The Royal Wolverhampton NHS Trust

Big data, smart dashboards: monitoring and reducing disparities in laboratory medicine

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Potential disparities in laboratory medicine

- Physiologic stratification
  - Age
  - Sex
  - Ethnicity
  - Pregnancy status
  - Time of day
  - Season
- Geography
- Socio-economic factors, access
- Pre-analytical disparities
  - Inconsistent instructions
  - Language barrier, literacy
  - Hydration, posture
  - Phlebotomy-related factors
  - Sample storage and transport
  - Time of day, season
- Analytical disparities
  - Operator-related factors
  - Capabilities of equipment
  - Change in performance
  - Lack of harmonisation
  - Interference
- Post-analytical disparities
  - Delayed communication
  - Language barrier, literacy
  - Access to digital devices
- Comorbidity-related interpretive confounding (or disease-associated biological variation)

Big data and me

Necessity is the mother of all interests!

In-house LAMP stack LIMS 2009-2012

- Validation rulebase
- Order-comms and reporting system
- Interface and middleware
- IQC package
- Test demand/utilisation reports
- QMS – PDF → DocuWiki

Ahead of the pack – web-based

Provided maintenance backup, but did nothing clinical

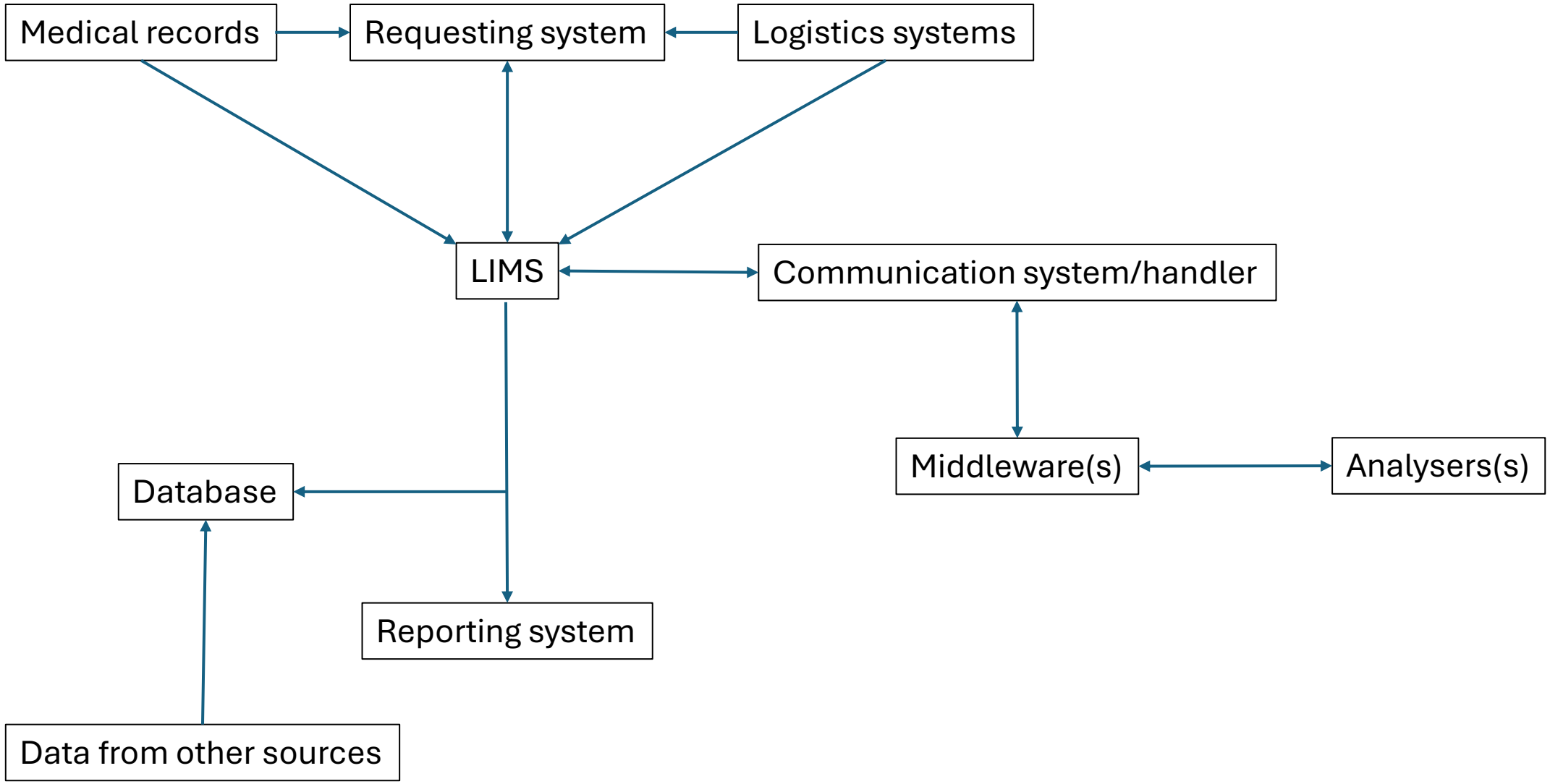
Lessons

- Consolidated detailed data is the key and the lack of access to queryable data is generally the biggest hurdle
  - Database vs data warehouse
- Have clear objectives
  - Outcome focused
  - Aligned with needs
- Look at the bigger picture – in space (width) and in time (possible future needs)
- Stay firm, insistent (and perhaps even repetitive!)
- Create resources – human and non-human
- Cut losses
- LLMs are a blessing

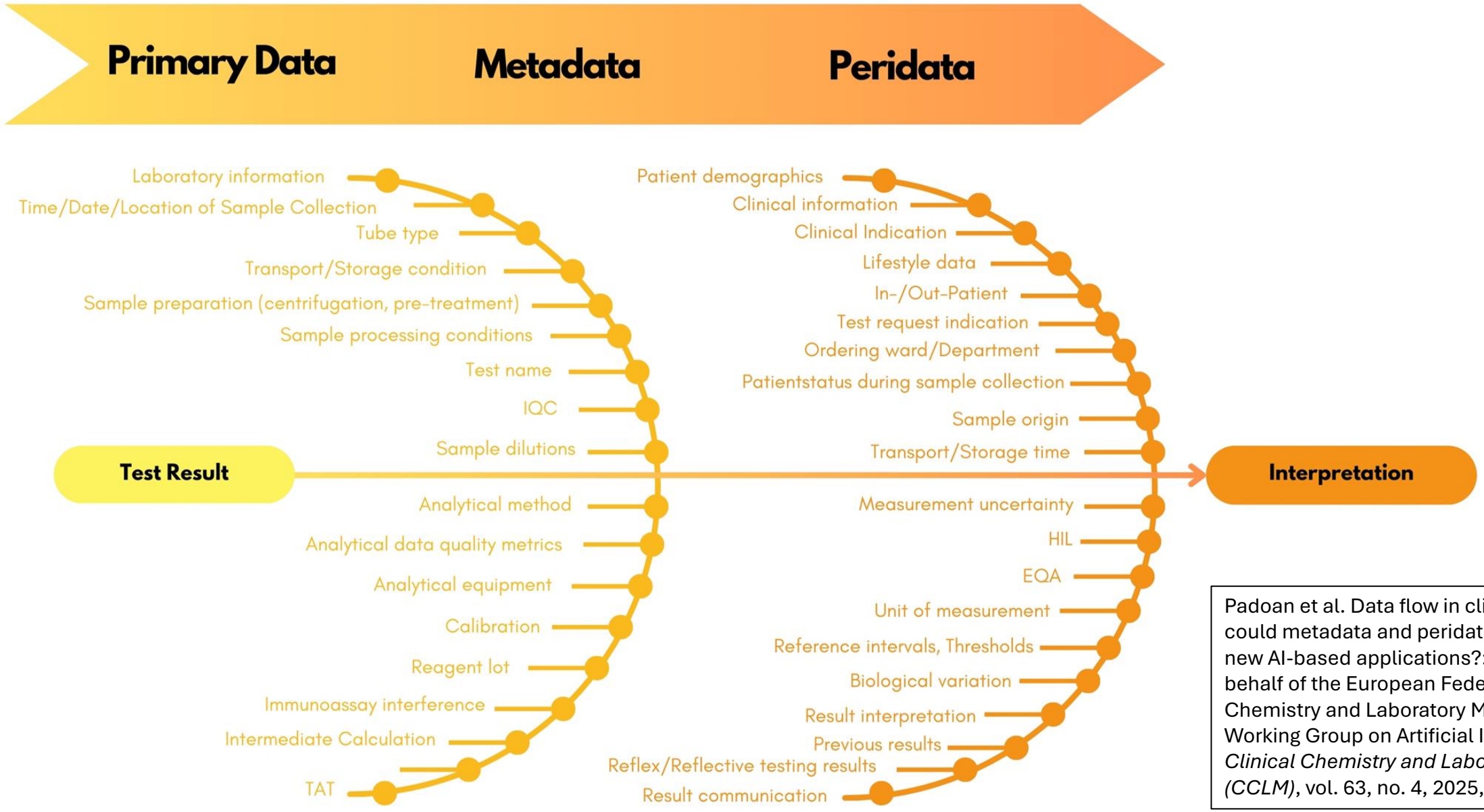
Using data to understand physio-pathology, find answers, and help solve issues

Digital (histo-)pathology

Dataflow and possibilities



Test result database vs data warehouse



Padoan et al. Data flow in clinical laboratories: could metadata and peridata bridge the gap to new AI-based applications?: An investigation on behalf of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group on Artificial Intelligence (WG-AI). *Clinical Chemistry and Laboratory Medicine (CCLM)*, vol. 63, no. 4, 2025, pp. 684-691.

Microsoft Azure SQL Database: options to query

- Power BI

- Azure Portal Query Editor

- R/ R Studio
- Python

- Visual Studio (VS) code + MSSQL extension
- SSMS (SQL Server Management Studio)

A few examples of

- *Dashboards*
- *Detection and mitigation of disparities*
- *Expected insights from big data*
- *Other than expected insights from big data*

Calcium patient mean/ bias monitoring

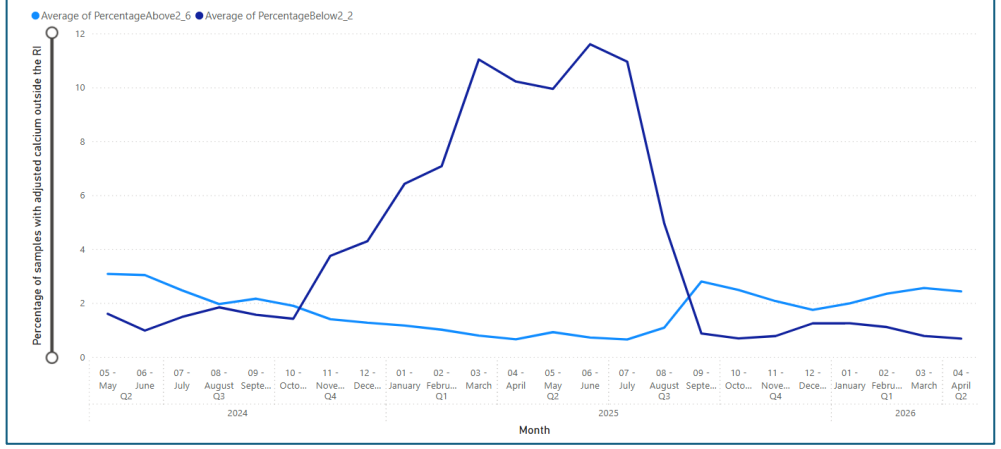
- Simple
- On ‘live’ database – ‘refresh’
- Analytical disparity/ assay provider related disparity
- *Additional insight:* likely to be calibrator issue rather than the assay

Serum albumin, total calcium and adjusted calcium daily averages of primary care samples

Albumin

Adjusted calcium

Percentage of samples from primary care locations with serum adjusted calcium <2.2 mmol/L and >2.6 mmol/L



Additional insight: likely to be calibrator issue rather than the assay

Cavalier et al on behalf of the European Federation of Clinical Chemistry and Laboratory Medicine Committee: Chronic Kidney Diseases and the Joint International Osteoporosis Foundation Working Group and International Federation of Clinical Chemistry and Laboratory Medicine Committee on Bone metabolism,. "Albumin-adjusted ("corrected") calcium should no longer be reported: a position statement from the Joint IOF Working Group and IFCC Committee on Bone Metabolism and EFLM Committee on CKD" *Clinical Chemistry and Laboratory Medicine (CCLM)*. https://doi.org/10.1515/cclm-2026-0545

Test count dashboard

- Utilisation
- Demand
- Differential requesting patterns
- New insights
- Non-obvious opportunities e.g. serum amylase

Test Count Dashboard

295K	11K	33K	1	0.05
Total Tests	Tests This Month	Tests YTD	Unique Test Codes	MoM % Change

Test Date
21/05/2024
31/03/2026

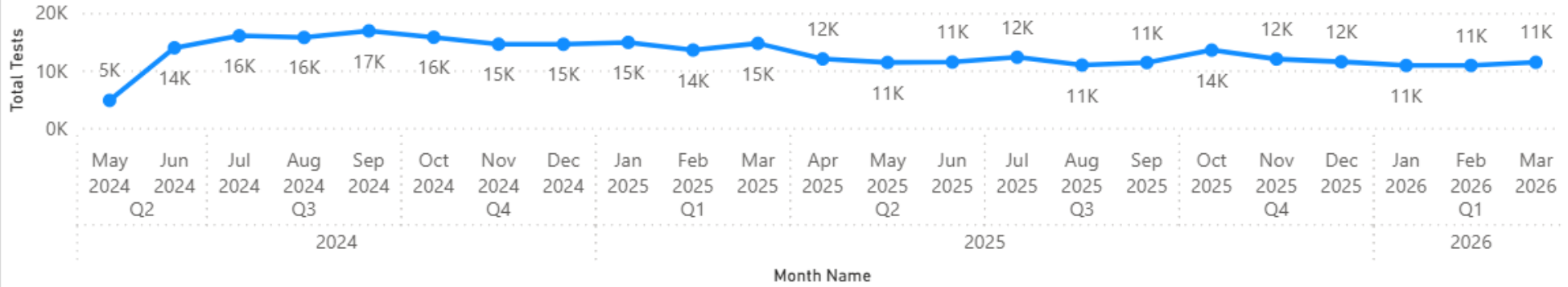
Broad Area
All

Requesting Location
All

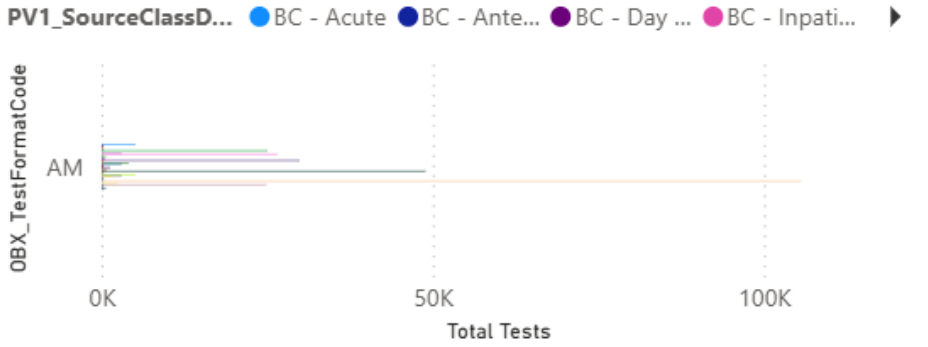
Test Code
AM

Test Profile Name
All

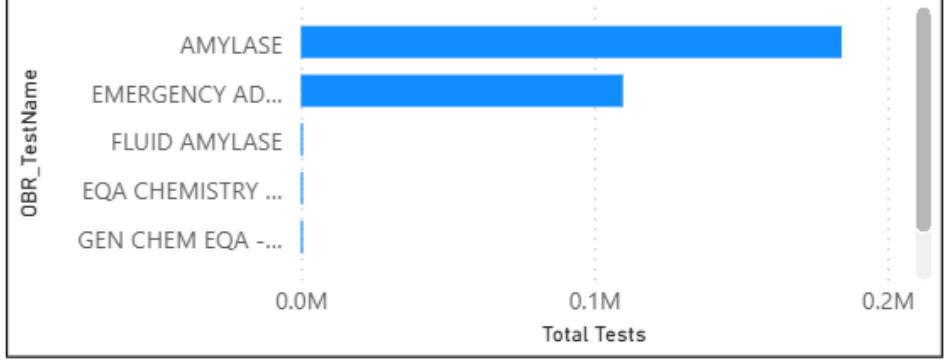
Test Volume Over Time



Top 20 Test Codes by Volume



Top 20 Test Profiles by Volume



Test Demand by Requesting Location

Test volume heatmap

OBX_TestFormatCode	2024	2025	2026	**Total**
AM	112190	149513	33130	**294833**
Total	**112190**	**149513**	**33130**	**294833**

Test Count Dashboard

106K	3K	8K	1	0.01
Total Tests	Tests This Month	Tests YTD	Unique Test Codes	MoM % Change

