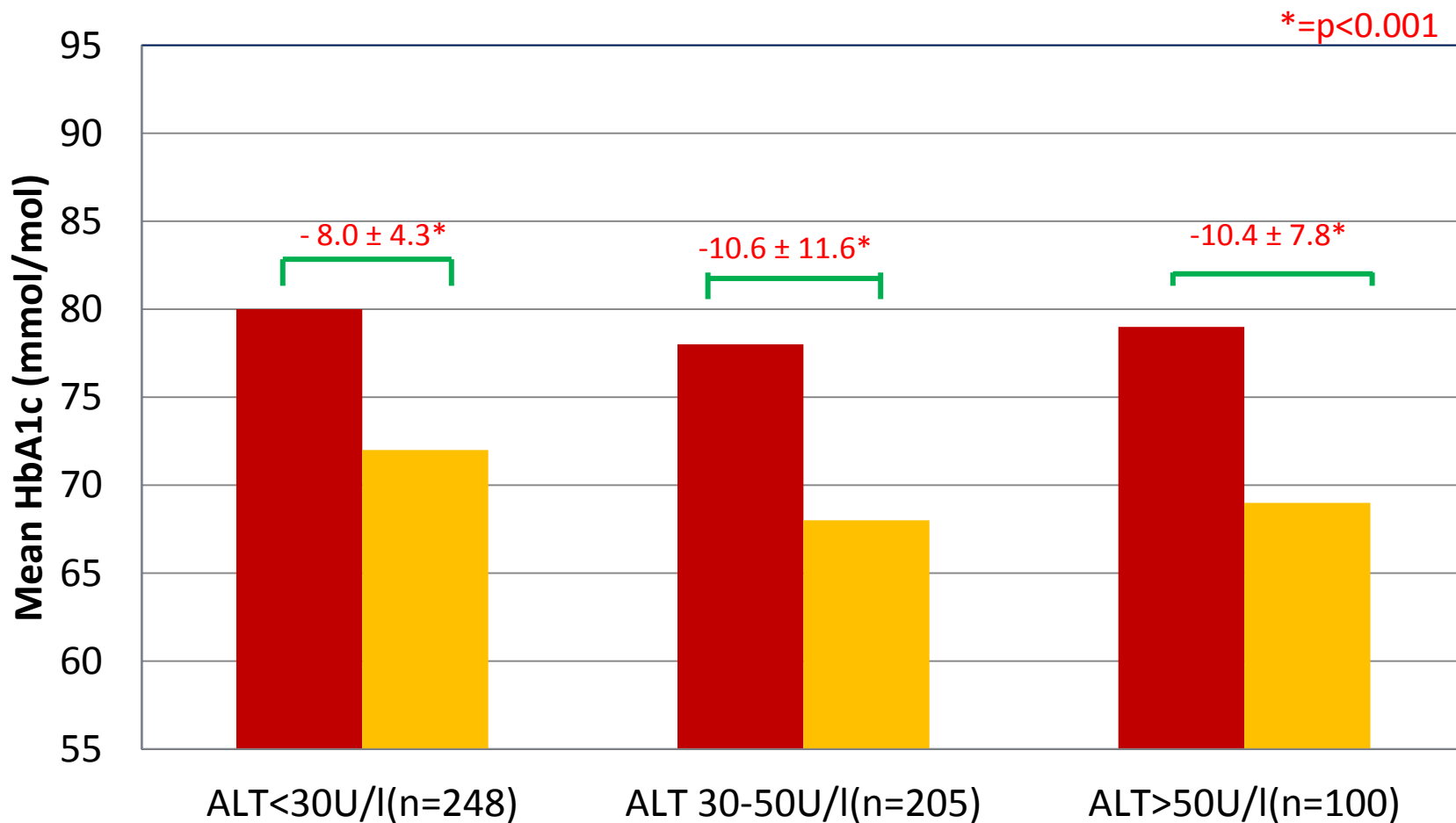
n(%)	ALT<30U/l n=250 (44.8)	ALT 30-50U/l n=209 (37.1)	ALT>50U/l n=101(18.1)	P value
Males(%)	49.2	65.2	66.3	<0.001
Age(yrs)	58.9±10.1	57.1±10.3	55.9±8.5	<0.001
Diabetes of Duration(yrs)	12.0(7.0-17.0)	9.0(3.0-15.0)	6.0(4.0-12.5)	<0.01
HbA1c(mmol)	79.2±16.9	78.1±17.5	79.2±16.7	<0.001
HbA1c(%)	9.4±1.5	9.3±1.3	9.4±1.3	<0.001
BMI(Kg/m ²)	35.8±8.4	36.2±9.9	35.7±6.7	<0.01
Weight(Kg)	99.2±21.9	103.3±24.1	103.1±19.6	<0.01
ALT(U/l)*	21.0(17.0-25.0)	37.0(33.0-41.0)	63.0(57.0-73.5)	n/a

