Lies, Damned Lies and Calculations

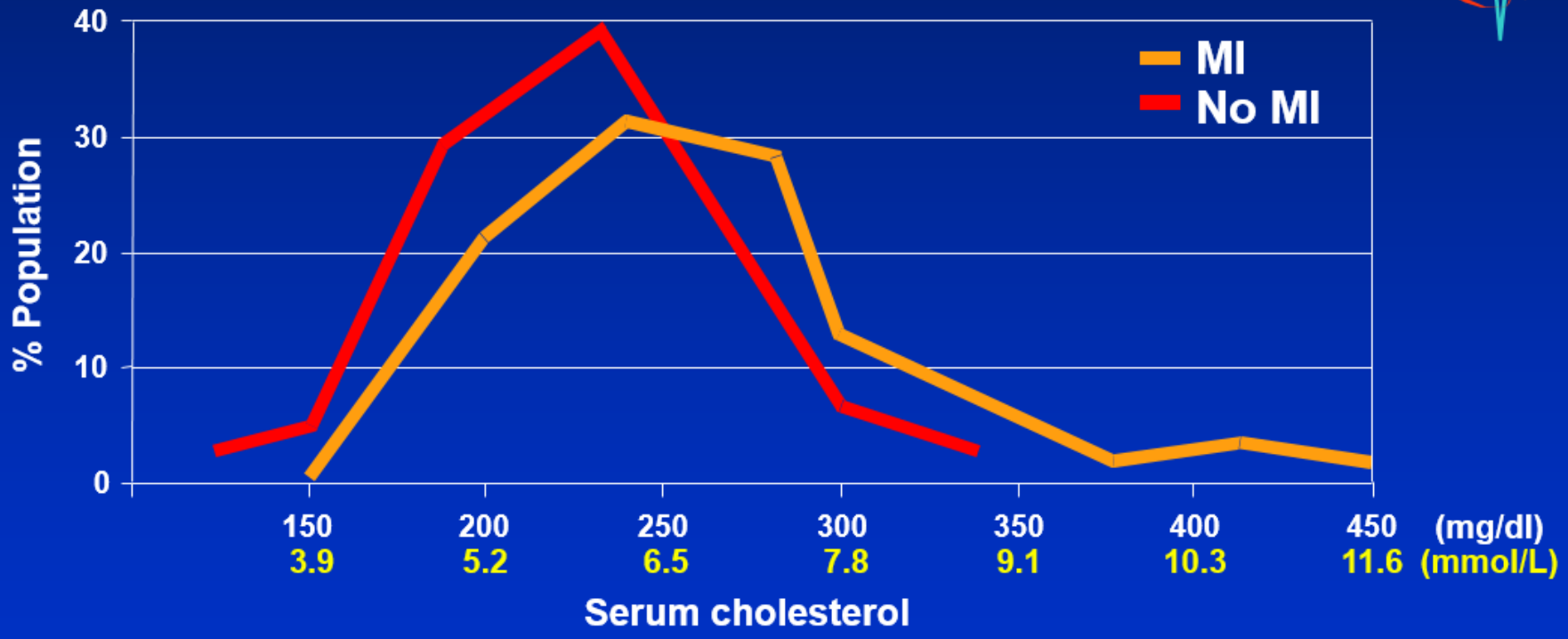
Prof. Pat Twomey

Consultant Chemical Pathologist


FRAMINGHAM - MEMORIAL

Serum Cholesterol Levels in Men*