Test Date
21/05/2024 — 31/03/2026

Broad Area
All

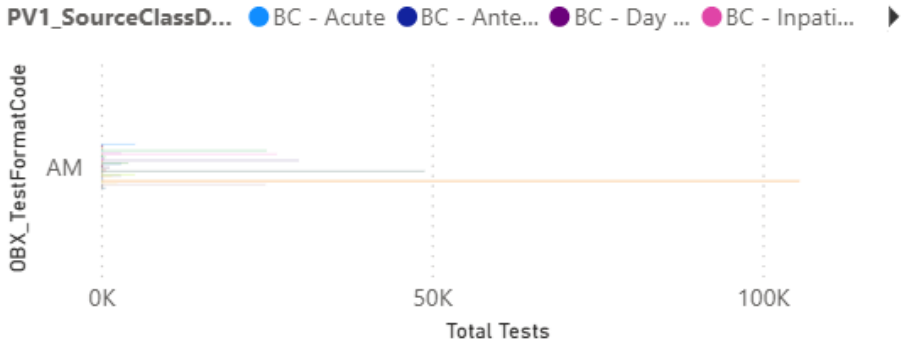
Requesting Location
All

Test Code
AM

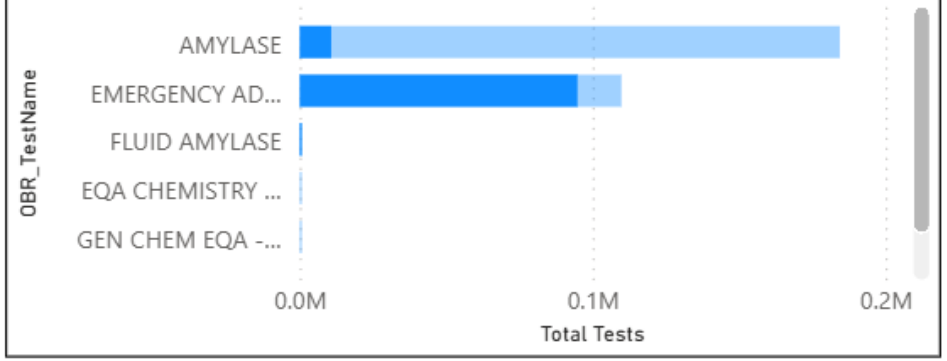
Test Profile Name
All

Test Volume Over Time

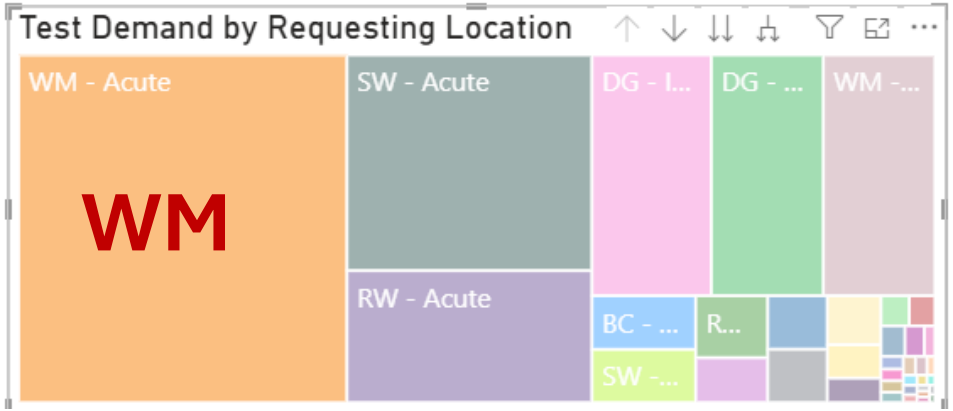
Top 20 Test Codes by Volume



Top 20 Test Profiles by Volume



Test Demand by Requesting Location



Test volume heatmap

OBX_TestFormatCode	2024	2025	2026	**Total**
AM	49108	48244	8203	**105555**
Total	**49108**	**48244**	**8203**	**105555**

The ideal reference population!!!

But for what???

- *Individuals without the disease*

But

- *Tested in the same circumstances as individuals with the disease.*
- *And the disease in question was one of the possibilities.*

Some merit in keeping serum lipase as the first line test

Ethnic differences in serum amylase

- Amylase isozymes: salivary (S-type) and pancreatic (P-type) coded by the AMY1 and AMY2 genes.
- Variability in copy number between populations - specifically of AMY1.
- This may reflect evolutionary adaptation to starch contents in the diet of different populations.
- Tsanios et al (1982) measured salivary amylase activity in 92 well people (split into 3 ethnic groups: white British, Indian and West Indian) and noted that mean total amylase activity was highest in the West Indian subgroup followed by the Indian subgroup.
- Since this paper in 1982, there has been minimal work focussing on ethnicity specific amylase other than one of the CALIPER studies mentioning the ethnicity related differences and the need for ethnicity-specific RIs.

Methods

- The data below was collected for all amylase requests from multiple hospital sites from 01/06/2019 to 30/09/2025:
  - Age on the day of sample collection
  - Sex
  - eGFR – calculated using the CKD-EPI formula without ethnicity adjustment (as per NICE)
  - Known diabetes
  - HbA1c
  - Ethnicity
- The dataset was split up into 2 groups: a derivation cohort (01/06/2019 to 31/05/2025) and a verification cohort (01/06/2025 to 30/09/2025)
- Multivariable linear regression was used to model serum amylase as a continuous outcome .
  - Ethnicity, diabetes mellitus, sex and assay method were used as categorical predictors.
  - Spline terms were used for eGFR and age as continuous predictors for serum amylase.
  - Individual predictor contribution to amylase variation was calculated using the relaimpo package in R.
- Reference intervals were derived using refineR and then verified on the verification dataset.

Clinical Importance

If the laboratory's current reference interval (28 – 100 U/L) is applied to all ethnicities:

Ethnicity group	Reference interval derivation dataset		
	n	% <LRL	% >URL
White	114063	10.2	5.8
Asian	29640	2.5	13.4
Black	8882	2.0	22.4

In the context of any presentation of abdominal pain this could lead to exhaustive and unnecessary pancreatic investigations or misdiagnosis.

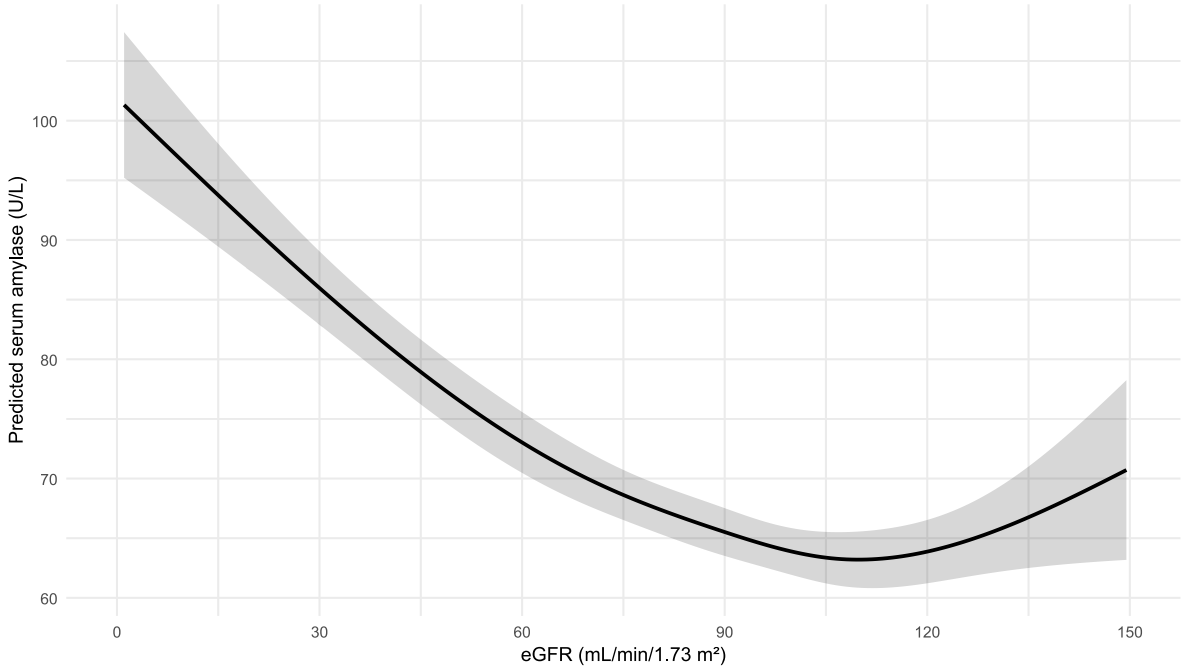
Kalaria T, More AM. Unpublished data.

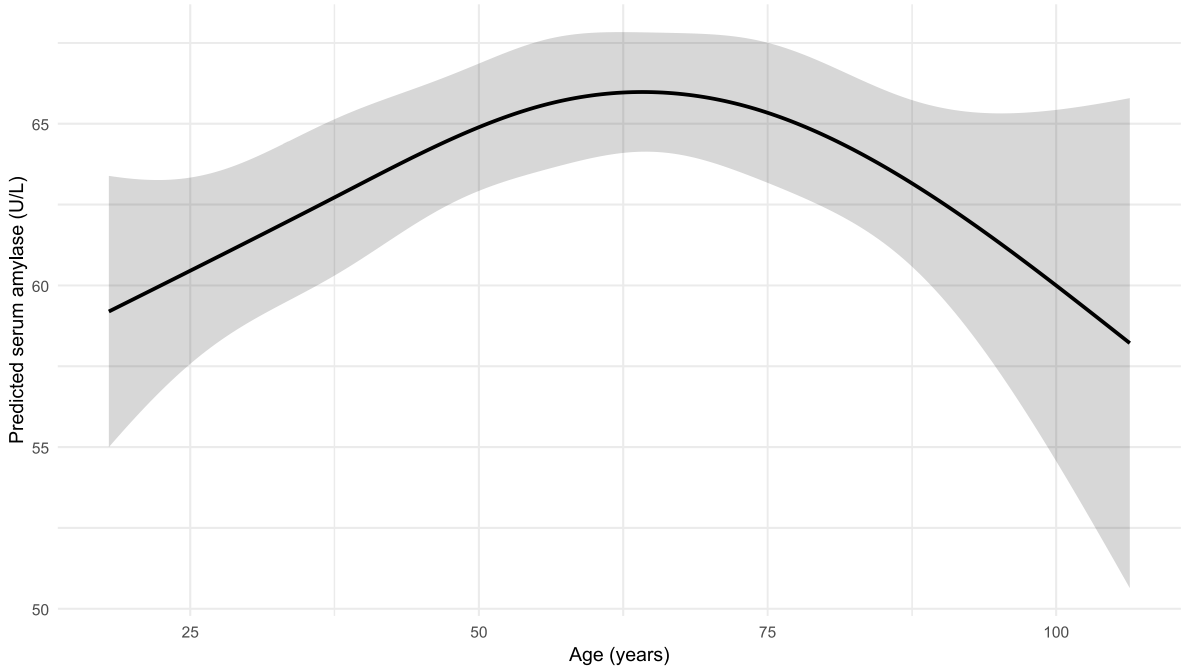
Results: Factors Affecting Serum Amylase Variation

- Data from 176,555 individuals were included
- Ethnicity was the largest contributor to explained amylase variation (57% of the model's total explained variance)
- eGFR was the second largest contributor to amylase variation – it was inversely associated with serum amylase – accounting for 30% of the model's total explained variance ($p<0.001$)
- Together – ethnicity and eGFR accounted for 87% of the total explained variance of the model
- Age was the third most important predictor – 7% of the model's total explained variance
  - There was an inverse U-shaped relationship seen between age and serum amylase levels
  - When adjusted for predictors including eGFR, serum amylase increased up to the 6th decade and then decreased
- Abbott serum amylase results were on average 3.2 U/L higher than Roche results.

Relationship of serum amylase with (a) eGFR and (b) age from spline adjusted multiple variable model. The plots show fitted mean predicted serum amylase as central line with 95% confidence interval of mean as shaded band.

Additional insight

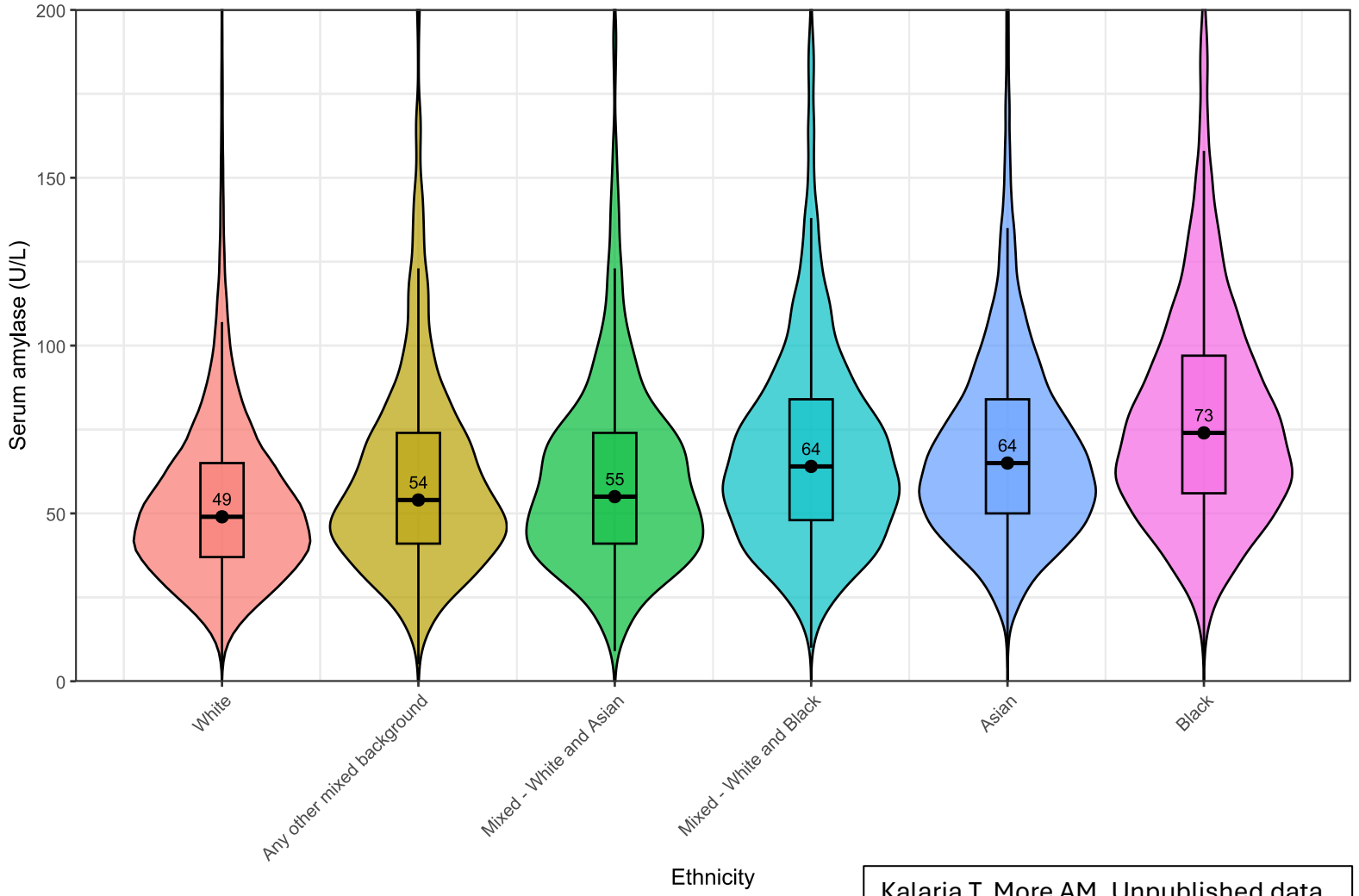




Kalaria T, More AM. Unpublished data.

Distribution of Serum Amylase by Ethnicity

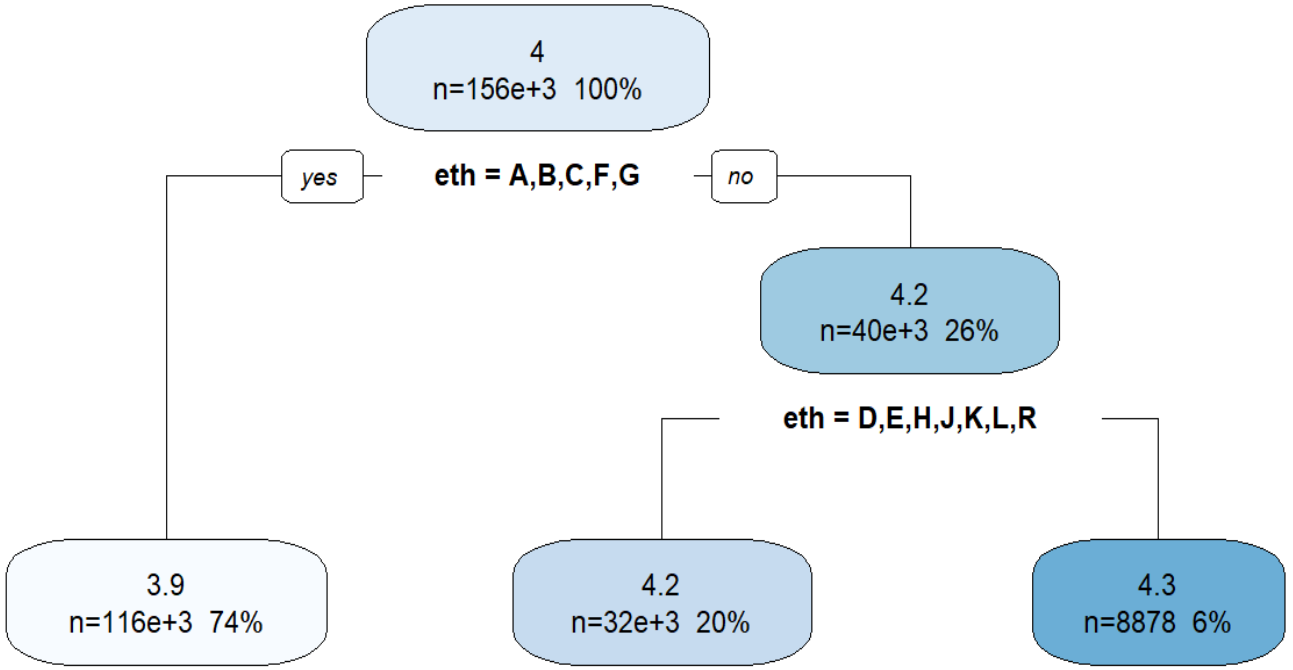
- Individual ethnicity subgroups from the ethnicity code data were grouped into 3 broad ethnic groups: White, Asian and Black. Mixed ethnicities were grouped.
- Amylase distributions in individuals of mixed ethnicities were approximately half-way between those of the two parent ethnicities.