Vs Combined Clinical Trials-
Dapagliflozin

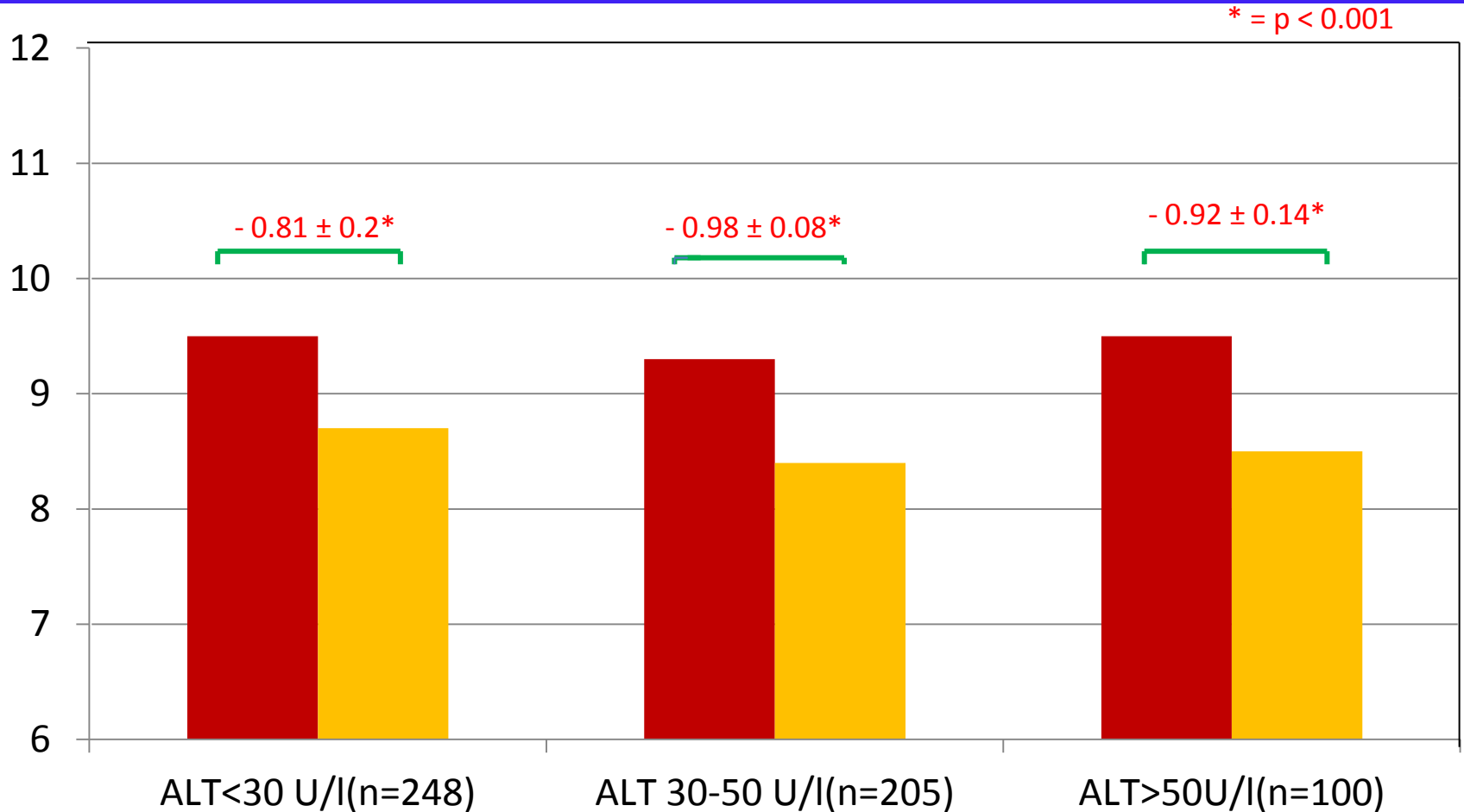
7.96

32.16

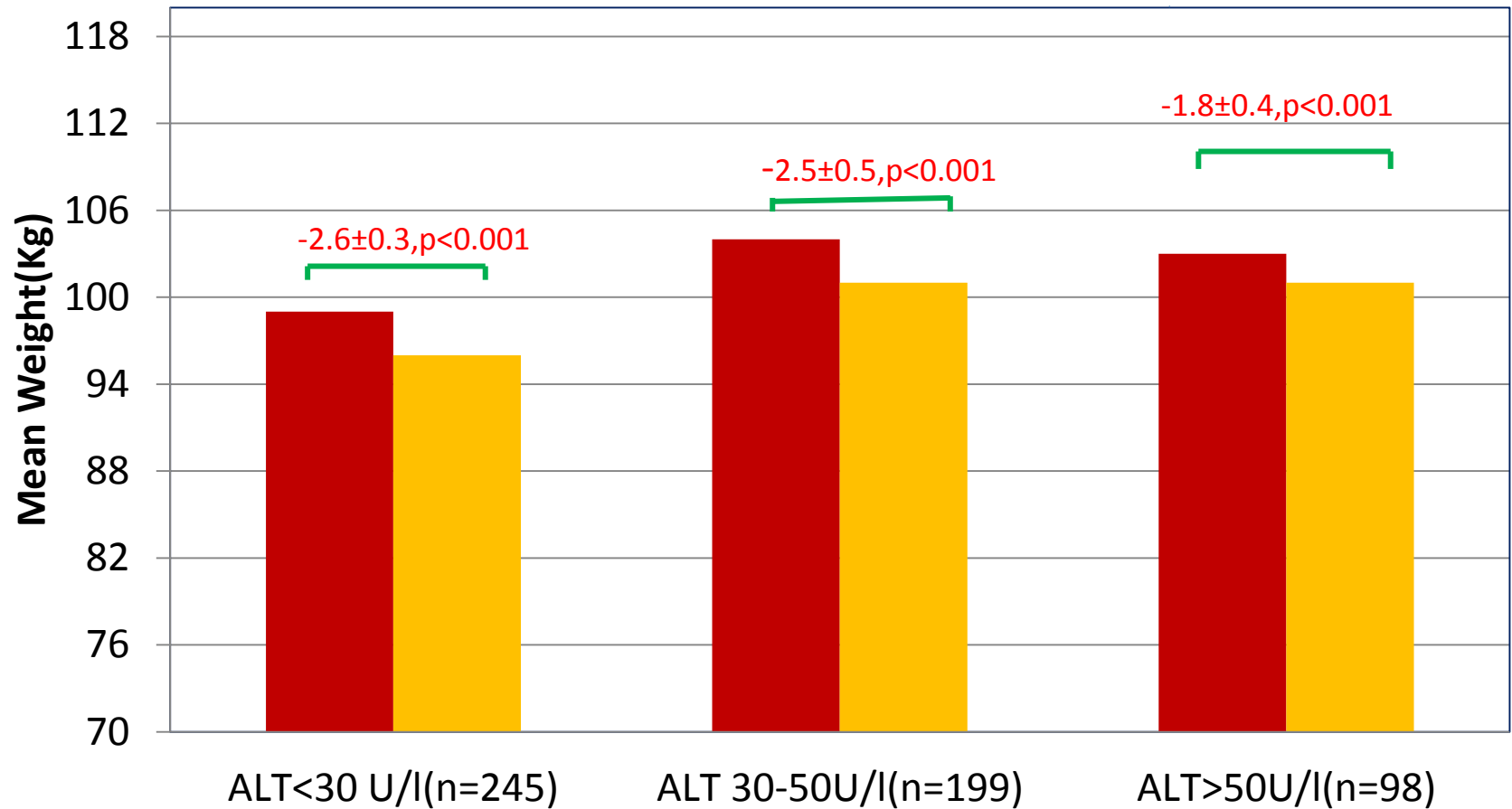
HbA1c Response to Dapagliflozin



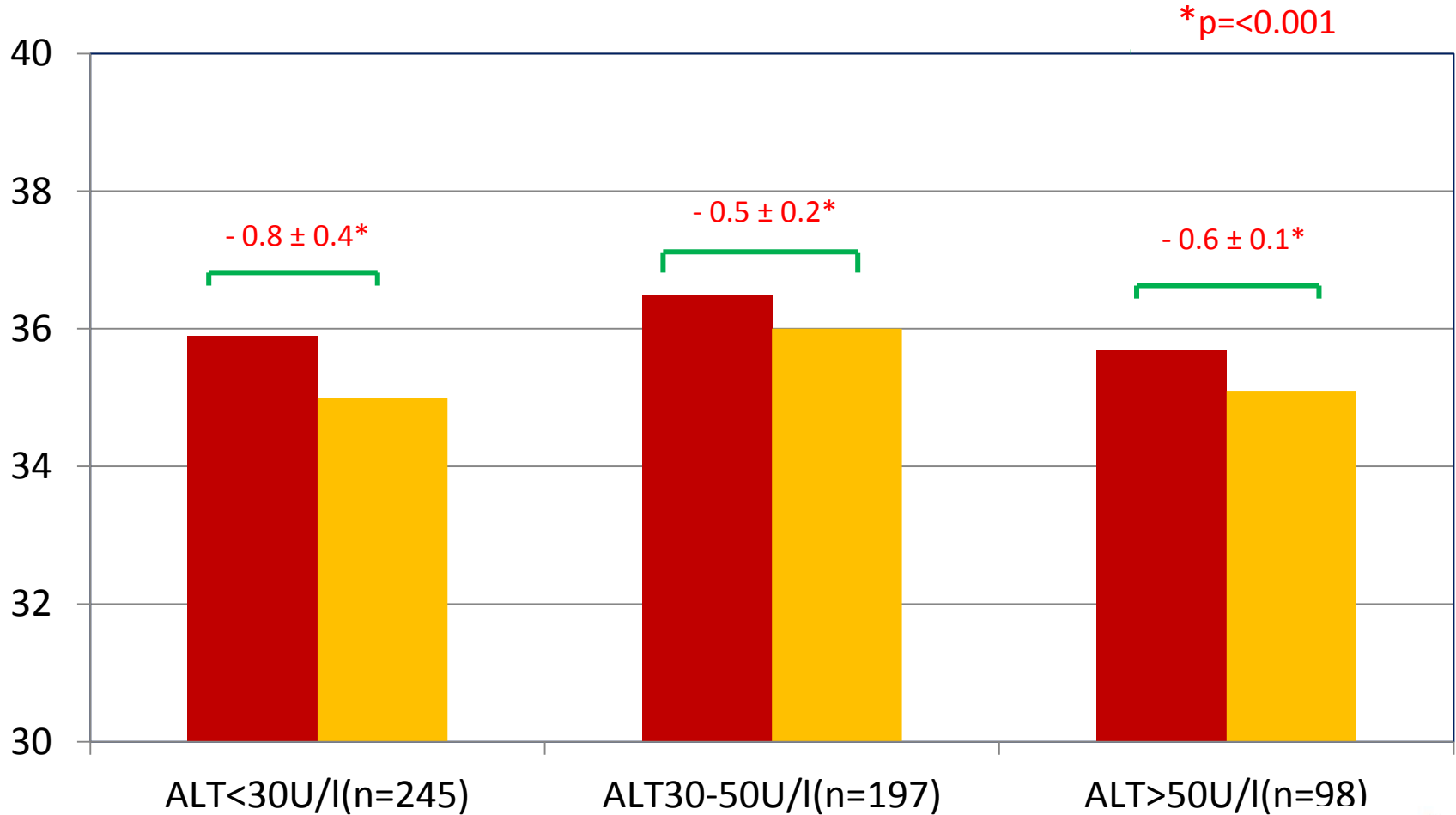
HbA1c Response to Dapagliflozin