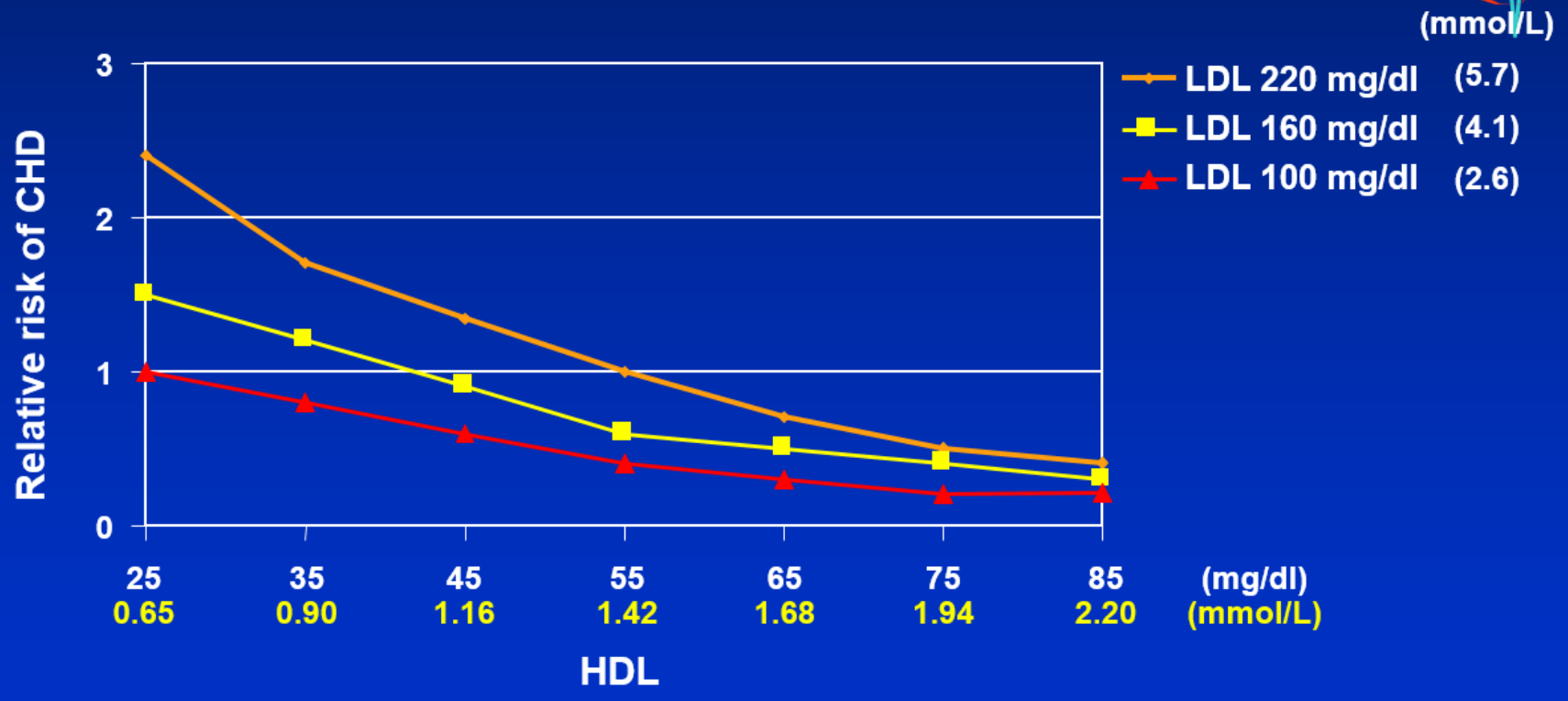
Framingham Heart Study



*During first 16 years of study: Entry ages 30–40 years
Adapted from Castelli WP *Can J Cardiol* 1988;4(suppl A):5A-10A.