Kalaria T, More AM. Unpublished data.

Serum amylase ethnicity partition analysis

Serum amylase results of the derivation cohort (n = 156380) were partitioned by UK national ethnicity codes using a classification and regression tree (CART) using anova method in package rpart



Kalaria T, More AM. Unpublished data.

Ethnicity Specific Reference Intervals

Median serum amylase was 1.3 and 1.5 times higher in Asian and Black individuals compared to those of White ethnicities

Group	Number of individuals	Lower reference limit# (U/L)	Median# (IU/L)	Upper reference limit# (U/L)
Laboratory's current reference intervals				
Age 1 year to <18 years*	-	25	-	101
Age ≥18 years^	-	28	-	100
Derived ethnicity-specific reference intervals (age ≥7 year and eGFR ≥60 mL/min/1.73m^2)				
White	114063	22 (18 – 23)	49 (47 – 50)	103 (90 – 107)
Asian	29640	30 (27 – 31)	64 (61 – 64)	128 (110 – 133)
Black	8882	32 (28 – 35)	73 (69 – 74)	155 (126 – 161)

The point estimates are the median of 1000 bootstrap iterations. The numbers in the brackets indicate 95% confidence intervals (CI) of percentiles.
* Source: CALIPER Paediatric Reference Interval Database
^ Source: Manufacturer provided reference interval

Kalaria T, More AM. Unpublished data.

Verification of RIs

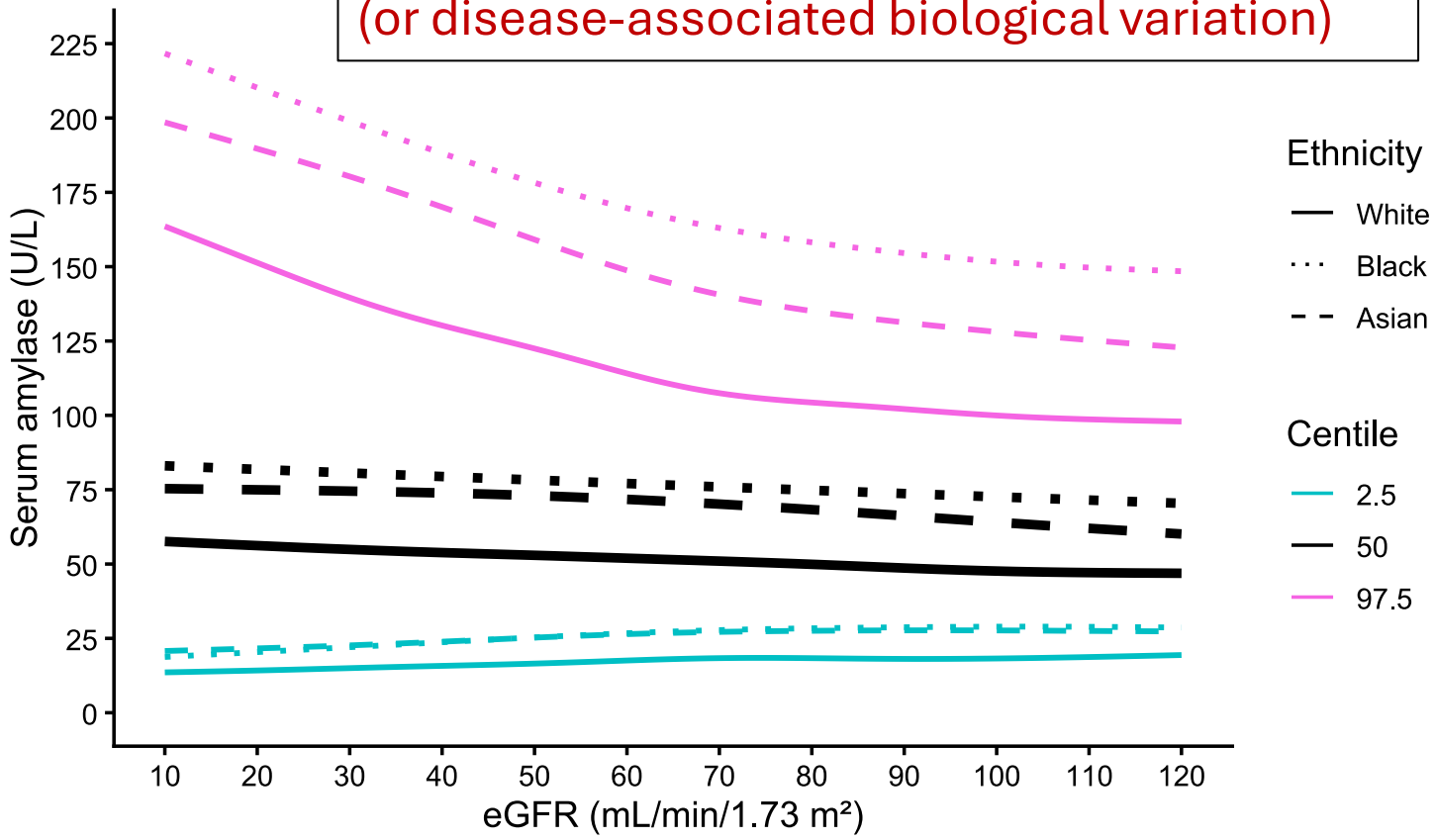
Ethnicity group	Reference interval derivation dataset			Verification dataset		
	n	% <LRL	% >URL	n	% <LRL	% >URL
Laboratory's current ethnicity non-specific reference intervals						
White	114063	10.2	5.8	6684	10.3	5.0
Asian	29640	2.5	13.4	2843	2.6	11.2
Black	8882	2.0	22.4	992	1.7	21.7
Applying ethnicity-specific reference intervals derived in this study						
White	114063	4.3	5.3	6684	4.2	4.6
Asian	29640	3.4	5.6	2843	3.6	5.0
Black	8882	3.5	4.4	992	3.3	3.2

Kalaria T, More AM. Unpublished data.

Serum amylase in individuals with decreased renal function

Additional insight
Comorbidity-related interpretive confounding
(or disease-associated biological variation)

- A total of 22,770 individuals had eGFR between 30 to 59 mL/min/1.73 m^2 (19,336 White, 2,251 Asian and 1,183 Black) and 6447 individuals had eGFR < 30 mL/min/1.73 m^2 (5,209 White, 836 Asian and 402 Black).
- Insufficient to derive robust partitioned RIs.
- Smoothened serum amylase 2.5th, 50th and 97.5th percentile curves for eGFR range may aid interpretation of serum amylase results in individuals with chronic kidney disease.

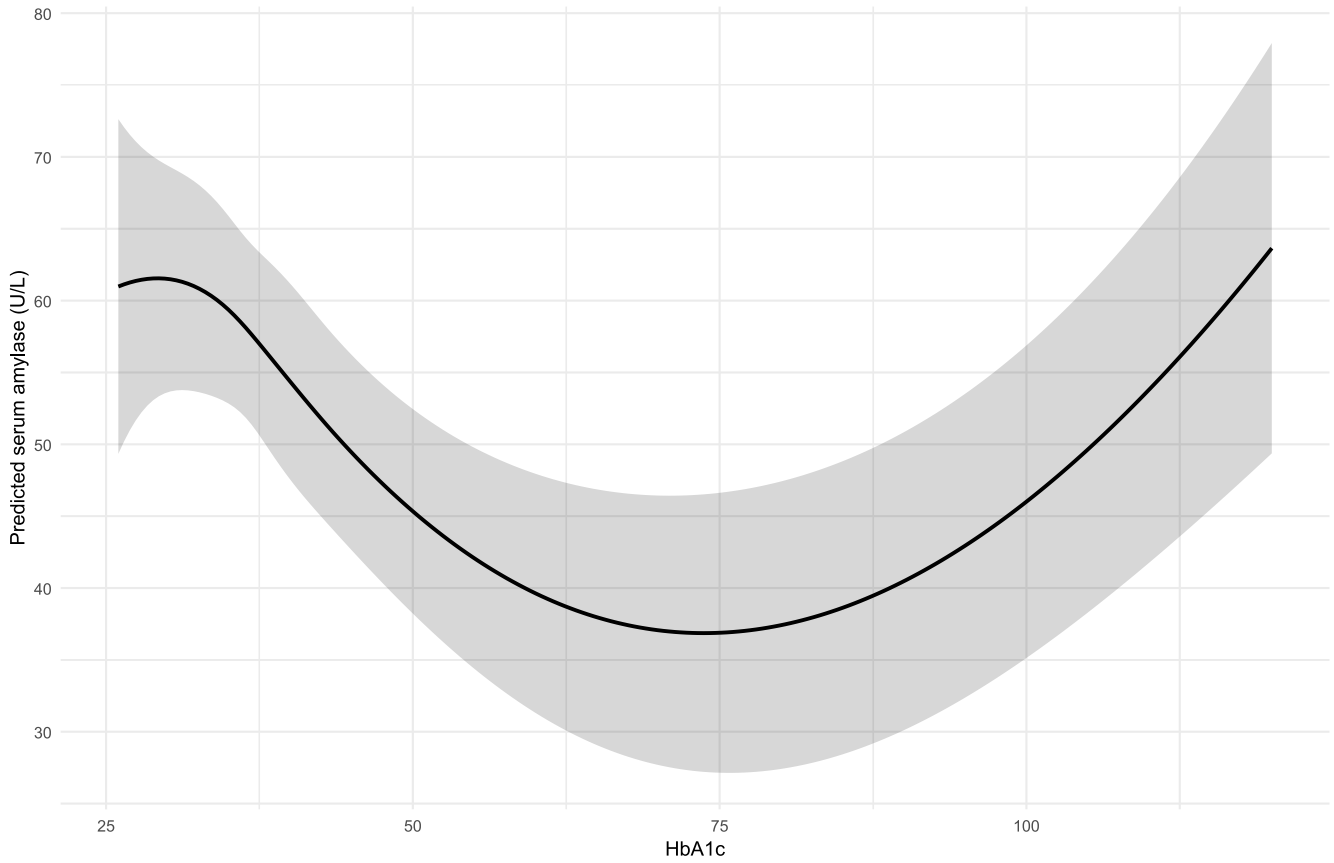


Kalaria T, More AM. Unpublished data.

Serum amylase in diabetics

Additional insight

- Individuals with diabetes mellitus had lower serum amylase levels by 6.1 U/L on average compared to non-diabetics in multiple variable model ($p < 0.001$, < 0.01% of total variance).
- Of 176,555 individuals, 7619 had HbA1c result in the same set of bloods. For these 7619 individuals with available concurrent HbA1c result, a separate multivariable linear regression model using ethnicity, sex and assay method as categorical predictors and spline terms for HbA1c, eGFR and age as continuous predictors for serum amylase demonstrated a non-linear U-shapped relationship of serum amylase with HbA1c (ANOVA $p<0.001$ for spline vs linear model fit).



Kalaria T, More AM. Unpublished data.

Ethnic differences in CK

- *Community paediatrician doing developmental delay clinic*
- *Rheumatologist running a muscle biopsy service*

Sex- and ethnicity-specific CK values from US population data of the National Health and Nutrition Examination Survey (NHANES) 2011–2014 are available as a guide to reference intervals.

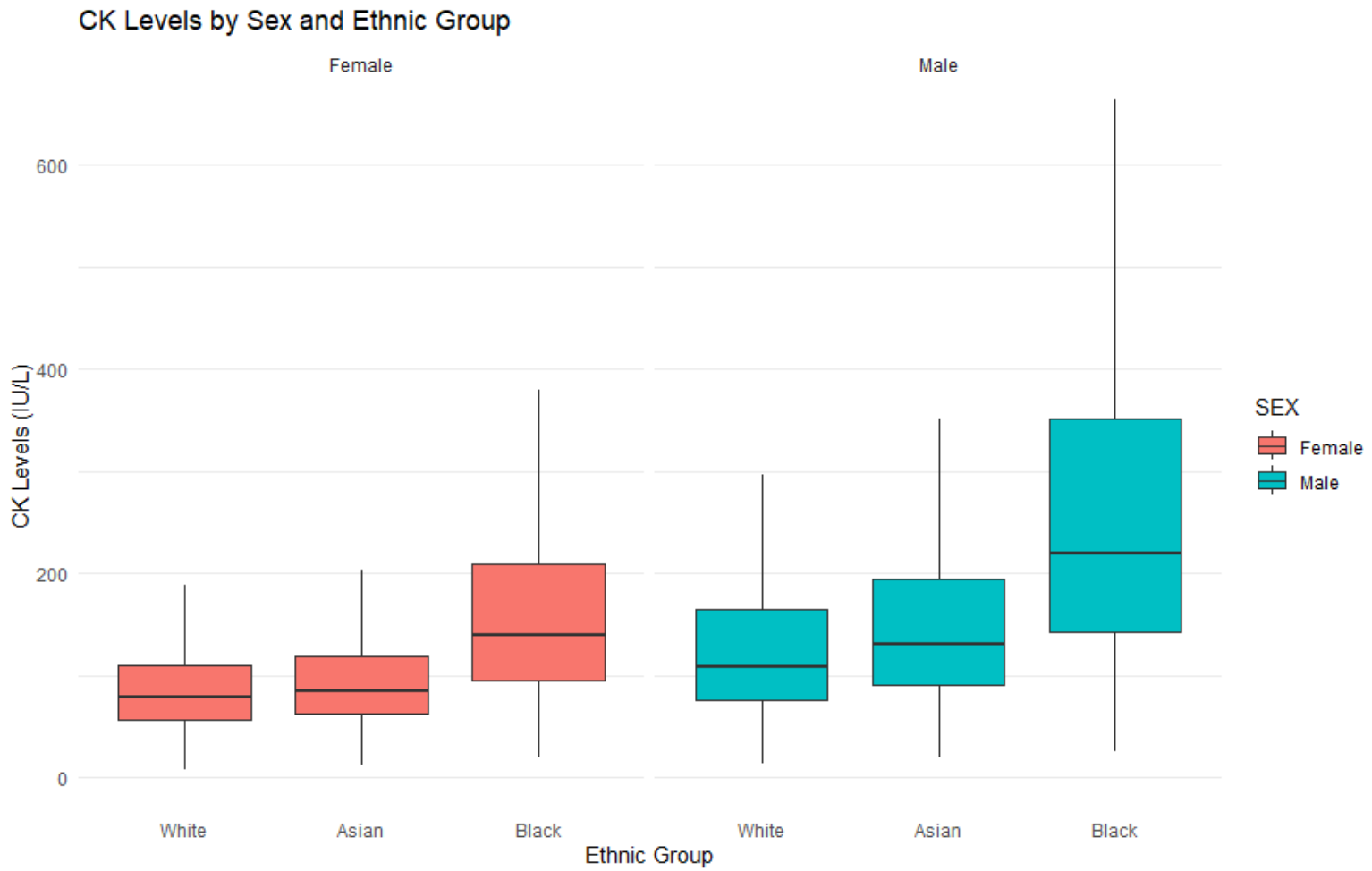
Datasets

Derivation

- Deidentified CK results, age on the day of sample collection, sex and ethnicity were retrieved for all primary care CK requests from 01/01/2008 to 30/04/2024 (n = 59,644)