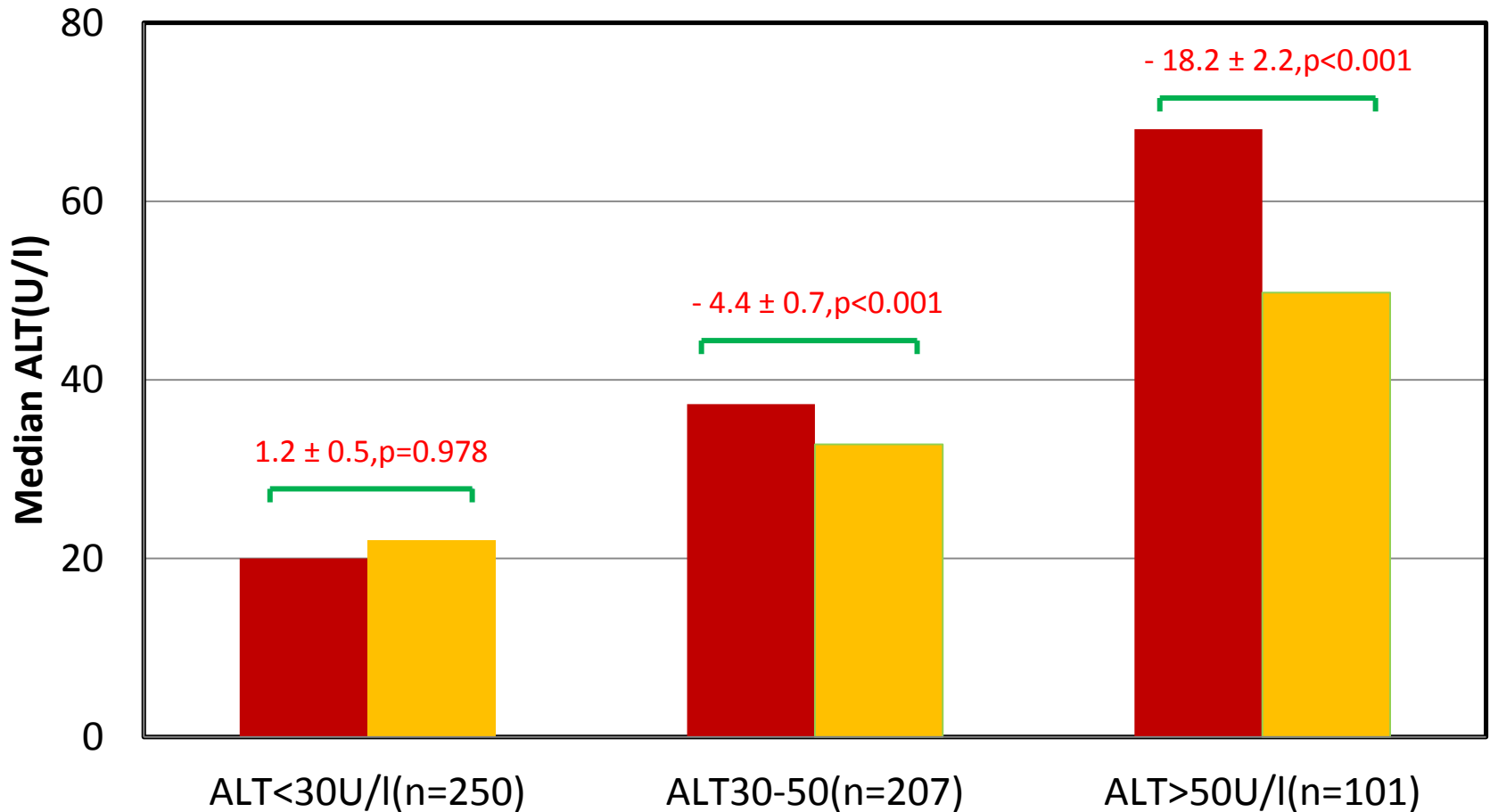
Weight Response to Dapagliflozin



BMI response to Dapagliflozin



ALT response to Dapagliflozin



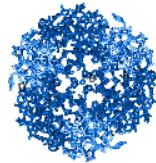
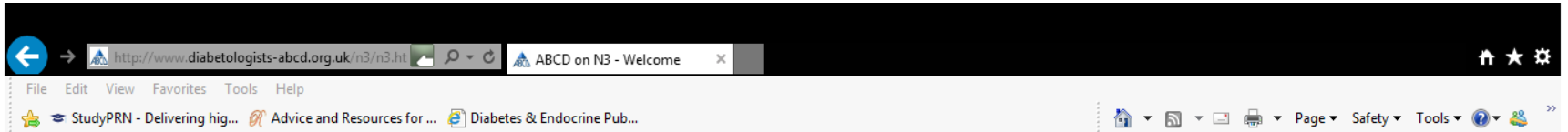
Correlation

Change in ALT correlation with:	Spearman's Rank Correlation coefficient [®]	P-value
Change in HbA1c	0.1	<0.05
Change in weight	- 0.06	0.18
Baseline ALT	0.5	<0.01

Conclusions

- Dapagliflozin has a clinically and statistically significant response on ALT reduction in Type 2 diabetes patients with high baseline ALT > 30U/l.
- This result may have implications regarding the insulin resistance associated with fatty liver and non-alcoholic fatty liver disease.