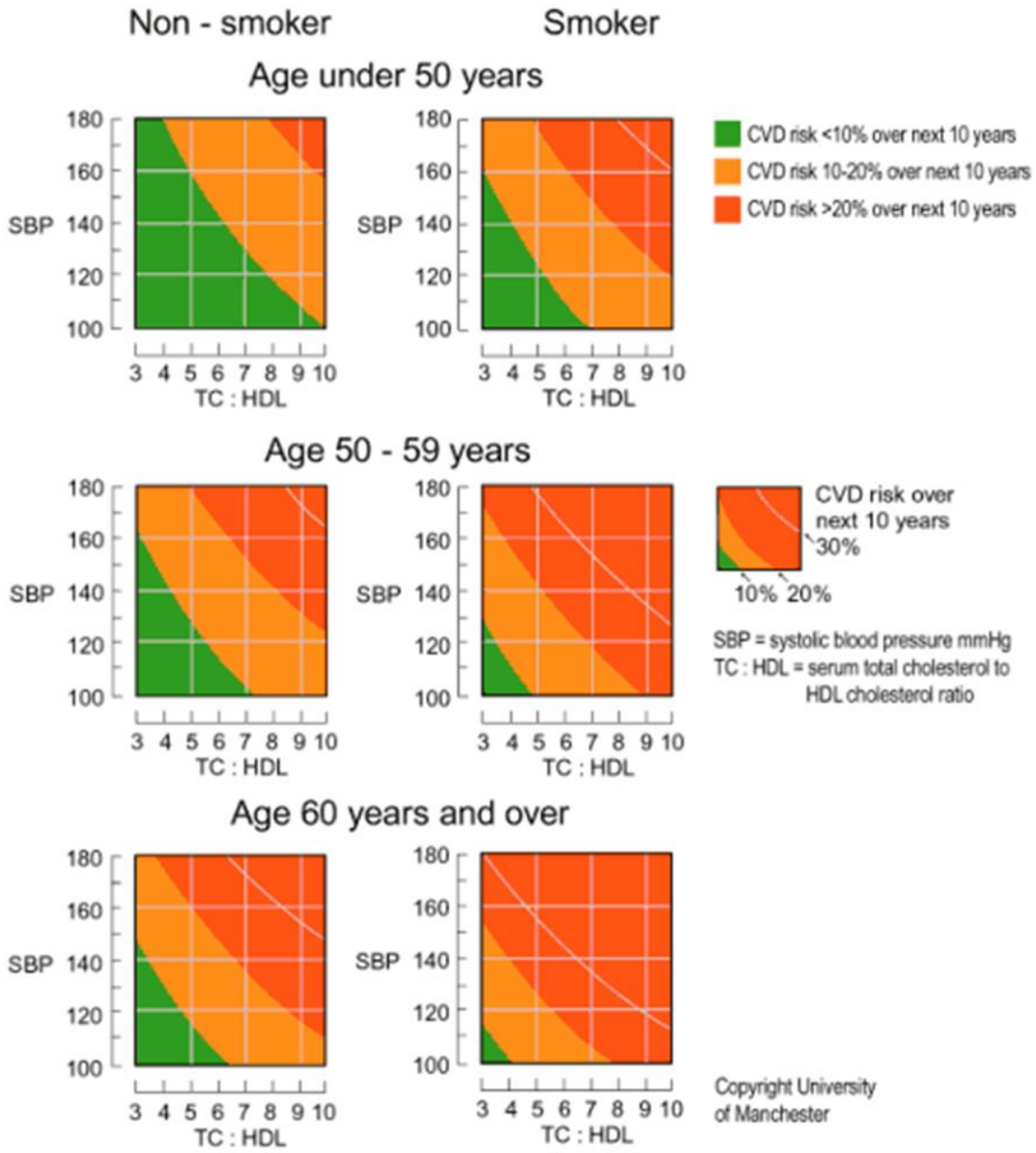
Increased HDL and Reduced CHD Incidence

Framingham Study



Adapted from Kannel WB. Status of risk factors and their consideration in antihypertensive therapy. *Am J Cardiol* 1987;59:80A-90A.

Nondiabetic Women



FRAMINGHAM EQUATIONS

$$\mu =$$

$$15.5305 + (28.4441 * sex) + (-1.4792 * \ln(age)) + (-14.4588 * \ln(age) * sex) + (1.8515 * (\ln(age)^2) * sex) + (-0.9119 * \ln(sysBP)) + (-0.2767 * smoker) + (-0.7181 * \ln(t\text{-}cho/HDL\text{-}cho)) + (-0.1759 * diabetes) + (-0.1999 * diabetes * sex) + (-0.5868 * LVH)$$

$$\sigma = e^{(0.9145 + (-0.2784 * \mu))}$$

$$p(CHD - 10\text{-}yr) = 1 - e^{(-e^{(\ln(10) - \mu/\sigma)})}$$

Sex: Male = 0; female = 1
DM, smoke, LVH: 0 = No; 1 = Yes

Cardiovascular disease risk profiles Am Heart J 1991; 121:293-8.

Lipid calculations

- TC / HDL-C ratio
- Non HDL-C (TC – HDL-C)
- cLDL-C = TC – HDL-C – Trigs/2.2
- Apo B / Apo A1
- Non HDL-C / Apo B
- Trigs / Apo B

Simple calculation

- On the next page, I will show a simple calculation for you to work out in your head

- The calculation is as presented so no questions please about the calculation!

- Please keep the answer to yourself

Simple calculation

$$1 + 2 \times 3 = ?$$

Simple calculation

9

7

Neither 9 or 7

B - Brackets

Complete anything in the brackets first

O - Orders

Next apply any orders of - square roots, indices etc.

D&M - Division or Multiplication

Then do any divisions or multiplications (if both are in the same calculation, complete them left to right)

A&S- Addition or Subtraction

Lastly, complete any additions or subtractions (if both are in the same calculation, do them from left to right)

Simple calculation

It is easy to miscalculate!