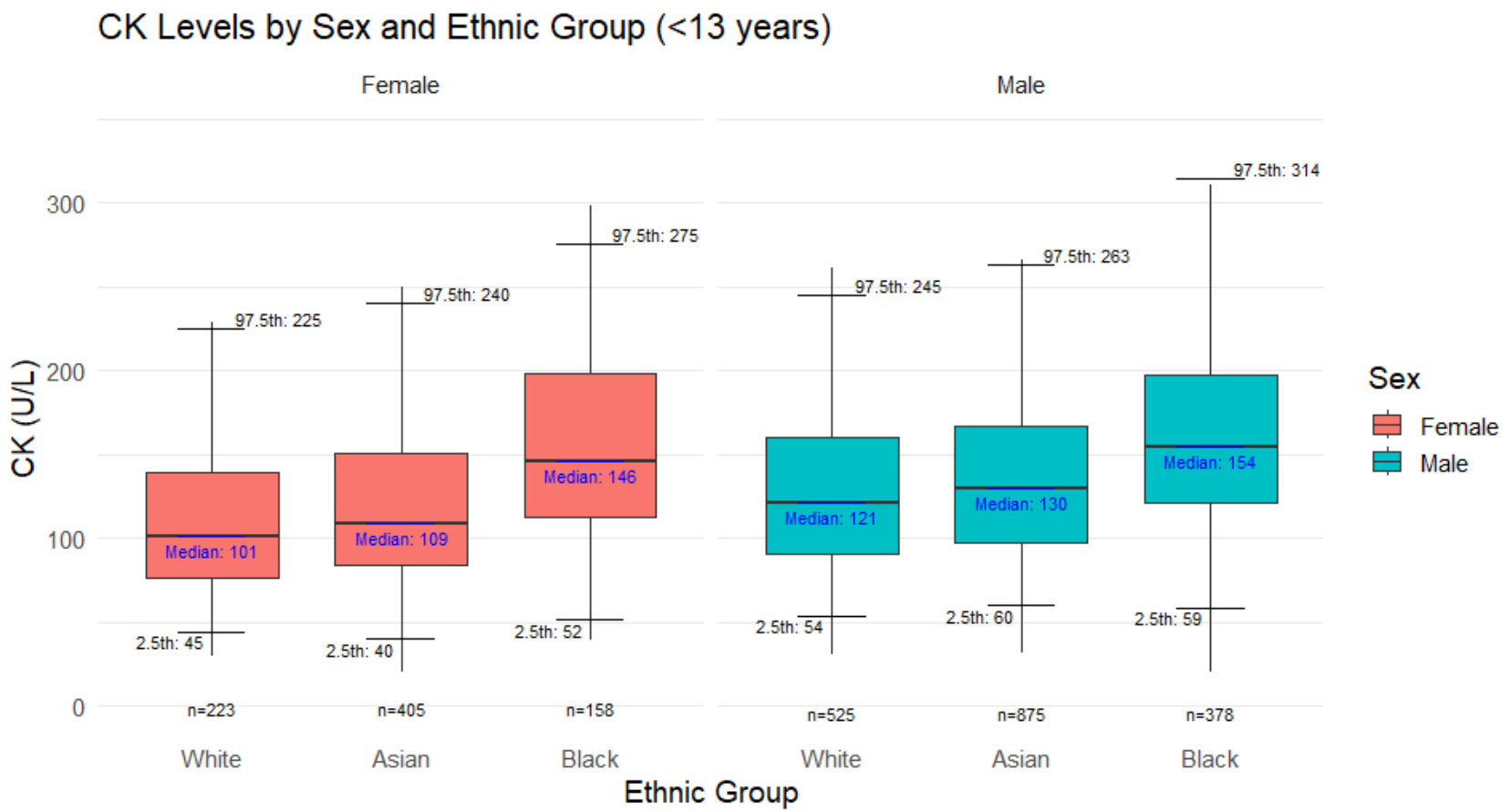
Verification

- Primary care CK results between 01/05/2024 and 31/10/2024 from the Black Country
- Primary care CK results between 26/01/2023 and 22/10/2024 from the South-West region of London



CK distributions in females and males of White, Asian and Black ethnicities in individuals ≥13 years of age

Kalaria T, Griffiths RL. Unpublished data.



Creatine kinase (CK, U/L) in female and male children <13 years of White, Asian and Black ethnicities. Boxplots are plotted after removing outliers within each Sex×Ethnicity subgroup using Tukey's rule (values <Q1−1.5×IQR or >Q3+1.5×IQR). Horizontal ticks mark the 2.5th and 97.5th percentiles of the trimmed distributions. Counts under the X-axis labels are post-exclusion numbers.

Kalaria T, Griffiths RL. Unpublished data.

Sex- and ethnicity-specific serum CK reference intervals for individuals aged 13 years and older. UK Pathology Harmony CK reference intervals, for White Caucasians only, are included for comparison.

Group	Number of individuals	CK lower reference limit# (IU/L)	Median# CK (IU/L)	CK upper reference limit# (IU/L)
Female				
UK Pathology Harmony	-	25	-	200
White	18978	29 (27 - 32)	75 (71 - 77)	170 (142 - 188)
Asian	10894	35 (32 - 37)	82 (76 - 85)	188 (141 - 206)
Black	4007	46 (41 - 49)	137 (133 - 140)	389 (345 - 422)
Male				
UK Pathology Harmony	-	40	-	320
White	13927	35 (34 - 37)	106 (104 - 108)	314 (294 - 333)
Asian	7927	44 (42 - 46)	125 (122 - 128)	357 (329 - 386)
Black	2363	58 (50- 64)	218 (210 - 227)	757 (660 - 842)

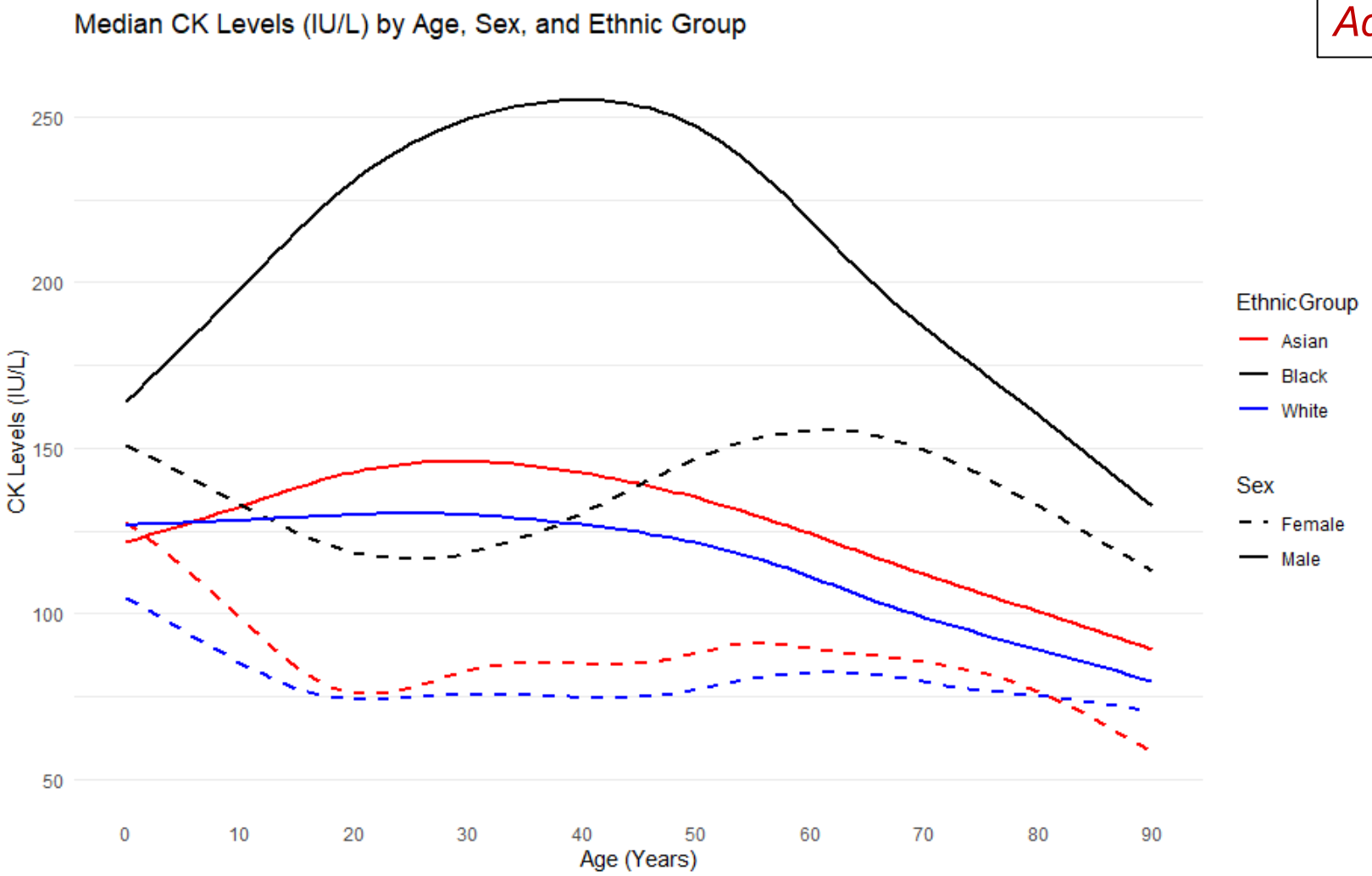
The point estimates are the median of 1000 bootstrap iterations and numbers in the brackets indicate 95% confidence intervals (CI).

Kalaria T, Griffiths RL. Unpublished data.

Assessment of derived sex- and ethnicity-specific CK reference intervals to compare the proportion of results outside the reference intervals for individuals aged 13 years and over in the dataset from which the reference intervals are derived and two additional datasets.

Group	West Midlands 1 (dataset from which reference intervals are derived)				West Midlands 2 (subsequent data from the same geography and laboratories)			South-West London		
	n	% <LRL	% >URL	% > 5xURL	n	% <LRL	% >URL	n	% <LRL	% >URL
Applying sex- and ethnicity-specific reference intervals derived in this study										
Female										
White	18978	2.3%	8.0%	0.26%	1229	3.1%	8.1%	709	2.7%	10.2%
Asian	10894	2.7%	6.7%	0.19%	489	4.5%	7.4%	287	4.2%	7.3%
Black	4007	2.4%	6.5%	0.35%	155	2.6%	9.7%	337	3.0%	6.2%
Male										
White	13927	2.5%	6.0%	0.45%	805	3.7%	7.8%	511	1.2%	7.6%
Asian	7927	2.3%	7.2%	0.63%	327	3.1%	6.7%	249	1.6%	8.0%
Black	2363	1.6%	6.6%	0.68%	70	1.4%	5.7%	183	1.6%	7.1%
If sex specific but ethnicity non-specific UK Pathology Harmony reference intervals are to be applied to all ethnicities										
Female										
White	18982	1.2%	5.1%	0.25%	1229	1.6%	5.7%	709	2.0%	6.2%
Asian	11006	0.6%	5.7%	0.17%	489	1.2%	6.5%	287	2.1%	4.9%
Black	4442	0.1%	28.1%	0.80%	155	0.7%	22.6%	337	0.3%	28.2%
Male										
White	13927	3.9%	5.8%	0.45%	805	4.5%	7.7%	511	2.4%	7.4%
Asian	7997	1.6%	9.0%	0.75%	327	2.1%	9.5%	249	1.6%	8.8%
Black	2594	0.2%	30.3%	1.82%	70	0.0%	24.3%	183	0.6%	29.0%

Additional insight

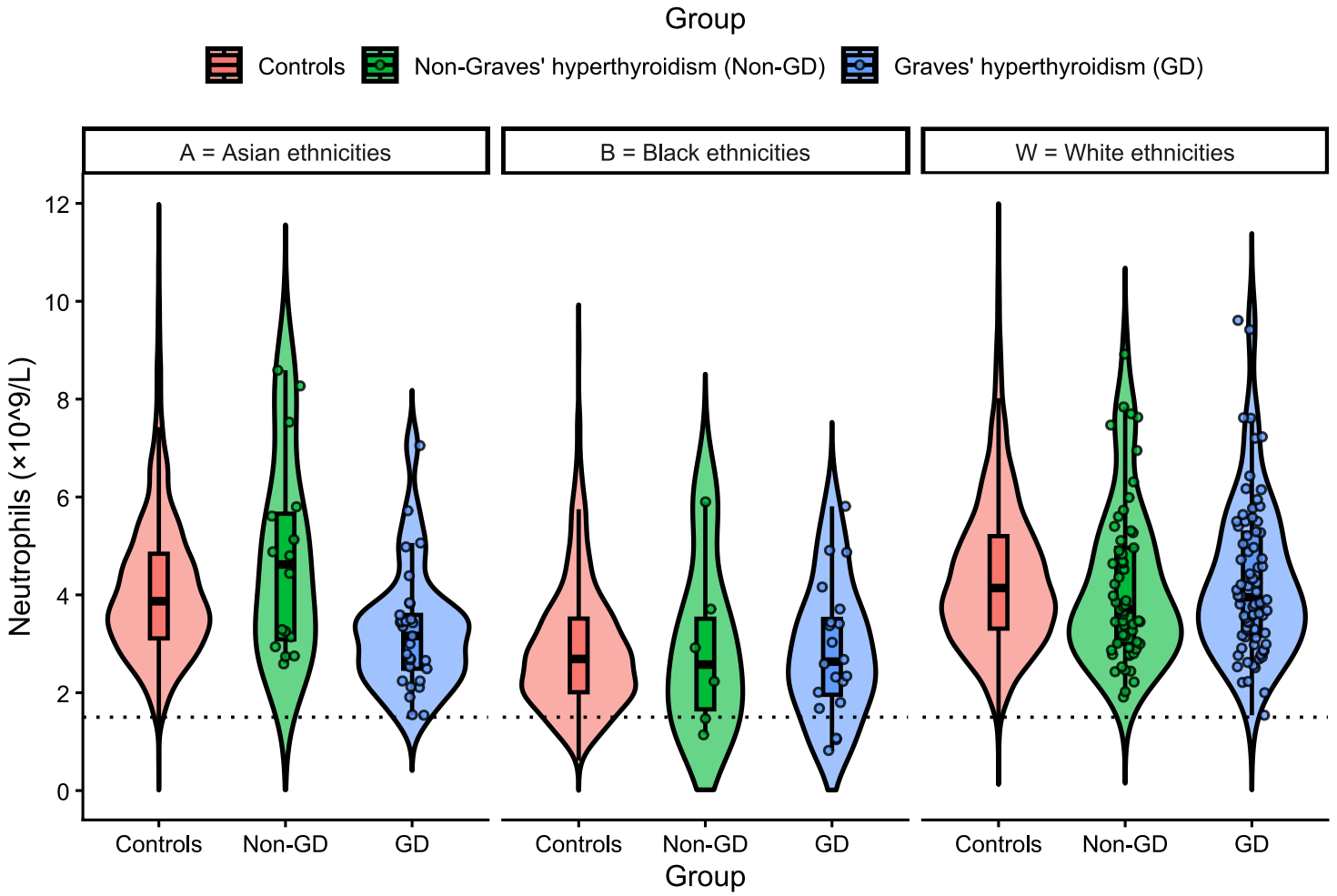


Median CK levels by age for sex and ethnicity groups

Kalaria T, Griffiths RL. Unpublished data.

Is it safe to start antithyroid medications in this ‘neutropenic’ newly diagnosed hyperthyroid individual?

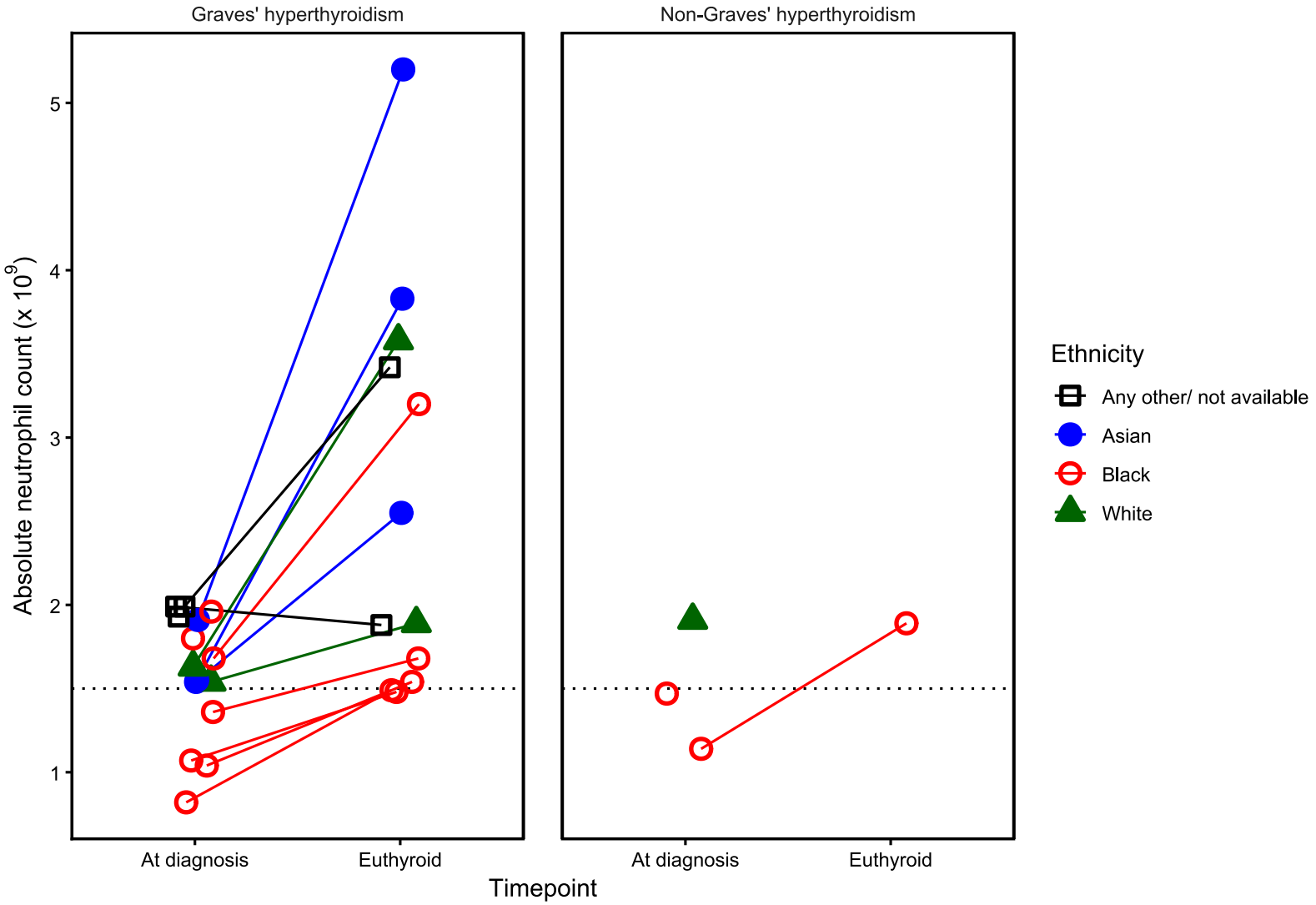
A retrospective cross-sectional analysis with an ethnicity-matched control cohort examining the relationship between free thyroxine (FT4), thyroid-stimulating hormone receptor antibody (TRAb) and absolute neutrophil count (ANC) in **newly diagnosed hyperthyroidism**, and assessing the influence of ethnicity on ANC.



