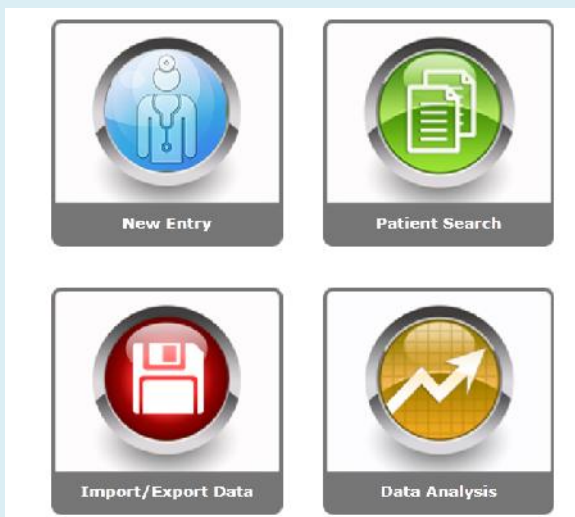


Does Liraglutide therapy affect the metabolic response in patients with elevated alanine aminotransferase and type 2 diabetes mellitus?

ABCD Nationwide Liraglutide Audit



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Background: Liver disease in diabetes

- Non-alcoholic fatty liver disease (NAFLD):
 - prevalent (42.6%) in diabetes¹
 - Can progress: non-alcoholic steatohepatitis (NASH), cirrhosis
- Diagnosis:
 - clinical features, imaging, liver enzymes, biopsy
 - Non-invasive scores e.g. NAFLD fibrosis, APRI, BARD, FIB-4
 - Alanine aminotransferase (ALT) may be a surrogate biomarker of liver injury

1. Williamson RM et al. Diabetes Care 2011. 34: 1139–1144.

Background: ABCD Nationwide Liraglutide Audit

- Initiative launched Autumn 2009, UK
- The Audit remains ongoing:
 - collects data on *real* clinical use of Liraglutide
 - demographics, medications, side effects, weight, HbA1c
 - blood tests include ALT

Audit Characteristics

Dates of Audit	2009-2013	
Centres	88	
Contributors	500	
Patients	5643	
Age (yrs)	55.5±11.0	
Duration of diabetes (yrs)*	9.0(6.0-13.0)	
Baseline HbA1c (%)	9.4±1.7	vs Combined Clinical Trials Liraglutide
BMI (kg/m ²)	38.8±7.3	8.5
Weight (kg)	110.5±22.8	31
Number of follow-up visits*	2 (2-3) Range: 0-15	
Duration of follow-up (months)	5.3(0-11.4) Range: 0-38.3	

Reported as mean±SD or median(IQR)*

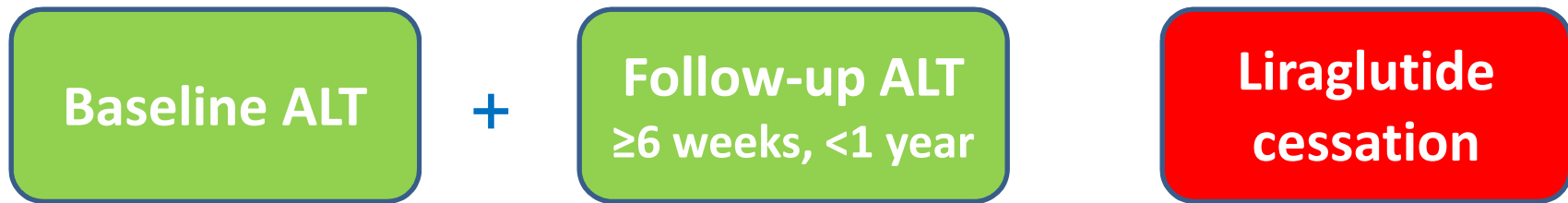
Aims

To evaluate the effect of:

1. Liraglutide on the metabolic response (HbA1c, weight, BMI, ALT) in patients with an elevated ALT
2. Variation in the baseline ALT on the metabolic response to liraglutide