ABCD Audits



Association of British Clinical Diabetologists

Welcome to ABCD on N3



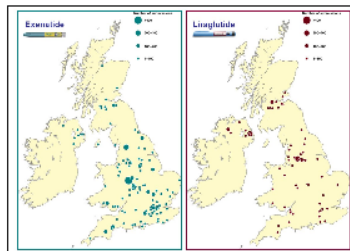
[Home](#)

[Live ABCD nationwide audits of new therapies](#)

[All ABCD nationwide audits](#)

[Future audits of new therapies](#)

[ABCD worldwide audits](#)



Above - centres contributing to the ABCD nationwide exenatide (left) and liraglutide (right) audits – click to enlarge

	Clinical trials combined	Real clinical use in UK (ABCD audit)
	Baseline HbA _{1c} (%)	
Exenatide	8.37	9.47
Liraglutide	8.5	9.40

The Association of British Clinical Diabetologists on N3

The Association of British Clinical Diabetologists (ABCD) is delighted to have achieved a presence on N3. This page is not itself on N3, as we wish the information to be universally available, but these pages form ABCD's portal into N3.

What is N3 and why a presence on it for ABCD?

N3 is the national broadband network for the National Health Service (NHS), connecting all NHS locations, in particular linking acute hospitals and GP surgeries. The important thing from ABCD's point of view is that it is the official secure place for storing patient data of NHS patients and therefore the most appropriate and secure place for holding our nationwide audit data in the future. Centres joining the national audit effort will be able to access their own patient data on their local NHS computers as they do with their other local clinical systems. They will be able to access and audit their own local data in order to learn from the local experience.

[Main ABCD homepage](#)

[ABCD canagliflozin audit](#)

[ABCD dapagliflozin audit](#)

[ABCD exenatide QW audit](#)

[Apply for both exenatide qw and dapagliflozin audits](#)

[ABCD degludec audit](#)

[ABCD liraglutide audit](#)

[ABCD exenatide audit](#)

[ABCD worldwide audits](#)

[ABCD endobarrier study](#)

[Contact us](#)



ABCD nationwide dapagliflozin audit contributors

The following are those whom we know about.

ABCD nationwide dapagliflozin audit – initial setup, maintenance and nationwide analysis: Ryder REJ, Adamson K, Bailey CJ, Walton C, Thong KY, Sen Gupta P, Cull ML, Yadagiri M. Statistician: Blann A