Distribution of absolute neutrophil count by thyroid disease status and ethnicity:

Violin plots show neutrophil counts in controls (n=9056), non-Graves’ (non-GD, n=85) hyperthyroidism and Graves’ hyperthyroidism (GD, n=152) across Asian, Black and White ethnic groups. Boxplots within each violin represent the median and interquartile range. Individual data points for hyperthyroidism patients are overlaid, but data points for the control group are not shown because of the large sample size. The dotted horizontal line represents 1.5 x10^9/L threshold for neutropenia.

Kalaria T, More AM. Clinical Endocrinology (ahead of print)

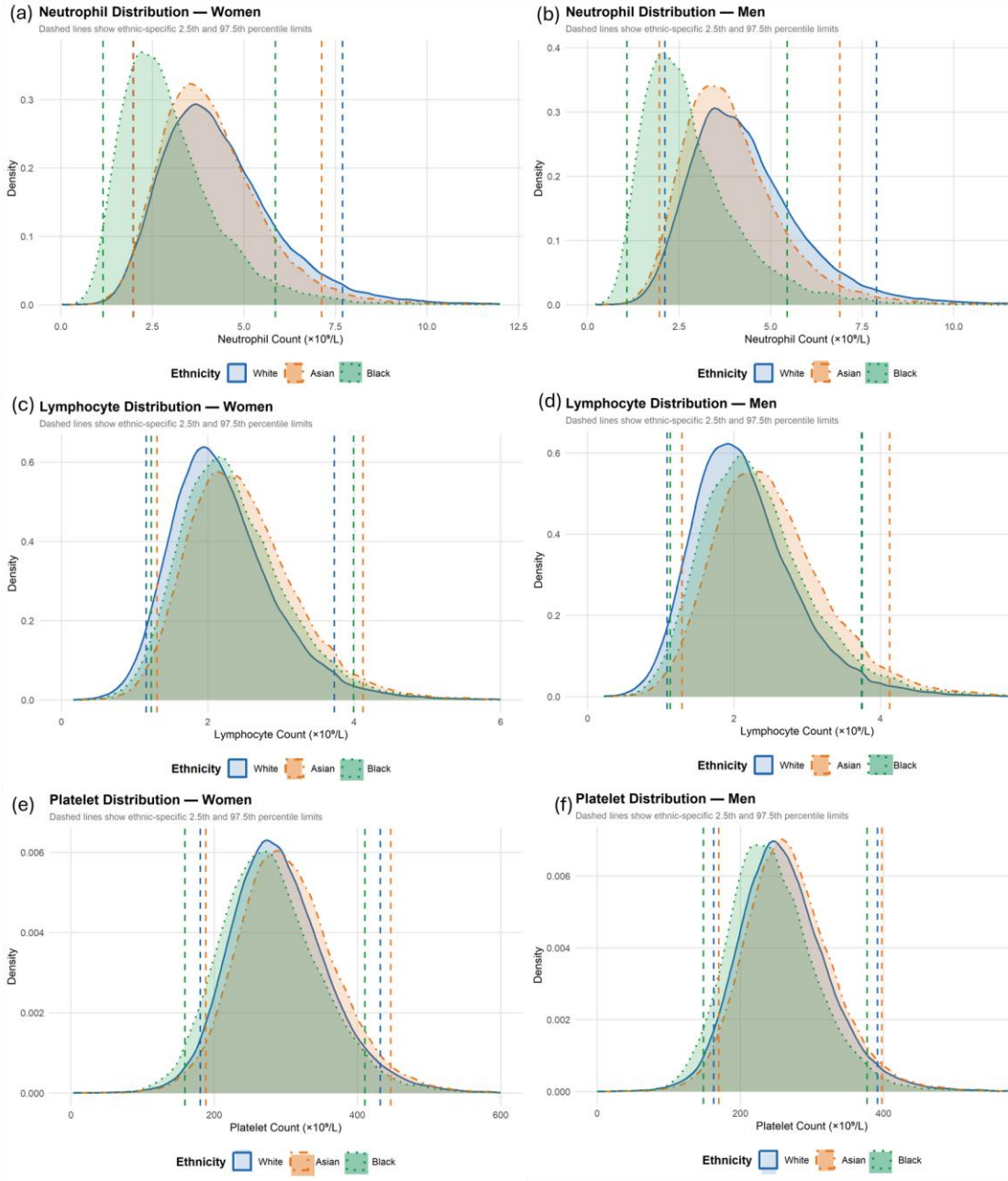


Absolute neutrophil counts (ANC) in Graves' and non-Graves' hyperthyroidism at diagnosis and after restoration of euthyroid status for 18 individuals with low ANC < 2.0 x10^9/L at the time of diagnosis. The horizontal dotted line represents the neutropenia threshold of 1.5 ×10^9/L.

Kalaria T, More AM. Clinical Endocrinology (ahead of print)

Ethnic differences in ANC

Ethnic Group	n	Reference Interval (2.5th–97.5th)	2.5th %ile (95% CI)	50th %ile (95% CI)	97.5th %ile (95% CI)
Laboratory's ethnicity non-specific	-	2.0–7.5	-	-	-
White	207,712	2.1–8.0	2.07 (2.00-2.11)	4.09 (4.05-4.11)	7.95 (7.53-8.05)
Asian	89,342	2.0-7.1	1.97 (1.95-2.06)	3.83 (3.81-3.85)	7.05 (6.89-7.24)
Black	25,910	1.1-5.9	1.13 (1.10-1.14)	2.61 (2.52-2.66)	5.93 (5.35-6.30)



Kabbani J, Kalaria T. Yet to be published data.

Differences in neutropenia severity classification in verification dataset (n= 46,171 samples, Nov–Dec 2025) when existing ethnicity-non-specific and the derived ethnicity-specific reference intervals are used.

Ethnic group	Ethnicity-non-specific RI				Ethnicity specific RIs
	% Low neutrophil count	% Mild Neutropenia	% Moderate Neutropenia	% Severe Neutropenia	% Low neutrophil count
White Men	2.3%	0.4%	0%	0%	3.0%
Asian Men	3.5%	0.5%	0.1%	0%	2.8%
Black Men	28.9%	8.9%	2.0%	0.1%	2.4%
White Women	2.7%	0.5%	0%	0%	2.6%
Asian Women	3%	0.6%	0%	0%	2.8%
Black Women	24.4%	7.4%	1.7%	0%	2.5%

DANC

Marginated neutrophil pool

Low neutrophil count was defined as neutrophil count <2.0 $\times 10^9$/L. Neutropenia severity classifications: mild 1.0–1.5 $\times 10^9$/L , moderate 0.5–1.0 $\times 10^9$/L, and severe <0.5 $\times 10^9$/L. Values are n (%).

Kabbani J, Kalaria T. Yet to be published data.

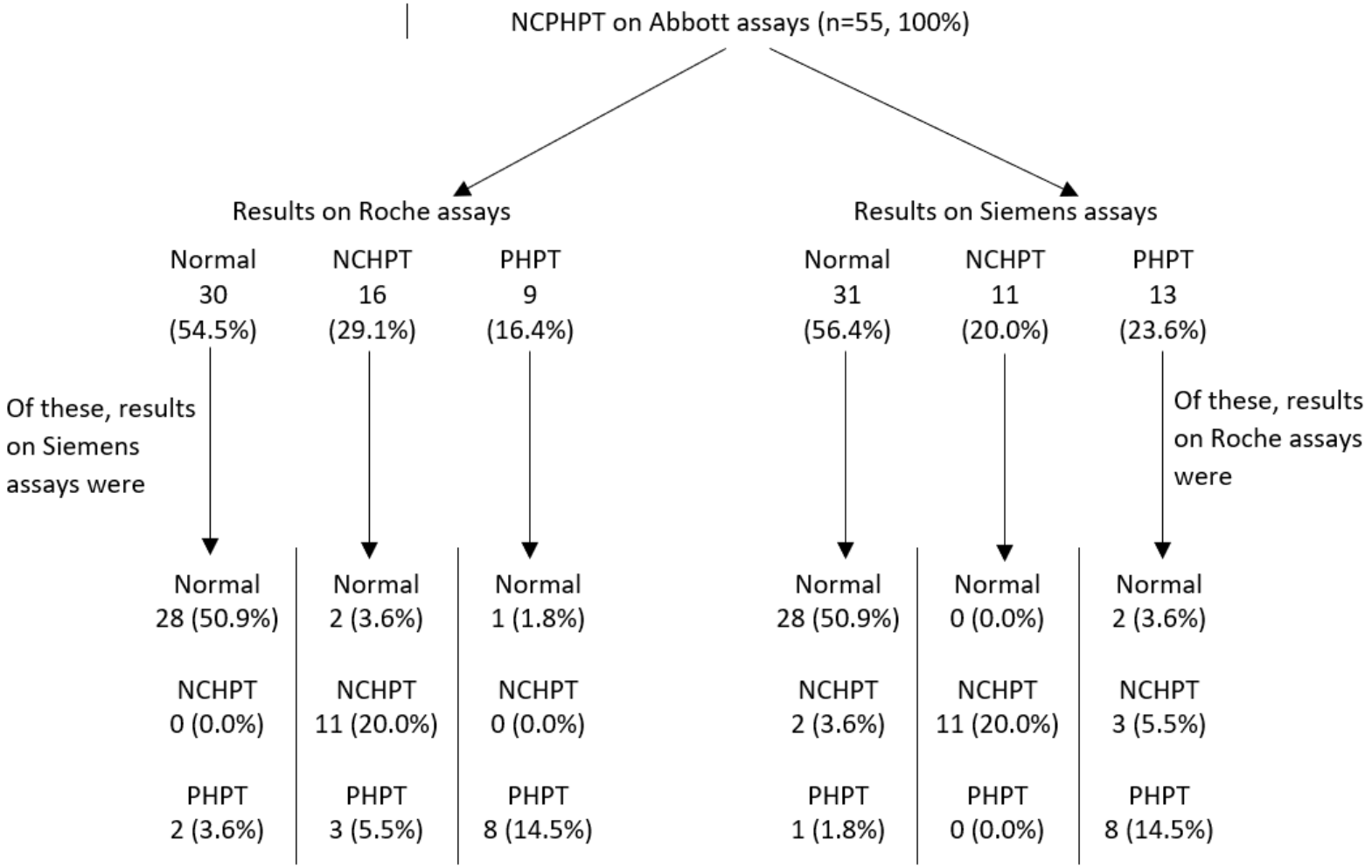
Ethnicity specific vs personalised RIs

- *For routine measurands (e.g. ANC), ethnicity-specific RIs are like a 'bridge' to personalised RIs and are likely to add value until personalised RIs become common-practice.*

  (Remember, it's *DANC*)

- *Thereafter, ethnicity-specific RIs may still add value for measurands not tested in routine bloods to have personalised RI information (e.g. CK, amylase).*

Assay related disparities in the diagnosis of NCPHPT



Identified consecutive NCPHPT at Nx

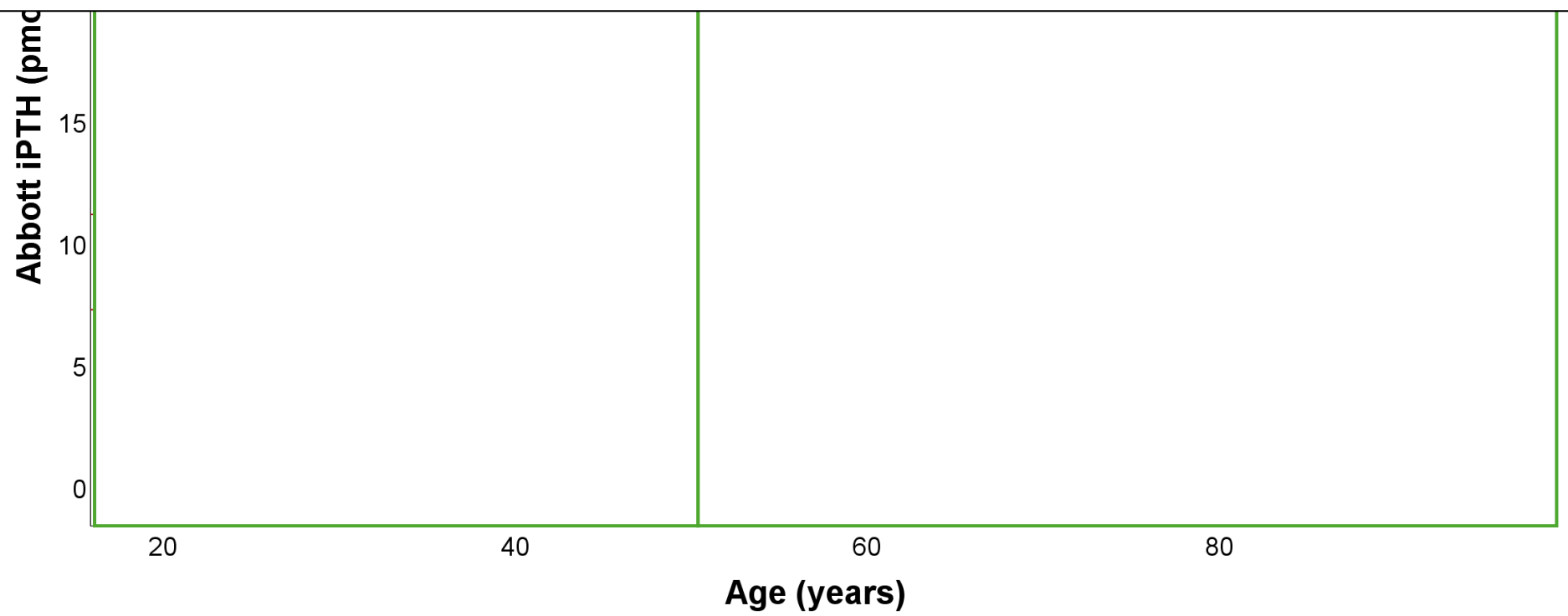
- Automated email alerts
- For 4 months
- Samples retrieved on completion of requested tests
- Divided in 3 aliquots
- Stored frozen at -80°C
- Transported frozen
- After thawing calcium, albumin and iPTH measured by Abbott Architect, Roche cobas and Siemens Atellica methods

- 55 patients, 48 females
- Age median 71 years, IQR 64-77

Kalaria T et al. Horm Metab Res. 2022 Jul;54(7):429-434.

Serum PTH results n=5935 from Sept 2015 to Nov 2022 for age ≥ 18 years, eGFR ≥60 mL/min, serum 25-hydroxyvitamin D >50 nmol/L, and serum albumin-adjusted calcium and serum phosphate (where available) within reference intervals.

Studying the assay related disparities made us aware of age-related disparities in the diagnosis of NCPHPT!!!