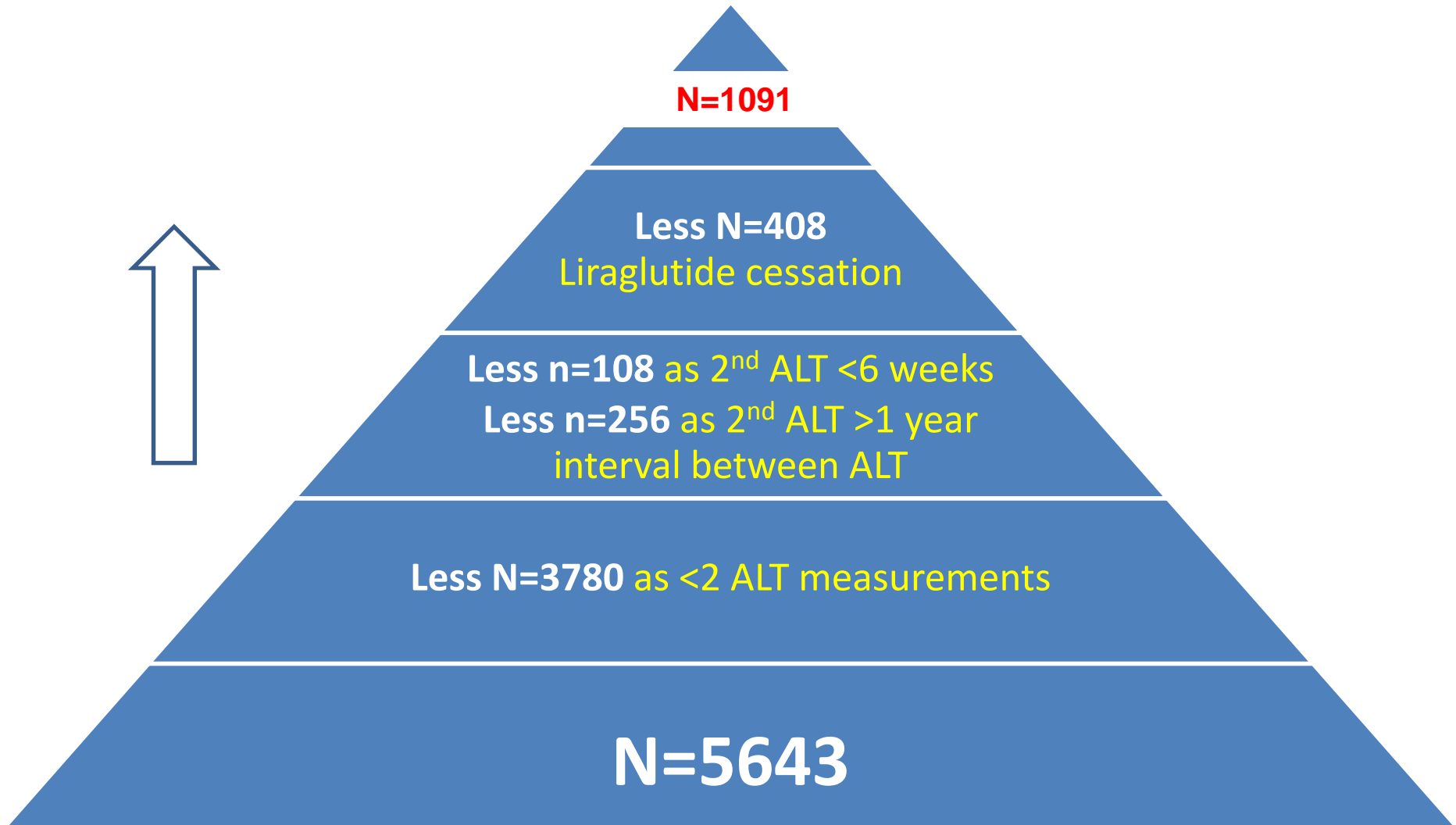
Methods

- Data obtained from ABCD liraglutide audit (2009-2013)
- Selection:



- Patients categorised into 3 groups depending on baseline ALT
 - Normal ALT ≤ 30 U/l
 - Abnormal ALT 31-50U/l
 - High abnormal ALT ≥ 50 U/l
- Descriptive statistics; Before and After liraglutide comparisons