J Clin Pathol 2000;53:807–812

Leaders

acp

Best Practice No 163

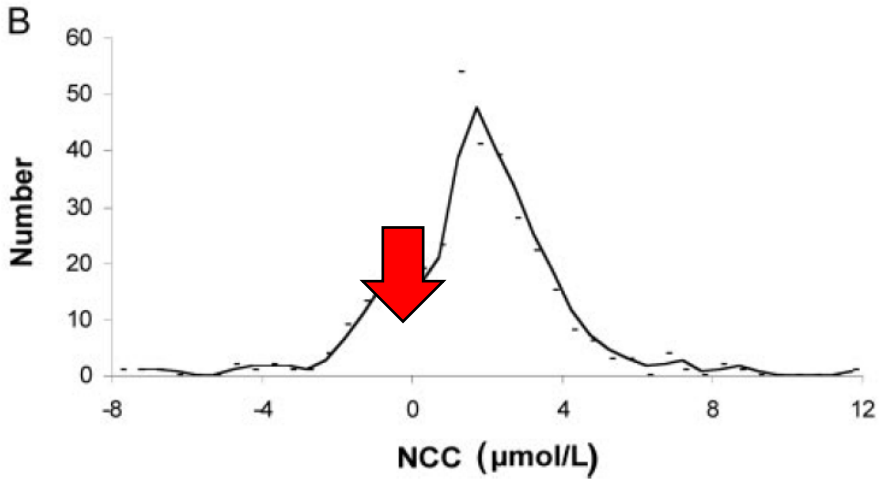
Wilson's disease: acute and presymptomatic laboratory diagnosis and monitoring

D Gaffney, G S Fell, D St J O'Reilly

Non-Cp-Cu (µmol/L) =

total serum Cu (µmol/L) – 0.047 × serum Cp (mg/L)

Non Caeruoplasmin bound Copper



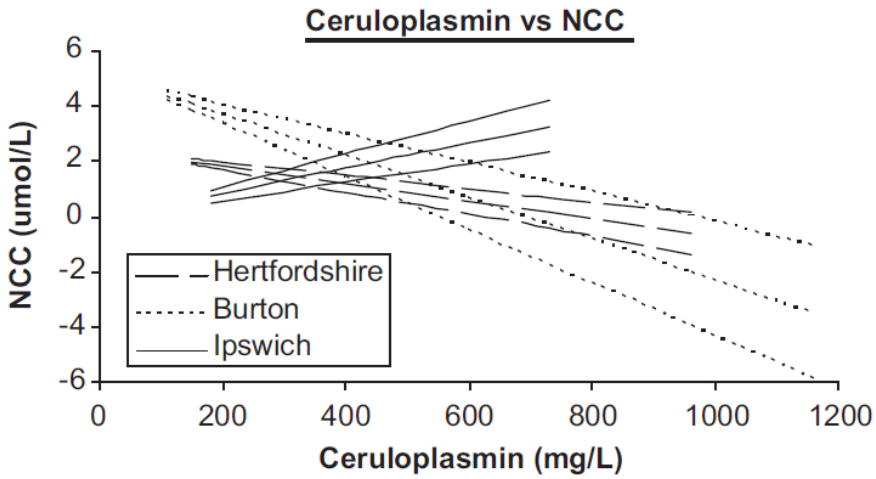


Fig. 1. Relationship between ceruloplasmin and copper concentrations (*A*) and NCC distribution plot (*B*) for 338 patients without Wilson disease.

"we did obtain negative values for 20.1% of patients. The upper reference limit is considered to be 1.6 umol/L, but 47.6% of results were above this cutoff"

DOI: 10.1373/clinchem.2005.052688

Available online at www.sciencedirect.com
ScienceDirect
ELSEVIER
Journal of Trace Elements in Medicine and Biology 22 (2008) 50–53
Journal of Trace Elements in Medicine and Biology
www.elsevier.de/jtemb

PATHOBIOCHEMISTRY

Non-ceruloplasmin-bound copper in routine clinical practice in different laboratories

Patrick J. Twomey[a,*], Adie Viljoen[b], Timothy M. Reynolds[c], Anthony S. Wierzbicki[d]

ORIGINAL ARTICLE

J Clin Pathol 2007;60:1048–1050. doi: 10.1136/jcp.2006.043547

Implications of method specific creatinine adjustments on General Medical Services chronic kidney disease classification