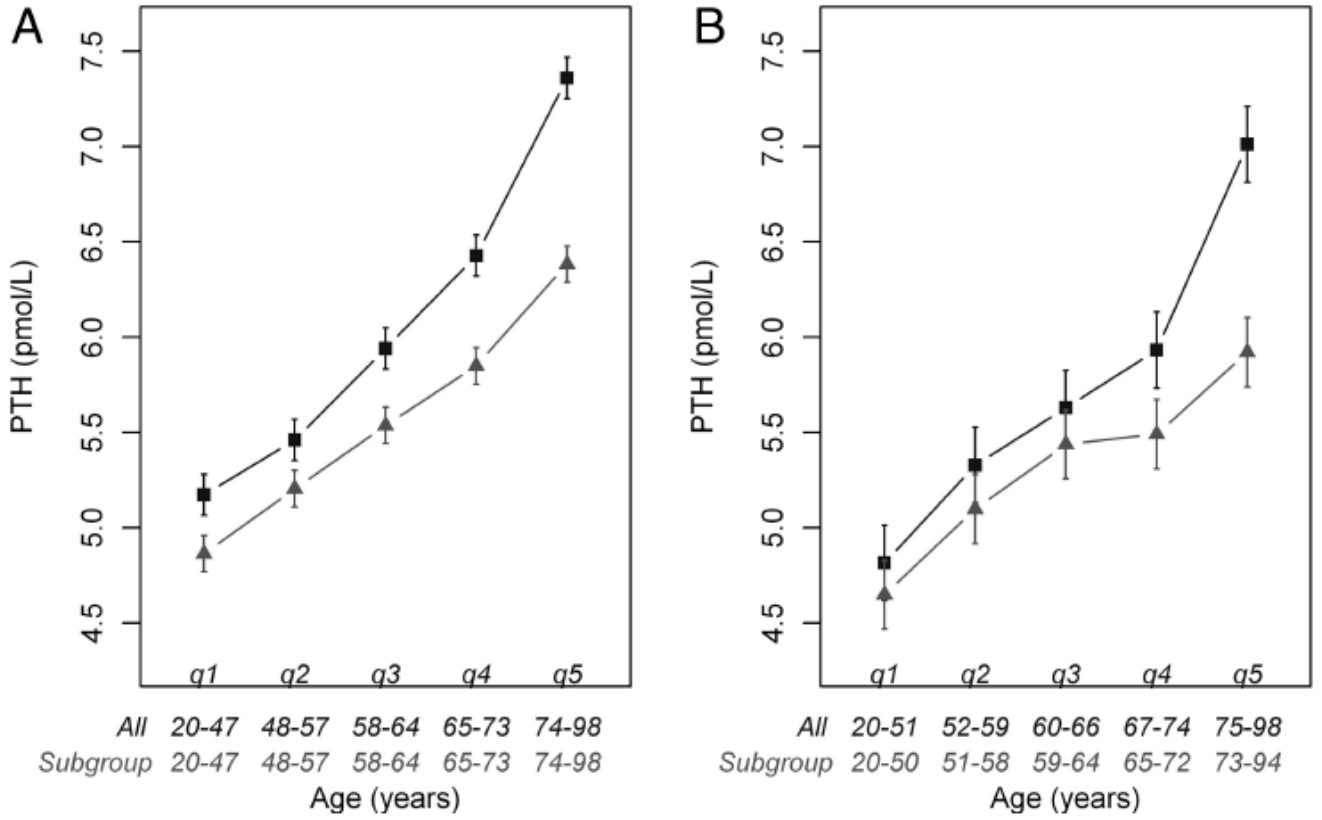
Kalaria T et al. J Endocr Soc. 2024 Jan 12;8(3):bvae004.

PTH increases with age

PTH concentration increases with age, and the increase is independent of 25-hydroxyvitamin D, renal function, ionized calcium, and phosphate levels.

In the subgroups, each 10-year increase in age was associated with a 6.1% increase in PTH (95% CI, 5.5%–6.8%; P < 0.001) in laboratory 1 and a 4.9% increase (95% CI 3.5%–6.2%; P < 0.001) in laboratory 2.

All (squares)= all results
Subgroup (triangles) = excluding eGFR <60 mL/min/1.73 m^2 or 25-hydroxyvitamin D of <50 nmol/L



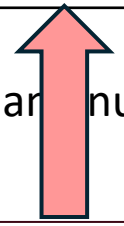
PTH analyzed by quintiles of age in laboratory 1 (A) and laboratory 2 (B). ■, all; ▲, subgroup. Error bars show mean ± 2 SEM.

Carrivick SJ et al. J Clin Endocrinol Metab. 2015;100(5):2131-2134.

Abbott serum iPTH reference intervals in adults

Group	Sample size	Lower reference limit# (pmol/L)	Median# (pmol/L)	Upper reference limit# (pmol/L)
All ages	5935	**2.0** (1.9-2.1)	4.8 (4.7-4.9)	**11.2** (10.3-12.1)
Age 18 to 45 years	712	**1.6** (1.2-1.8)	4.0 (3.7-4.2)	**8.6** (6.9-10.7)
Age 46 to 60 years	1259	**1.8** (1.6-2.0)	4.6 (4.4-4.8)	**9.5** (8.2-11.3)
Age 61 to 80 years	3181	**2.0** (1.9-2.1)	4.9 (4.7-5.0)	**11.3** (9.9-12.0)
Age 81 to 95 years	783	**2.3** (1.6-2.4)	5.5 (5.0-5.6)	**12.3** (9.1-13.4)

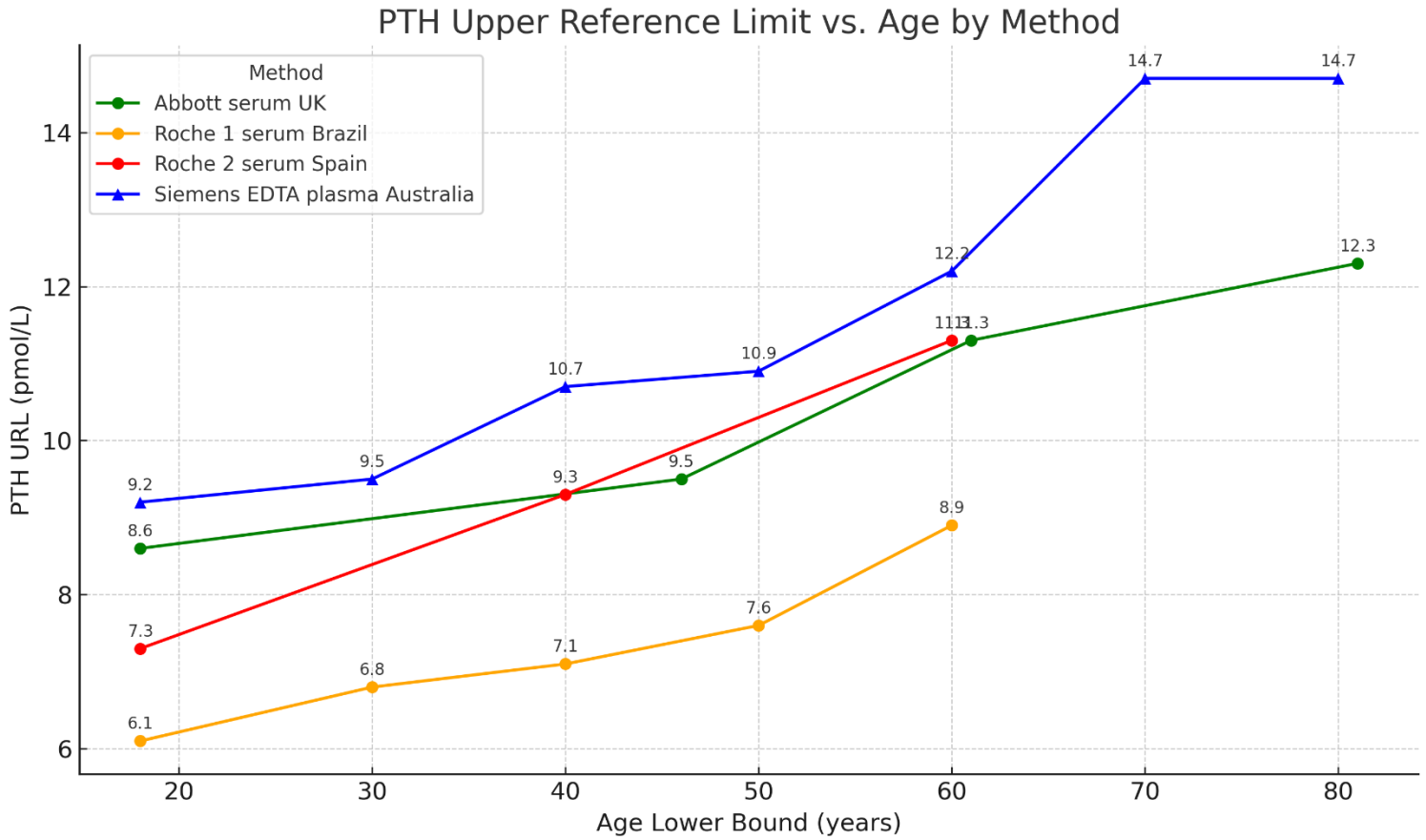
The point estimates are the median of 1000 bootstrap iterations and numbers in the brackets indicate 90% confidence intervals (CI).



5% to 6% every 10 years

Kalaria T et al. J Endocr Soc. 2024 Jan 12;8(3):bvae004.

Comparison of different age-specific iPTH reference intervals



Farrell C-JL et al. Clin Endocrinol (Oxf) 2018; 88(2):311–317.

Siemens ADVIA Centaur, EDTA plasma, 4 years, N= 10788, 25-hydroxyvitamin D >= 75 nmol/L, albumin adjusted serum calcium 2.1 to 2.6 mmol/L, eGFR >=60 mL/min/1.73m2. Non-parametric percentile + Bhattacharya analysis.

Delgado JA et al. Clin Chim Acta 2020; 508217–220.

Roche cobas, serum, N= 2279, non-parametric percentiles. Within reference intervals creatinine (64 - 110 µmol/L), 25-hydroxyvitamin D (75 - 250 nmol/L), calcium (2.10 - 2.55 mmol/L), albumin (0.53 - 0.76 mmol/L), and phosphate (0.74 - 1.52 mmol/L).

Cavalcante LBCP et al. J Endocrinol Invest 2023; 46(12):2525–2533.

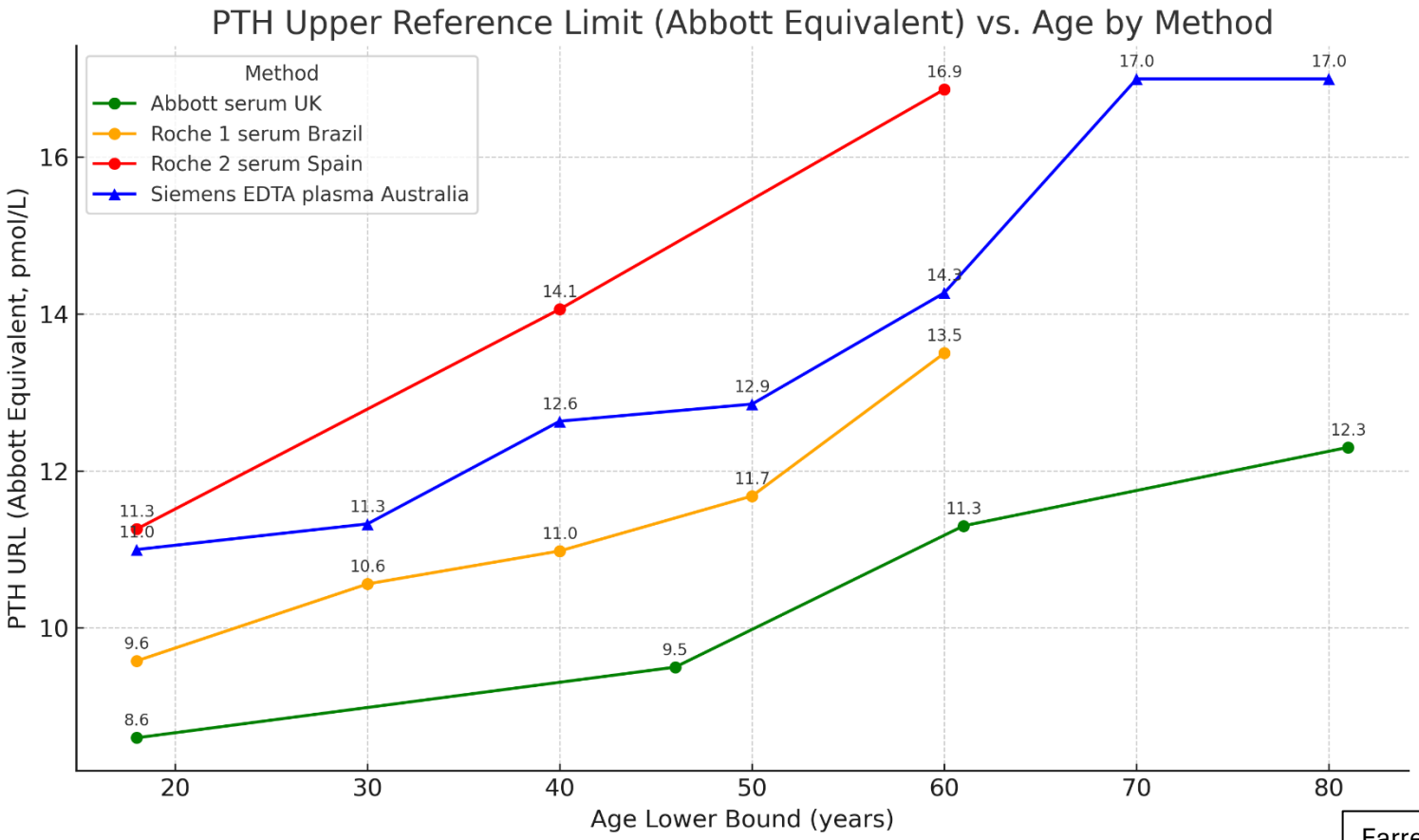
Roche cobas, serum, 3 years, N= 263,242 for 25-hydroxyvitamin D >= 50 nmol/L and N = 160,660 for 25-hydroxyvitamin D >= 75 nmol/L, refine R. total calcium <= 2.57 mmol/L, eGFR CKD-EPI >=60 mL/min/1.73m2. Excluded patients with history of using lithium, furosemide, denosumab, zoledronic acid or teriparatide.

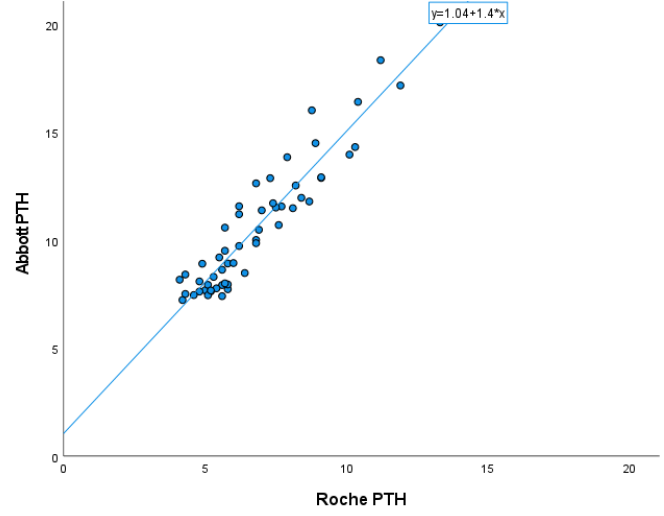
Kalaria T et al. J Endocr Soc. 2024 Jan 12;8(3):bvae004.

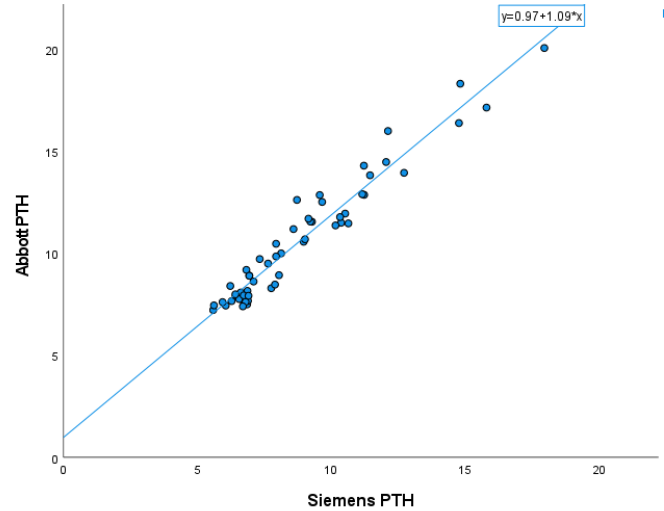
Abbott Architect, serum, 7 years, N= 5935, refine R. eGFR ≥60 mL/min, 25-hydroxyvitamin D >50 nmol/L, albumin-adjusted calcium 2.2 to 2.6 mmol/L, serum phosphate (where available) 0.8-1.5 mmol/L.

Comparison of different age-specific iPTH reference intervals

(Values converted to Abbott iPTH equivalent)







Abbott PTH = 1.04 +1.4*Roche PTH

Abbott PTH = 0.97 + 1.09*Siemens PTH

Farrell C-JL et al. Clin Endocrinol (Oxf) 2018; 88(2):311–317.