England

Aintree University Hospital NHS Foundation Trust (University Hospital Aintree): Wilding J, Yunus A. **Bromley CCG (Selsdon Park Medical Practice):** Cheah Y, Lovie K. **County Durham And Darlington NHS Foundation Trust (Darlington Memorial Hospital):** Kamaruddin S, Khan U, Partha P, Peter P, Tarigopula G, Tee SA. **Doncaster And Bassetlaw Hospitals NHS Foundation Trust (Bassetlaw Hospital):** Chaturvedi P, Payne G. **Dorset County Hospital NHS Foundation Trust (Dorset County Hospital):** Graja A, Macklin A, Wotherspoon F. **Dorset County Hospital NHS Foundation Trust (Cerne Abbas Surgery):** Murphy H, Wakeman C. **Dudley Group Hospitals NHS Foundation Trust (Russells Hall Hospital):** Pang T. **East and North Hertfordshire NHS Trust (Queen Elizabeth II Hospital):** Phylactou M, Darzy K, Winocour P. **East Sussex Healthcare NHS Trust (Conquest Hospital):** Batson D, Castro E, Combes A, Dashora U, Govindan R, Kumar S, Moor C, Ravelo M. **Great Western Hospitals NHS Foundation Trust (The Great Western Hospital):** Bhattacharya B, Broughton C, Ghaffar I. **Hull and East Yorkshire Hospitals NHS Trust (Hull Royal Infirmary):** Varghese J, Walton C. **King's College Hospital NHS Foundation Trust (Orpington Hospital):** Allinson R, Allitt C, Amo-Konado S, Barratt M, Cheah YS, Cunningham S, Fisher N, Hopkins D, Hussey S, Lewis D, Lovegrove-Saville L, Mukuva P, Mustafa O. **Lancashire Teaching Hospitals NHS Foundation Trust (Chorley And South Ribble Hospital):** Balmuri LMR, Imtiaz K. **London Medical, London (Private):** Abraham R, Palik E. **London North West Healthcare NHS Trust (Brent Community Services):** Anthony J, Carroll M, Godambe S, McCabe-Hughes F, Murali KS, Ogida L, Patel N, St-John J. **Maidstone And Tunbridge Wells NHS Trust (The Tunbridge Wells Hospital):** Agarwal G, Barnes D, Billings D, Butler C, Cairns S, Crosby Z, Danby T, Haq M, Ryan A. **Pennine Acute Hospitals NHS Trust (North Manchester General Hospital):** Tarpey S. **Pennine Acute Hospitals NHS Trust (Royal Oldham Hospital):** Tarpey S. **Royal Berkshire NHS Foundation NHS Trust:** Gallen JW. **Royal United Hospital Bath NHS Trust:** Robinson T. **Sandwell And West Birmingham Hospitals NHS Trust (Cape Hill Medical Centre, GP):** Gardner G. **Sandwell And West Birmingham Hospitals NHS Trust (City Hospital Birmingham):** Bajwa R, Basu A, Cull M L, De P, Lee B, Kaur A, Pickles O, Ryder R E J, Sen Gupta P, Taylor N, Wyres, M, Yadagiri M. **Sandwell And West Birmingham Hospitals NHS Trust (Tower Hill Medical Centre, Dr DK Nandis Practice, GP):** Bath S, Chiam W. **Sandwell And West Birmingham Hospitals NHS Trust (Norvic Family Practice, GP):** Pathan A, Charm E, Littlewood Z. **Sandwell And West Birmingham Hospitals NHS Trust (Sherwood House Medical Practice, GP):** Hoffman H. **Sandwell And West Birmingham Hospitals NHS Trust (Sundial Lane Surgery, Dr K Akhtar, GP):** Akhtar R, Baker O, Durk D, Woakes E. **Sandwell And West Birmingham Hospitals NHS Trust (Park House Surgery, GP):** Baker O, Hallan P. **Surrey and Sussex Healthcare NHS Trust (East Surrey Hospital):** Brockett K, Clark J. **The Royal Bournemouth And Christchurch Hospitals NHS Foundation Trust (Royal Bournemouth General Hospital):** Hampton K, Partridge H, Walker J, Williams E. **The Royal Wolverhampton NHS Trust (New Cross Hospital):** Aziz U, Lekakou L, Oguntolu V. **Whitstable Medical Practice (Dr Jm Ribchester & Partners, GP):** Brice R, Rollings R, Sansom H.

Scotland

Greater Glasgow & Clyde: Huang F, Jones G. **NHS Fife (Victoria Hospital, Kirkcaldy):** Baird J, Burns D, Chalmers J, Creagh M. **Royal Infirmary of Edinburgh NHS Trust:** Reid H. **West Lothian NHS Trust:** Adamson K, Reid H, Vanlook L. **Western General Hospitals NHS Trust:** Reid H.

Wales

Abertawe Bro Morgannwg University NHS Trust (Morriston Hospital): Bain S C, Eyles J, Kumar P, Min T, Price D, Stephens JW. **Abertawe Bro Morgannwg University NHS Trust (Neath Port Talbot Hospital):** Chokor M, Peter R. **Abertawe Bro Morgannwg University NHS Trust (Singleton Hospital):** Bain S C, Eyles J. **Abertawe Bro Morgannwg University NHS Trust (Swansea University):** Bain S C, Eyles J. **Betsi Cadwalader University Healthboard (Wrexham Maelor Hospital):** Ahmad S, Khalily N, Stanaway S. **Cardiff And Vale NHS Trust:** Roberts A.

Northern Ireland

Belfast Trust (Belfast): Johnston PC, Nugent A. **Northern Trust (Antrim Area Hospital):** Kennedy A, Strzelecka A.

Acknowledgment

The ABCD nationwide dapagliflozin audit is an independent audit supported by an unrestricted grant from Astra Zeneca