Selection of n=1091 (19.3%) for analysis

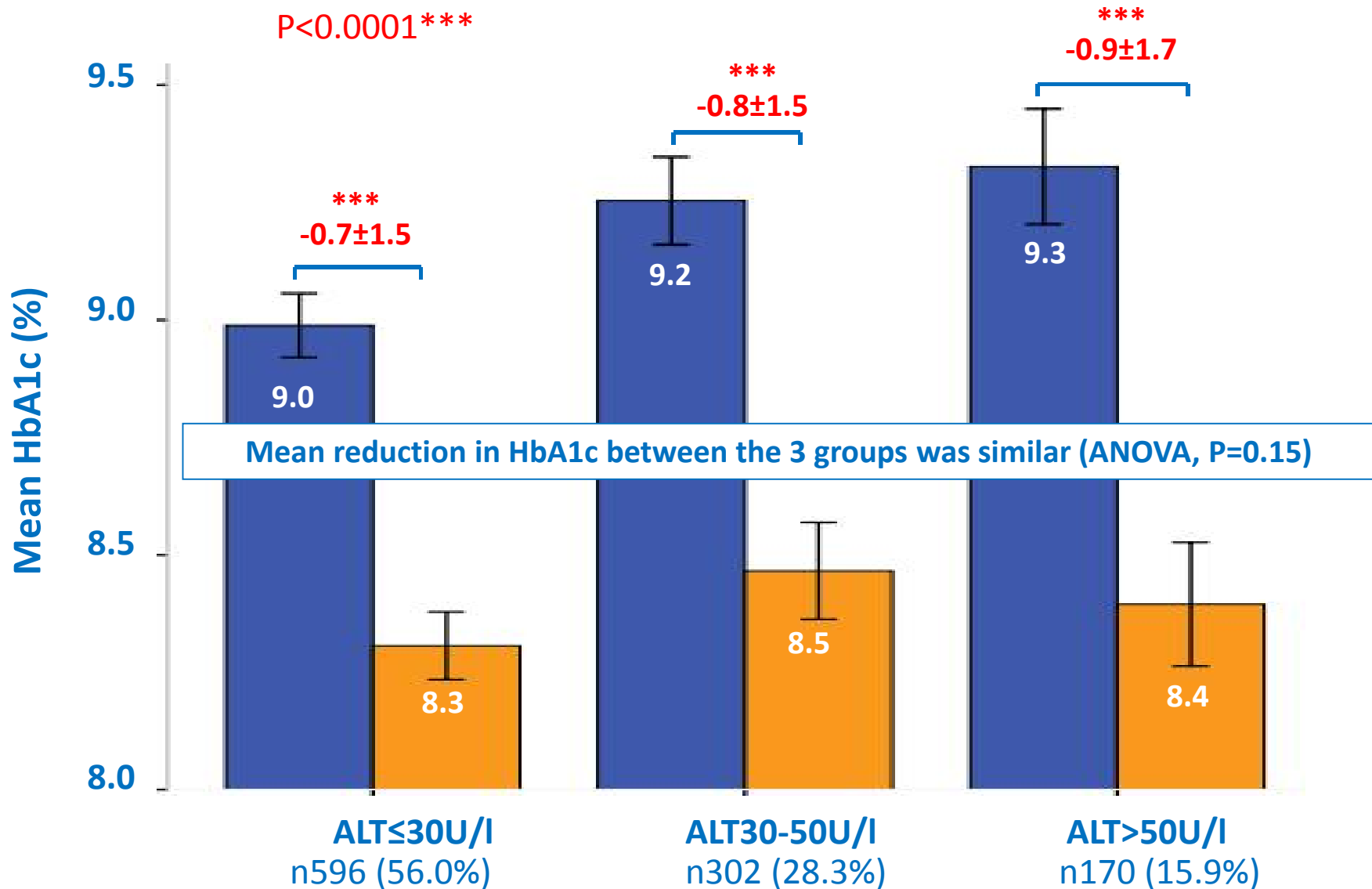


RESULTS: Baseline Characteristics (ALT ≤30; 31-50; >50)

n (%)	ALT ≤30 606 (55.5)	ALT 30-50 n314 (28.8)	ALT >50 N171 (15.7)	P-Value
Male (%)	49.3	58.3	70.8	<0.0001
Caucasian (%)	85.2	91.7	88.4	0.04
Age (yrs)	57.5±10.8	55.5±10.4	51.0±11.3	<0.0001
Diabetes Duration (yrs)	10(7.0-15.0)	9(6.0-13.0)	7(4.0-11.8)	<0.0001
On insulin (%)	44.7	44.6	32.2	0.01
HbA1c (%)	9.0±1.7	9.2±1.6	9.3±1.6	0.02
BMI (kg/m ²)	38.3±7.3	38.8±8.3	37.6±6.1	0.25
Weight (kg)	108.5±23.1	111.2±23.4	110.8±21.6	0.19
ALT (U/l)	22(17.0-25.0)	39(34.0-44.3)	65(56.0-78.0)	n/a
Liraglutide stop (%)	21.8	19.1	19.9	0.61