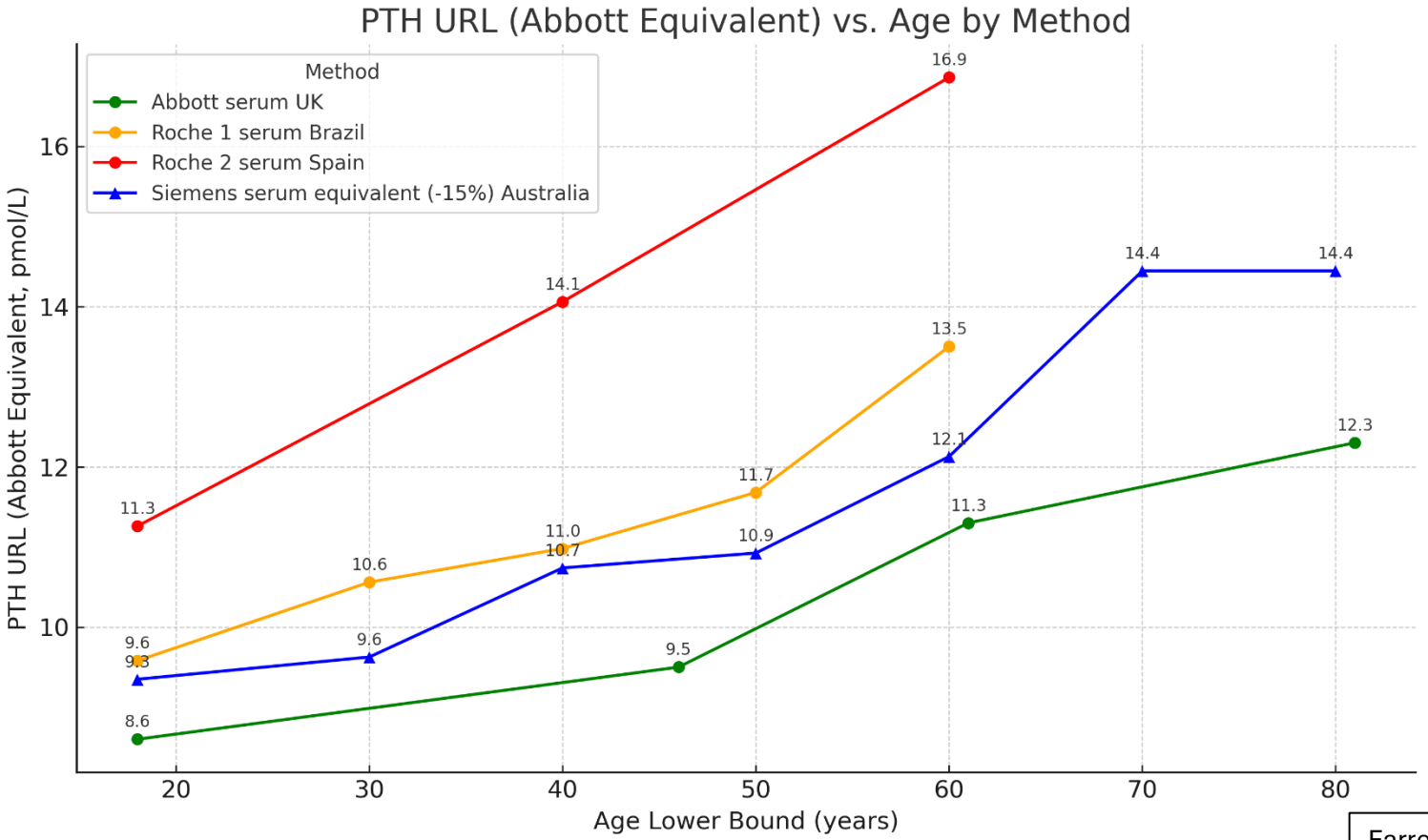
Delgado JA et al. Clin Chim Acta 2020; 508217–220.

Cavalcante LBCP et al. J Endocrinol Invest 2023; 46(12):2525–2533.

Kalaria T et al. J Endocr Soc. 2024 Jan 12;8(3):bvae004.

Comparison of different age-specific iPTH reference intervals

(Values converted to Abbott iPTH equivalent and Siemens EDTA plasma values decreased by 15% to make serum equivalent)



Abbott PTH = 1.04 +1.4*Roche PTH

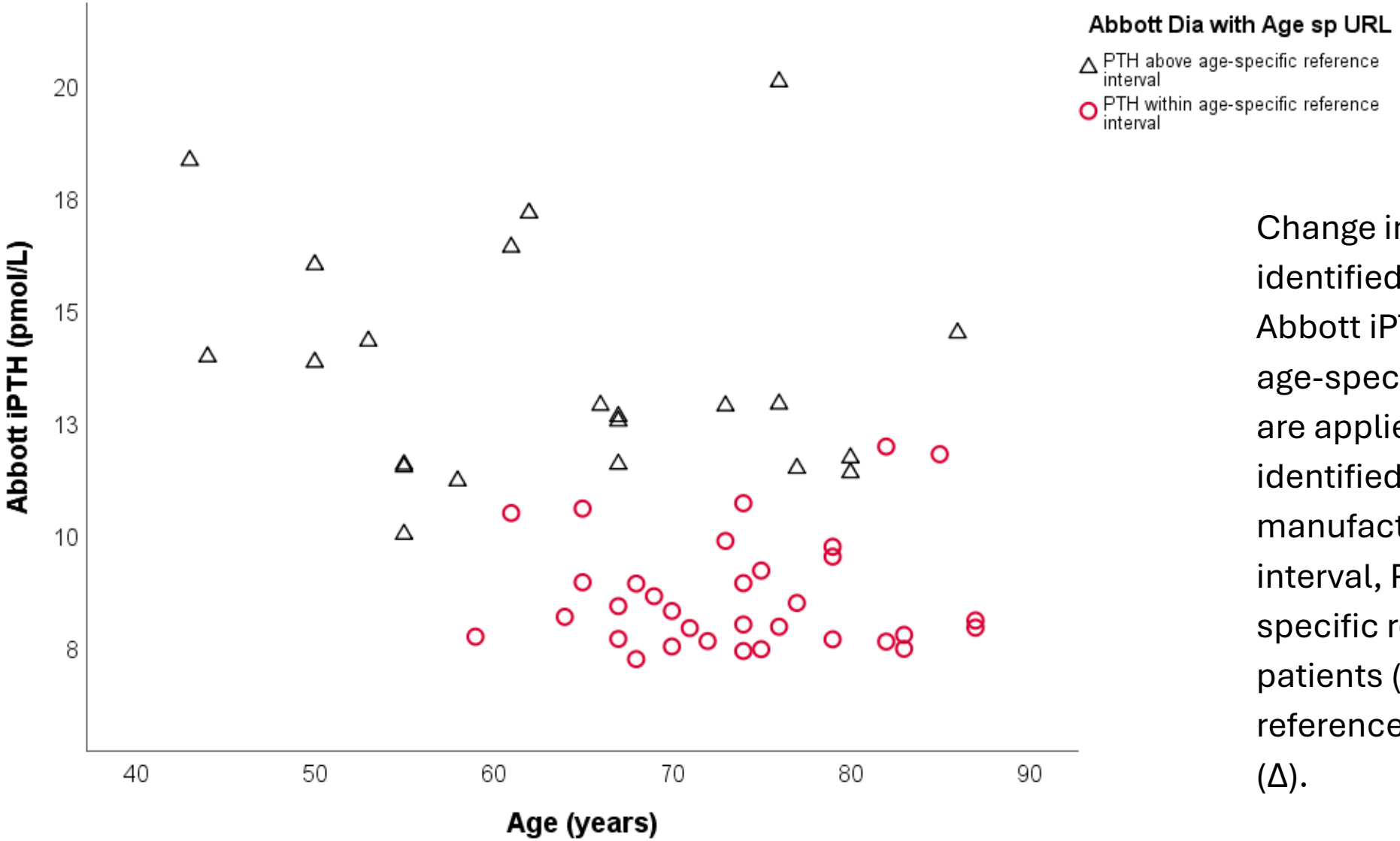
Abbott PTH = 0.97 + 1.09*Siemens PTH

Farrell C-JL et al. Clin Endocrinol (Oxf) 2018; 88(2):311–317.

Delgado JA et al. Clin Chim Acta 2020; 508217–220.

Cavalcante LBCP et al. J Endocrinol Invest 2023; 46(12):2525–2533.

Kalaria T et al. J Endocr Soc. 2024 Jan 12;8(3):bvae004.



Change in diagnosis of NCPHPT identified using manufacturer provided Abbott iPTH reference interval when age-specific iPTH reference intervals are applied. Of the 55 consecutively identified NCPHPT using the manufacturer provided iPTH reference interval, PTH was within the age-specific reference interval in 33 (60%) patients (O) and above the age-specific reference intervals in 22 (40%) patients (Δ).

Kalaria T et al. J Endocr Soc. 2024 Jan 12;8(3):bvae004.

NCPHPT N = 55 identified using Abbott assays
N = 9 with hypercalcaemic primary hyperparathyroidism (PHPT) on Roche assays were excluded
Remaining N = 46

Addressing the age-related disparities using real-world big data RIs addressed non-harmonised PTH assay related disparities to some extent!!!

		Abbott iPTH assay and age non-specific RI	
		Normal N (%)	NCPHPT N (%)
Roche iPTH assay and age non-specific RI	Normal N (%)	0 (0)	**30 (65.2)**
	NCPHPT N (%)	0 (0)	16 (34.8)

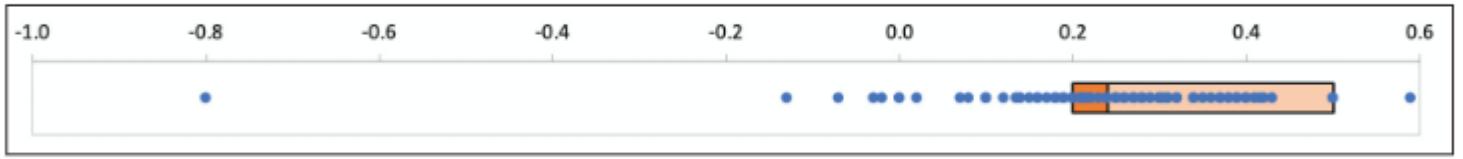
		Abbott iPTH age-specific RI	
		Normal N (%)	NCPHPT N (%)
Roche iPTH age-specific RI	Normal N (%)	**31 (67.4)**	8 (17.3)
	NCPHPT N (%)	0 (0.0)	7 (15.2)

Khalil H, Kalaria T et al. Horm Metab Res. 2025 Aug;57(8):471-476.

Potassium

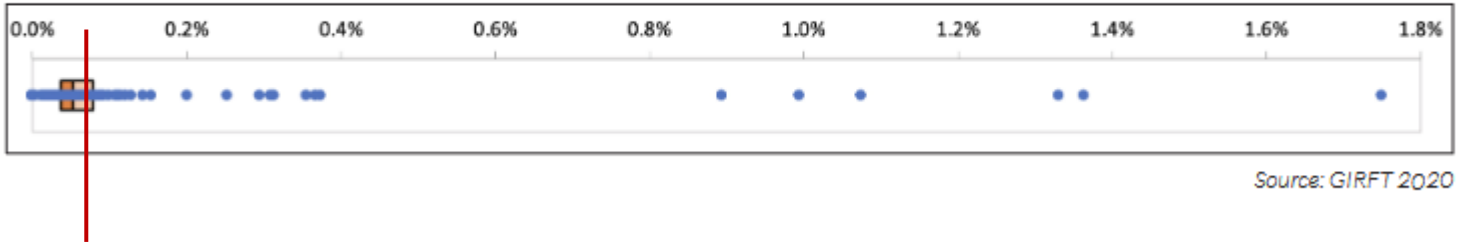
GIRFT

Figure 20: Difference in average potassium results for samples taken February 2019 and July 2018 (n=125)



Source: GIRFT 2020

Figure 21: Proportion of potassium tests with elevated level (above 6.5 mmol/L) from primary care (n=123)



Source: GIRFT 2020

BCPS

Jul'23 & Feb'24: 0.07 %

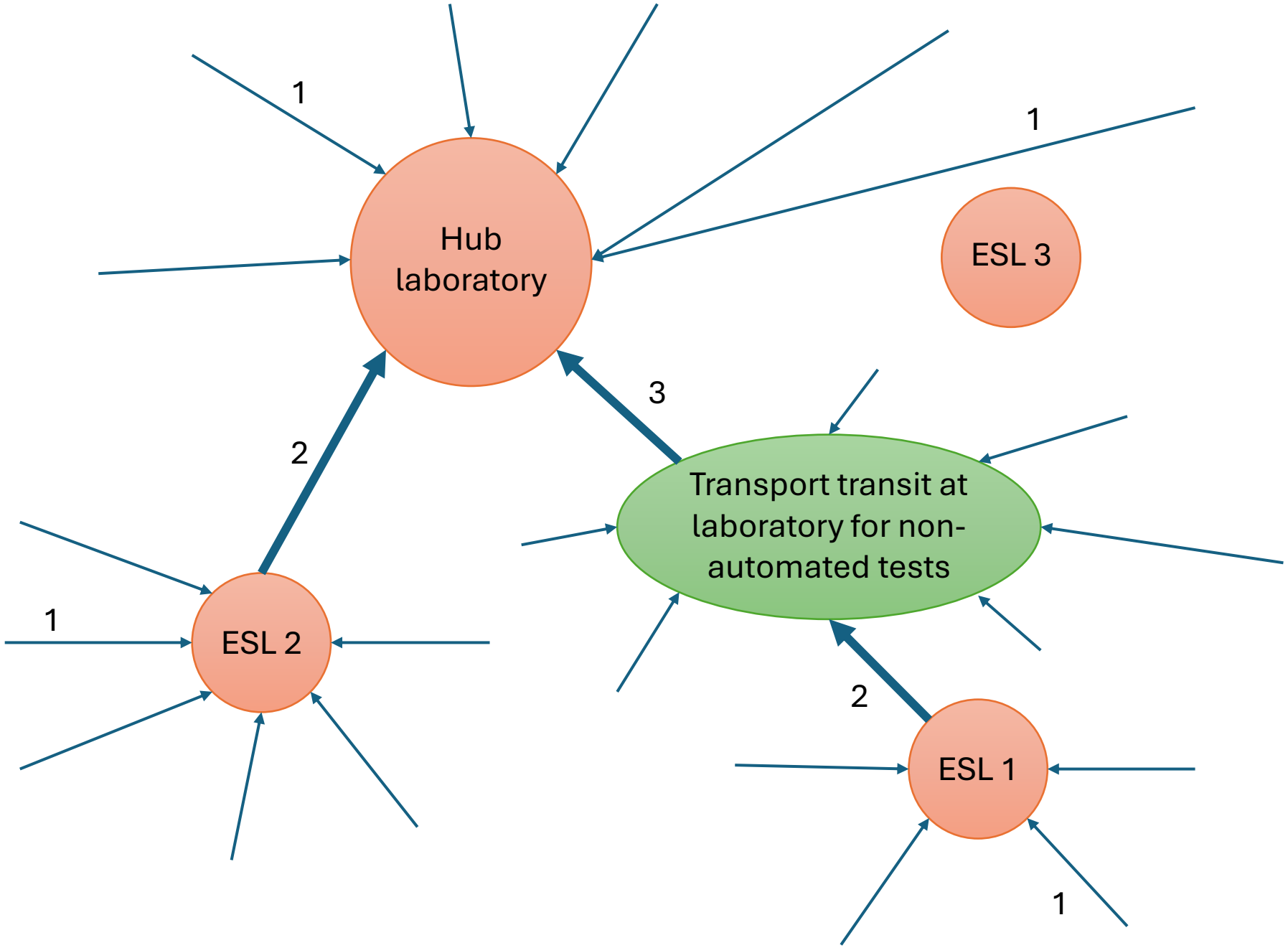
Jul'24 & Feb'25: 0.08 %

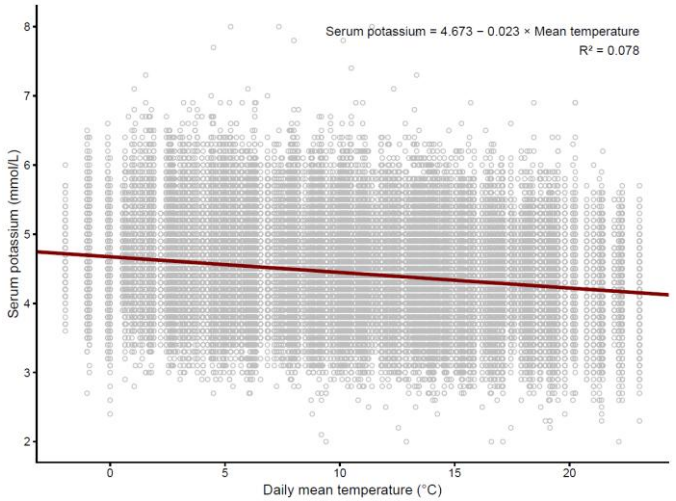
Jul'25& Feb'26: 0.08 %

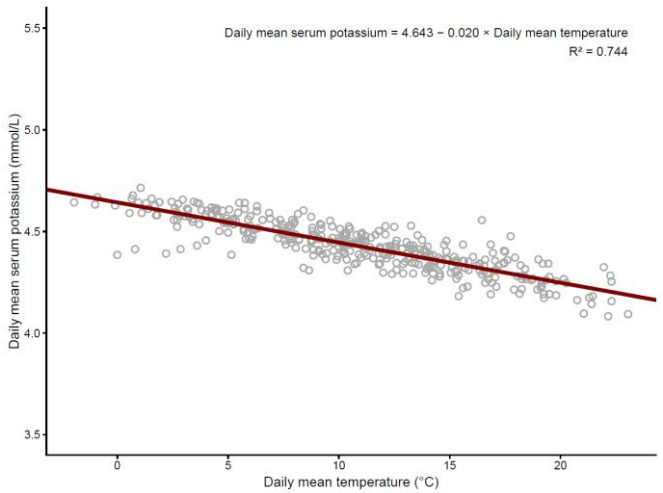
"We found that some labs never saw a potassium below the lower reference limit of 2.5 mmol/L. However, labs that had invested in sample stabilisation reported results below this limit in 0.75% of tests."