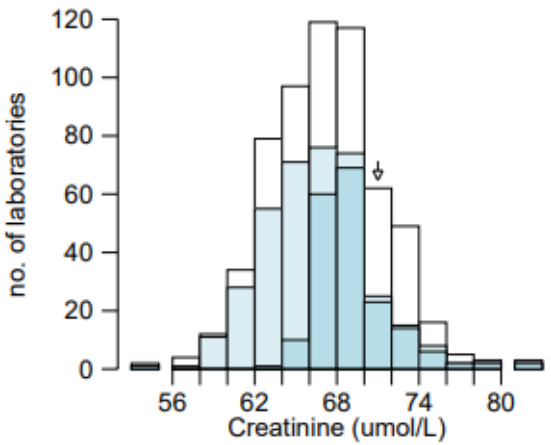
Timothy M Reynolds, Patrick J Twomey

From 01/04/2006, the DoH (England) added eGFR to the GP Quality Outcomes Framework

Table 1 Quality outcome framework for chronic kidney disease (ChKD)

Indicator	Points	Payment stages
ChKD1: The practice can produce a register of patients aged ≥18 years with ChKD (US National Kidney Foundation: Stage 3–5 ChKD)	6	
ChKD2: The percentage of patients on the ChKD register whose notes have a record of blood pressure measurement in the previous 15 months	6	40–90%
ChKD3: The percentage of patients on the ChKD register in whom the last blood pressure reading, measured in the previous 15 months, is ≤140/85 mm Hg	11	40–70%
ChKD4: The percentage of patients on the ChKD register who are treated with an ACE inhibitor or angiotensin receptor blocker (unless a contraindication or side effects are recorded)	4	40–80%

Specimen : 1105A	n	Mean	SD	CV(%)
All methods [ALTM]	582	67.7	4.0	5.9
Dry slide / Sensor	20	65.9	2.9	4.4
Compensated Kinetic Jaffe	209	69.2	4.0	5.7
Abbott Architect [10AB]	34	69.1	2.9	4.2
Beckman AU [10OL]	31	63.6	2.1	3.3
Roche Cobas [10BO]	109	71.0	3.0	4.3
Enzymatic	371	66.9	3.7	5.5
Abbott Alinity [9AB20]	41	64.7	1.8	2.8
Abbott Architect [9AB]	60	63.8	2.0	3.2
Beckman AU [9OL]	25	65.8	1.3	1.9
Roche Cobas [9BO]	190	69.4	2.3	3.3
Siemens ADVIA [9TE]	30	61.9	1.9	3.0



Your result	72
Target value (Enzymatic)	66.9
Standard Uncertainty	0.3
Your specimen: %bias	+7.6
Accuracy Index	141
Method Principle mean [GLTM]	66.9
Method mean [MLTM]	69.4

ORIGINAL ARTICLE

Implications of method specific creatinine adjustments on General Medical Services chronic kidney disease classification

J Clin Pathol 2007;**60**:1048–1050. doi: 10.1136/jcp.2006.043547

Timothy M Reynolds, Patrick J Twomey

The Department of Health (England) subsequently advised that GPs should allow laboratories to calculate eGFR and that laboratories should employ the updated four-variable MDRD equation.

$$[\text{eGFR} = 186 \times (\text{creatinine result}/88.4)^{-1.154} \times \text{Age}^{-0.203} \times [0.742 \text{ if female}] \times [1.212 \text{ if Afro-Caribbean}]^{3}$$

Take-home messages

- Estimated glomerular filtration rate (eGFR) is not a simple value that can easily be calculated.
- Different formulae for calculation of eGFR lead to different chronic kidney disease (ChKD) identification outcomes.
- Use of the "wrong" eGFR formula can significantly increase the screen positive rate (ie, numbers of patients with ChKD stage 3).
- Identifying more patients with ChKD3 increases general practitioner (GP) workload and costs, and also increases problems for patients.
- Laboratories and not GPs should calculate eGFR.