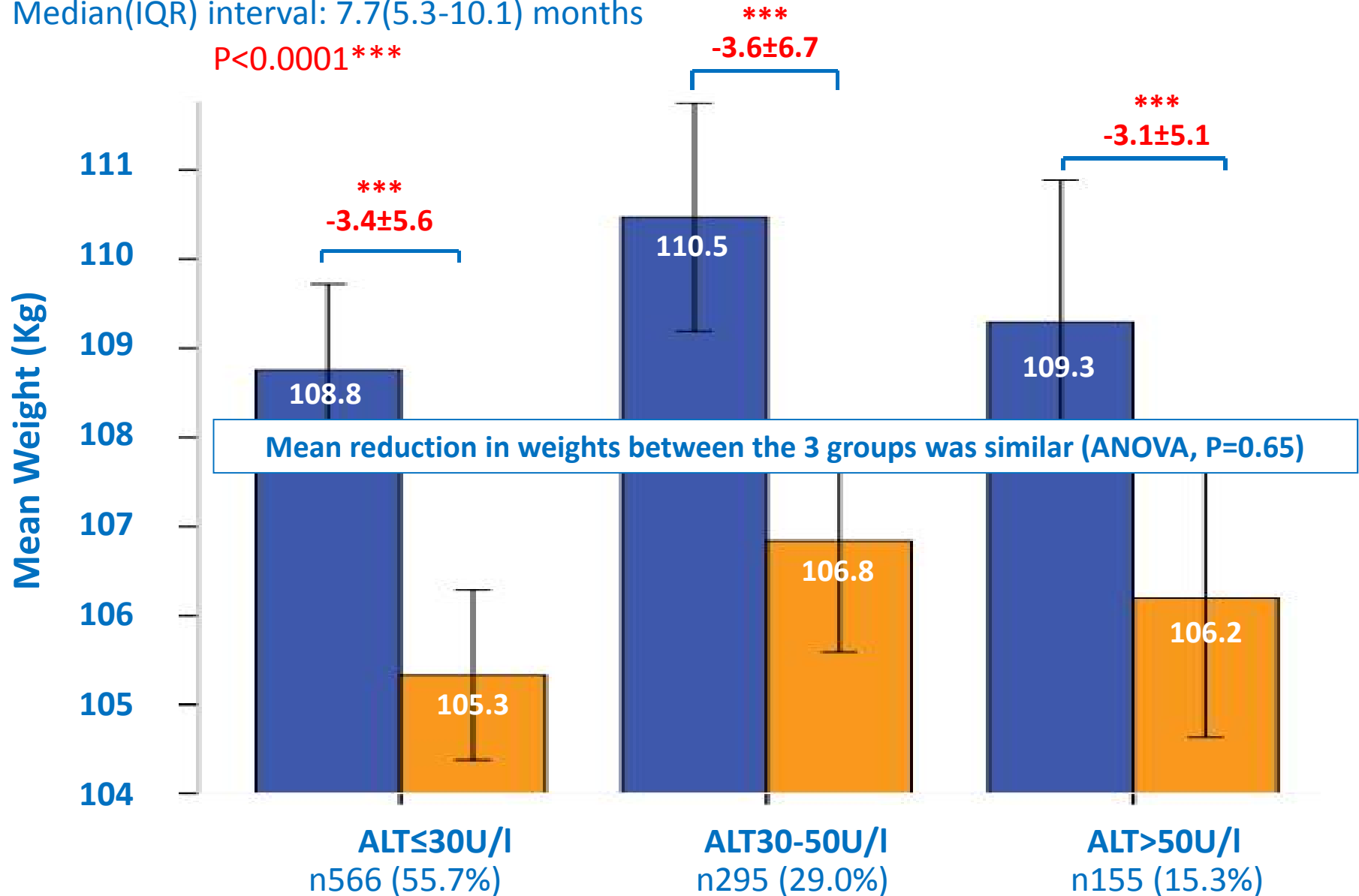
HbA1c response to Liraglutide; n=1068 (97.9%)