Pathology GIRFT Programme National Specialty Report (September 2021)

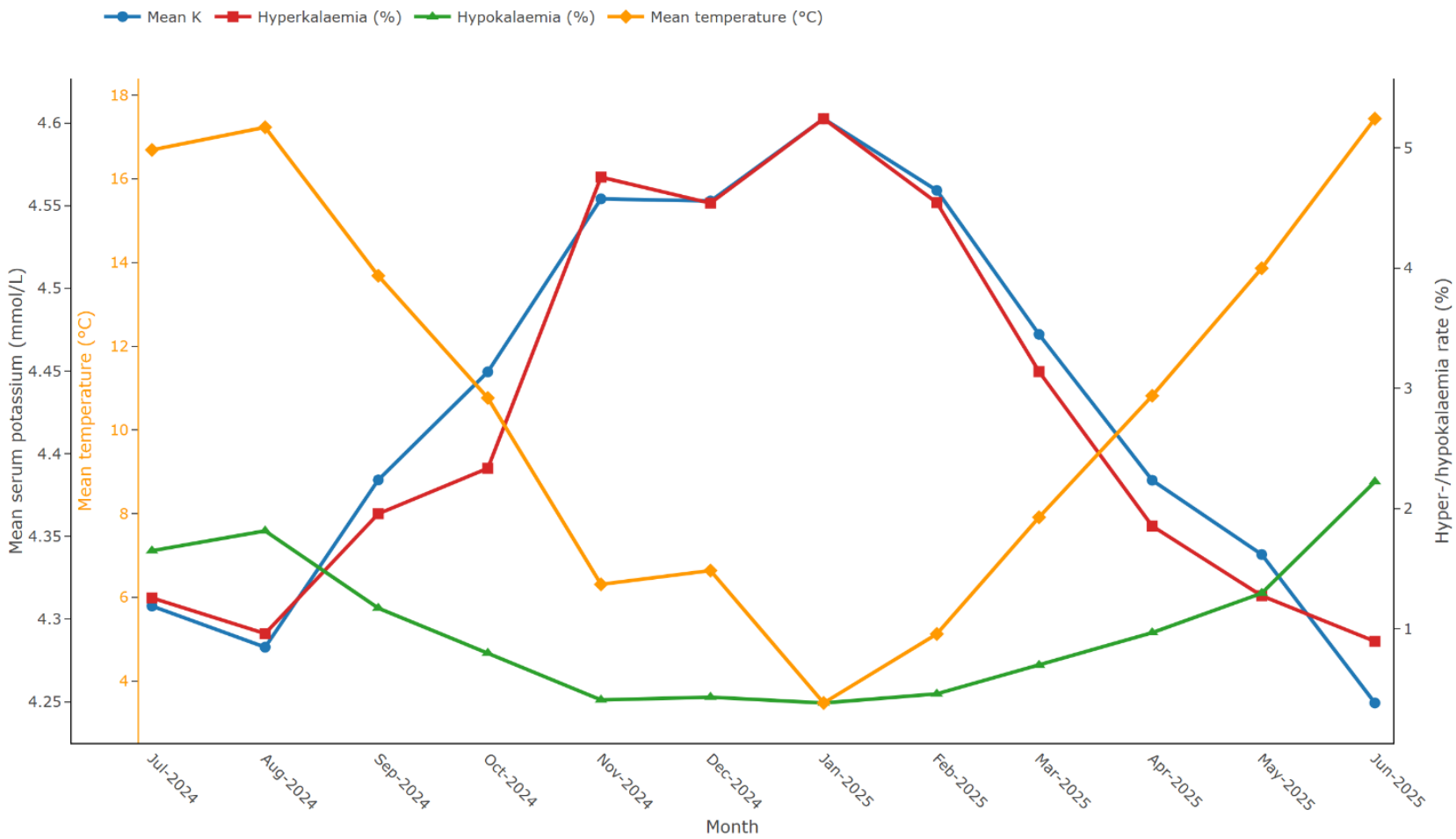
Potassium


1
1
Hub laboratory
ESL 3
3
2
Transport transit at laboratory for non-automated tests
1
ESL 2
2
ESL 1
1





Relationship between (a) daily mean ambient temperature (0900–0900, ° C) and all serum potassium results (n = 382,735) and (b) daily mean ambient temperature and daily mean serum potassium.



Monthly mean serum potassium concentration (blue line with circles, left axis), mean daily ambient temperature (0900–0900 h) from the nearest meteorological station (yellow line with rhombuses, second left axis), prevalence of hyperkalaemia (> 5.3 mmol/L, red line with squares, right axis) and hypokalaemia (< 3.5 mmol/L, green line with triangles, right axis) between July 2024 and June 2025 demonstrating seasonal variation in serum potassium with higher potassium and hyperkalaemia prevalence during colder months and the reverse pattern for hypokalaemia during warmer months.

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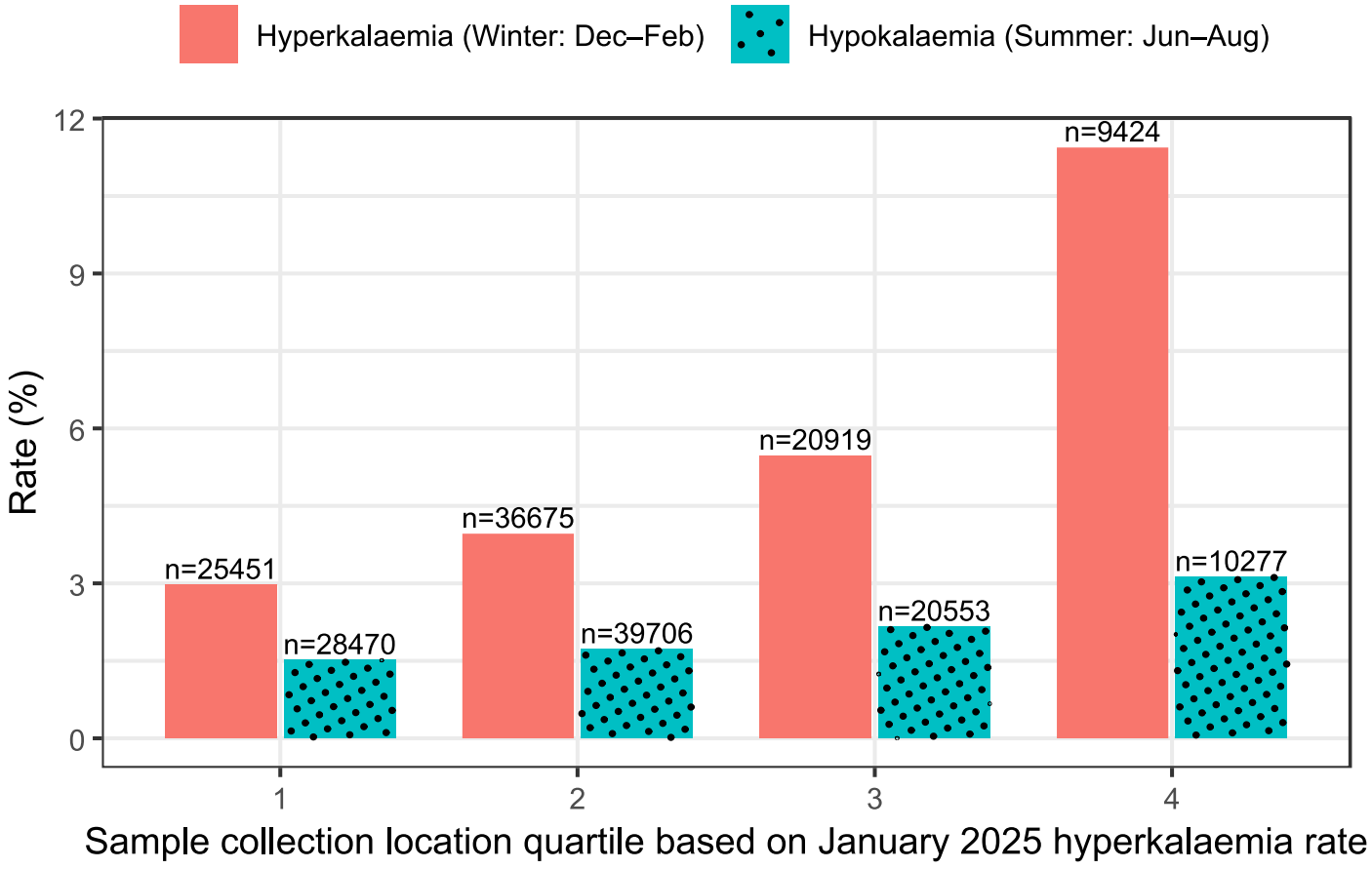
Additional insight



Not just efflux. Influx as well.

- Hyperkalaemia was 5.6 times higher in January compared to June; with hypokalaemia being 6.0 times higher in June compared to January.
- Locations in the highest January-2025 hyperkalaemia quartile Q4 exhibited both substantially higher winter hyperkalaemia (OR=4.22, 95% CI 3.33–5.35; $p < 0.0001$) and higher summer hypokalaemia (OR=2.10, 95% CI 1.36–3.23; p=0.0008) compared with the lowest quartile Q1.

Hyperkalaemia and hypokalaemia rates by sample collection location quartiles defined by the January 2025 hyperkalaemia rate.

Samples originating from locations with lowest hyperkalaemia rate in January 2025 are in the first quartile whereas samples from locations with highest hyperkalaemia are in the fourth quartile. Bars show the percentage of samples with pooled hyperkalaemia during winter (December 2024–February 2025) and hypokalaemia during summer (July–August 2024 and June 2025) months. Values are calculated across all samples within each quartile. The numbers above bars indicate the total number of samples contributing to each estimate.

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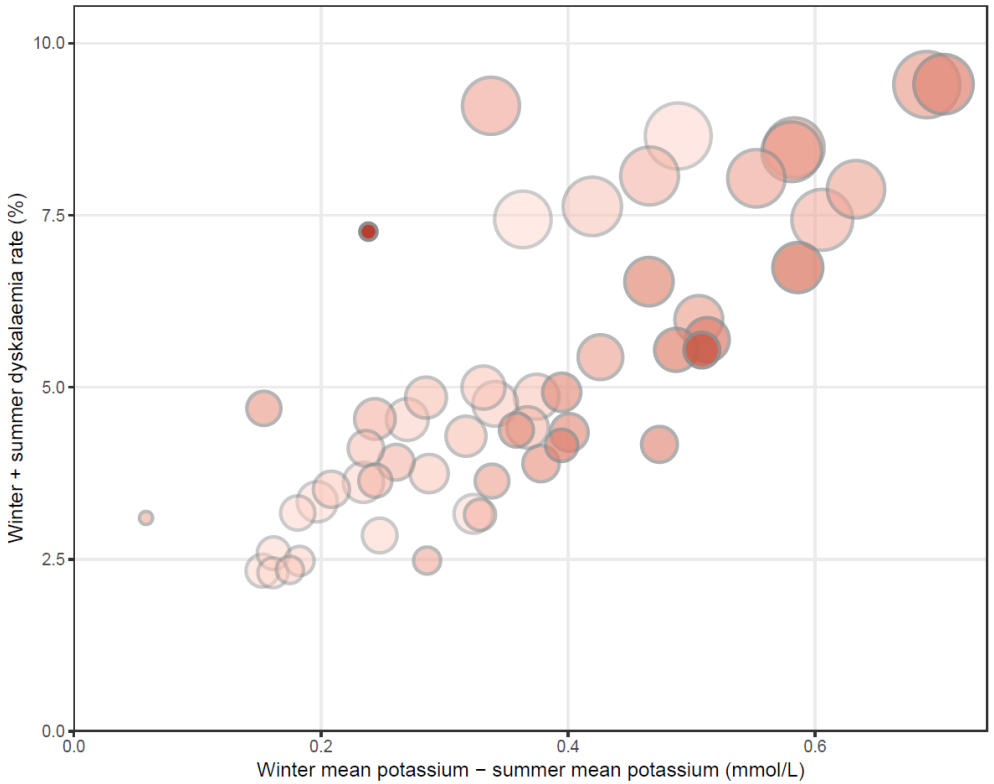

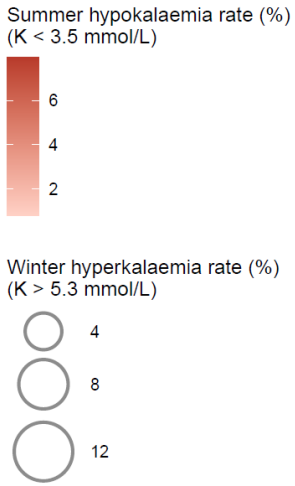

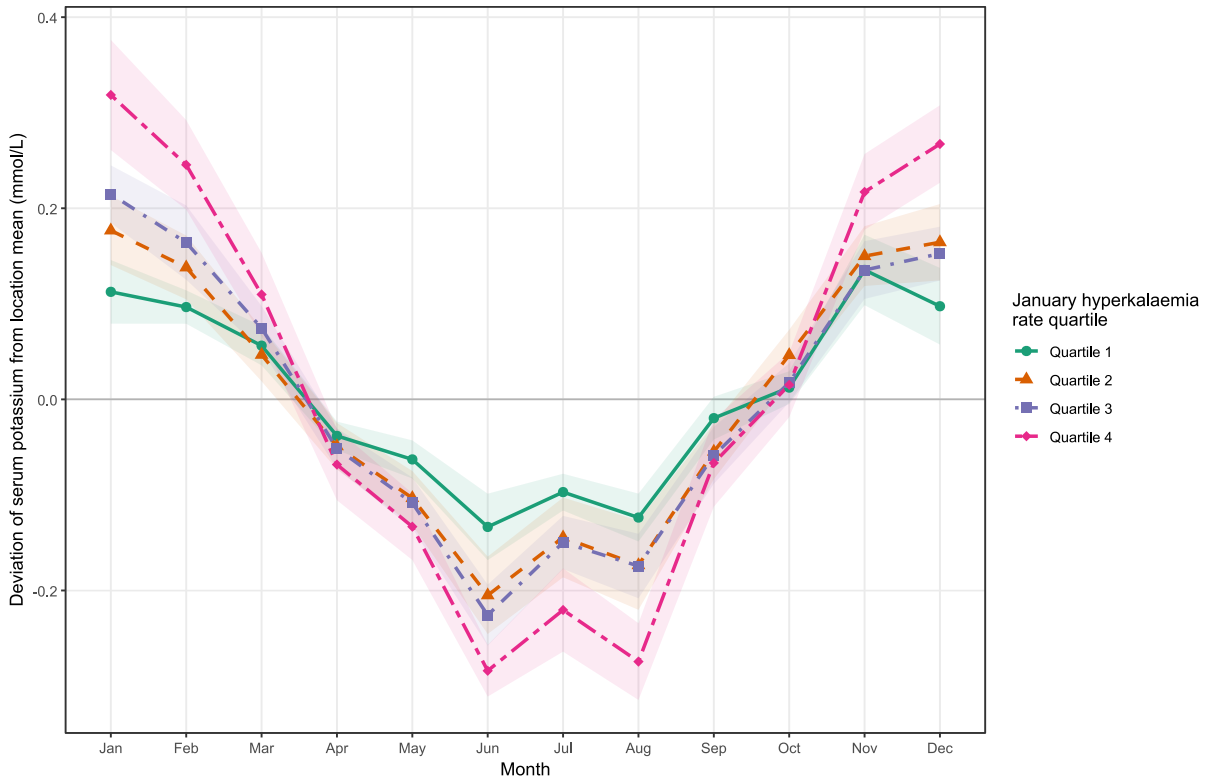

Seasonal shift in mean serum potassium and dyskalaemia rates by location (n = 54)

The x-axis shows the difference in mean serum potassium between winter (December, January and February) and summer (June, July and August) months. The y-axis shows the combined winter and summer dyskalaemia rate (%), calculated as the proportion of all winter and summer results with serum potassium outside the reference range. Bubble size is proportional to the winter hyperkalaemia rate (%), and bubble fill indicates the summer hypokalaemia rate (%).

Month-by-month deviation in mean serum potassium by January hyperkalaemia risk quartile

Lines show mean location-centred potassium deviation (monthly mean minus each location's overall mean, mmol/L) across calendar months, stratified by location quartiles defined by January hyperkalaemia rate. The shaded areas around the quartile lines indicate 95% confidence interval for the mean monthly deviation.

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Mitigations for seasonal dyskalaemia

- More indexor® deployed.
- Using Indexor® to book samples.
- Improved specimen reception flow at the ‘hub’ – sample lot queues, more evening staffing.
- Improved intra-laboratory logistics of off-track centrifugation during high-volume hours.
- Change in analyser maintenance schedules to make all analysers available during peak work times.
- Community services liaison to divert home-collection samples appropriately.
- Better matching of transport times and frequency to phlebotomy clinic times.
- More frequent transport for high volume locations.
- Deployment of centrifuges.
- One less transit location for the most affected area.
- Temperature control of transit locations.
- Temperature control of transportation vehicles/ insulated containers (expensive, logistic issues).
- Temperature control of specimen reception.
- A second primary care sample analysing site (‘mini-hub’).

Potential disparities in laboratory medicine

- Physiologic stratification
  - Age
  - Sex
  - Ethnicity
  - Pregnancy status
  - Time of day
  - Season
- Geography
- Socio-economic factors, access
- Pre-analytical disparities
  - Inconsistent instructions
  - Language barrier, literacy
  - Hydration, posture
  - Phlebotomy-related factors
  - Sample storage and transport
  - Time of day, season
- Analytical disparities
  - Operator-related factors
  - Capabilities of equipment
  - Change in performance
  - Lack of harmonisation
  - Interference
- Post-analytical disparities
  - Delayed communication
  - Language barrier, literacy
  - Access to digital devices
- Comorbidity-related interpretive confounding (or disease-associated biological variation)