Median(IQR) interval: 7.4(4.8-9.9) months



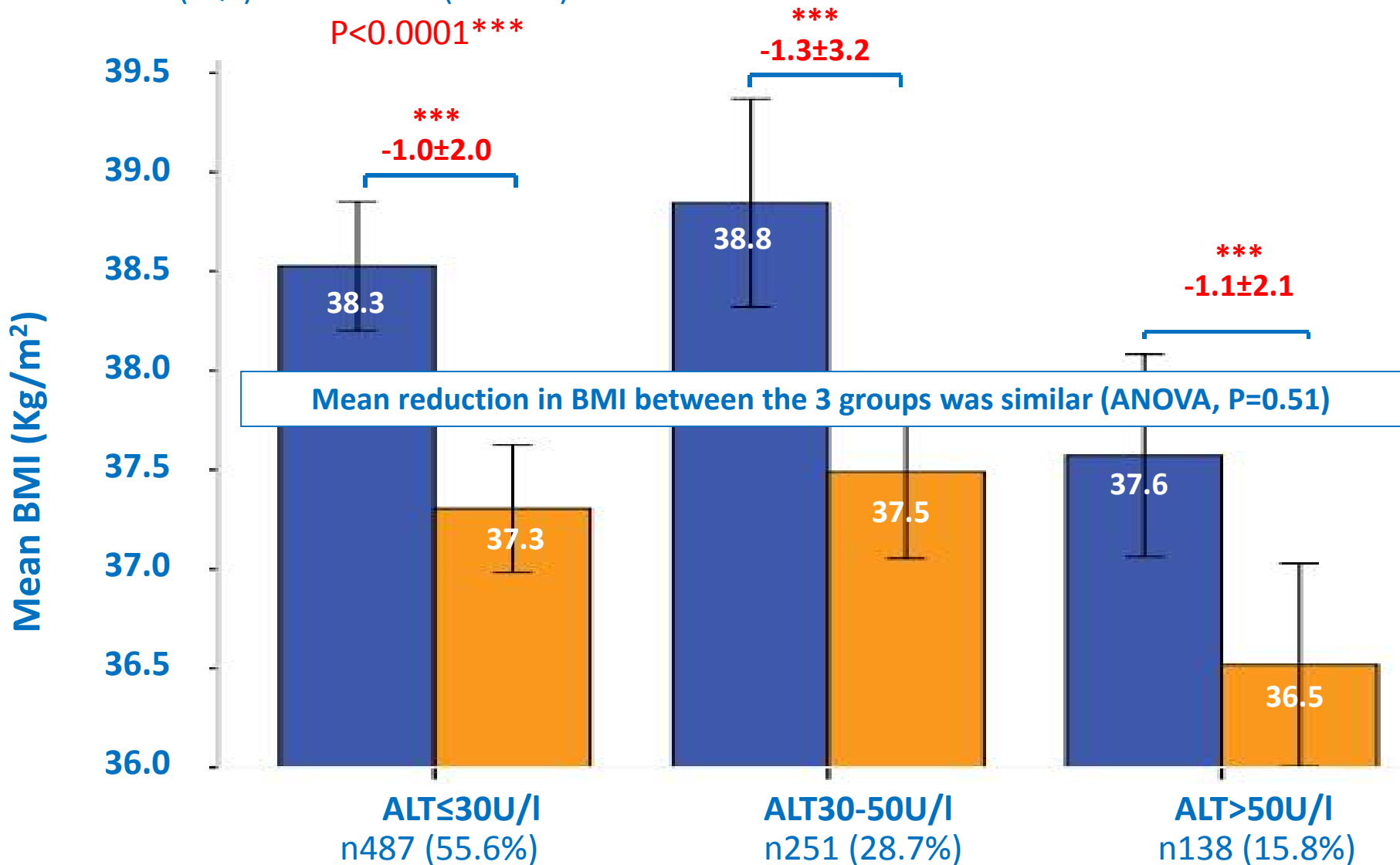
Weight response to Liraglutide; n=1016 (93.1%)

Median(IQR) interval: 7.7(5.3-10.1) months



BMI response to Liraglutide; n=876 (80.3%)

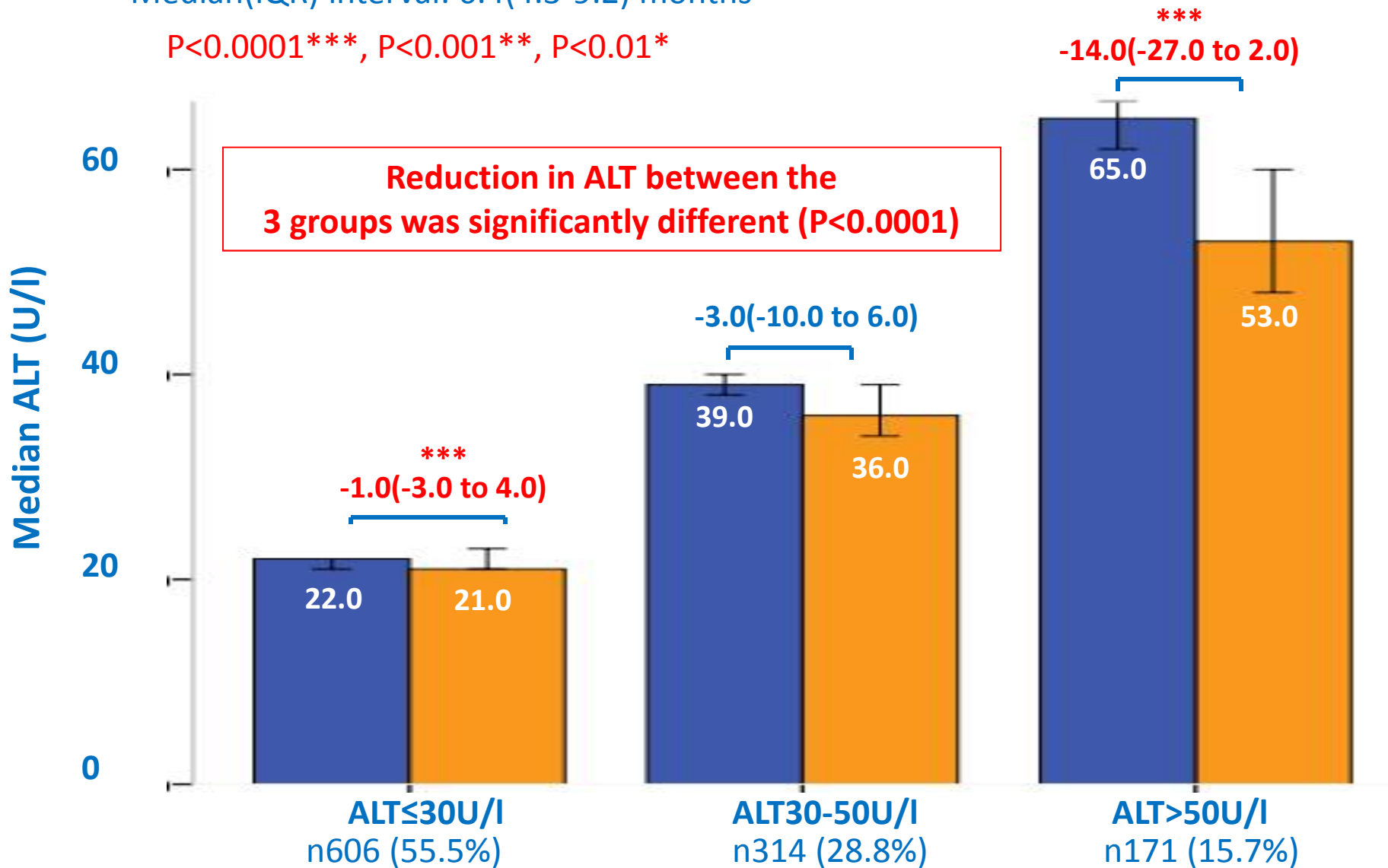
Median(IQR) interval: 7.4(4.9-9.9) months



ALT response to Liraglutide; n=1091 (100%)

Median(IQR) interval: 6.4(4.3-9.2) months

P<0.0001***, P<0.001**, P<0.01*



Correlation

Baseline ALT correlation with:	Spearman's Rank Correlation coefficient	P-value
Change in HbA1c	-0.05	0.09
Change in weight	0.02	0.53
Change in BMI	0.05	0.14
Change in ALT	-0.34	<0.0001

ANCOVA: ALT change over time (dependent)

Independent variables	df	F	P-value
Model	1	4.21	0.04
Age	1	0.56	0.46
Sex	1	0.26	0.61
Duration of diabetes	1	0.12	0.73
Baseline HbA1c	1	0.009	0.93
Baseline ALT	99	3.25	<0.0001

Summary

- There are marked differences observed in baseline characteristics in the high versus normal ALT group
- Liraglutide improves HbA1c, reduces weight and ALT
- Baseline ALT correlates inversely with ALT reduction

Conclusion

- Liraglutide use has a clinically and statistically significant impact on ALT reduction in T2DM patients with a high baseline ALT
- This analysis utilising serum ALT may have implications regarding NAFLD

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

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