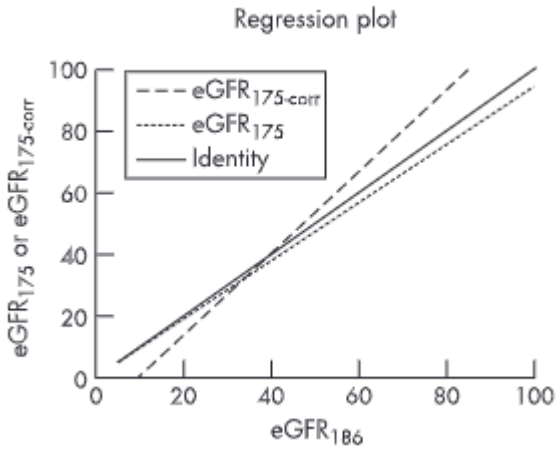


Table 1: Main eGFR equations.

Name	Age (years)	Sex			eGFR equation
CKD-EPI$_{Crea}$ (ASR) [8]	≥18	Female	SCr ≤ 0.70		$144 \times (SCr/0.70)^{-0.329} \times 0.9929^{Age} \times 1.159$ [if Black]
			SCr > 0.70		$144 \times (SCr/0.70)^{-1.209} \times 0.9929^{Age} \times 1.159$ [if Black]
		Male	SCr ≤ 0.90		$141 \times (SCr/0.90)^{-0.411} \times 0.9929^{Age} \times 1.159$ [if Black]
			SCr > 0.90		$141 \times (SCr/0.90)^{-1.209} \times 0.9929^{Age} \times 1.159$ [if Black]
CKD-EPI$_{Crea}$ (AS) [18]	≥18	Female	SCr ≤ 0.70		$143 \times (SCr/0.70)^{-0.241} \times 0.9938^{Age}$
			SCr > 0.70		$143 \times (SCr/0.70)^{-1.200} \times 0.9938^{Age}$
		Male	SCr ≤ 0.90		$142 \times (SCr/0.90)^{-0.302} \times 0.9938^{Age}$
			SCr > 0.90		$142 \times (SCr/0.90)^{-1.200} \times 0.9938^{Age}$
CKD-EPI$_{CysC}$ [86]	≥18	Female	ScysC ≤ 0.80		$133 \times (SCysC/0.80)^{-0.499} \times 0.9962^{Age} \times 0.932$
			ScysC > 0.80		$133 \times (SCysC/0.80)^{-1.328} \times 0.9962^{Age} \times 0.932$
		Male	ScysC ≤ 0.80		$133 \times (SCysC/0.80)^{-0.499} \times 0.9962^{Age}$
			ScysC > 0.80		$133 \times (SCysC/0.80)^{-1.328} \times 0.9962^{Age}$
CKD-EPI$_{Crea+CysC}$ (ASR) [86]	≥18	Female	SCr ≤ 0.70	ScysC ≤ 0.80	$130 \times (SCr/0.70)^{-0.248} \times (ScysC/0.80)^{-0.375} \times 0.9952^{Age}$
			SCr ≤ 0.70	ScysC > 0.80	$130 \times (SCr/0.70)^{-0.248} \times (ScysC/0.80)^{-0.711} \times 0.9952^{Age}$
			SCr > 0.70	ScysC ≤ 0.80	$130 \times (SCr/0.70)^{-0.601} \times (ScysC/0.80)^{-0.375} \times 0.9952^{Age}$
			SCr > 0.70	ScysC > 0.80	$130 \times (SCr/0.70)^{-0.601} \times (ScysC/0.80)^{-0.711} \times 0.9952^{Age}$
	≥18	Male	SCr ≤ 0.90	ScysC ≤ 0.80	$135 \times (SCr/0.90)^{-0.207} \times (ScysC/0.80)^{-0.375} \times 0.9952^{Age}$
			SCr ≤ 0.90	ScysC > 0.80	$135 \times (SCr/0.90)^{-0.207} \times (ScysC/0.80)^{-0.711} \times 0.9952^{Age}$
			SCr > 0.90	ScysC ≤ 0.80	$135 \times (SCr/0.90)^{-0.601} \times (ScysC/0.80)^{-0.375} \times 0.9952^{Age}$
			SCr > 0.90	ScysC > 0.80	$135 \times (SCr/0.90)^{-0.601} \times (ScysC/0.80)^{-0.711} \times 0.9952^{Age}$
CKD-EPI$_{Crea+CysC}$ (AS) [18]	≥18	Female	SCr ≤ 0.70	ScysC ≤ 0.80	$130 \times (SCr/0.70)^{-0.219} \times (ScysC/0.80)^{-0.323} \times 0.9961^{Age}$
			SCr ≤ 0.70	ScysC > 0.80	$130 \times (SCr/0.70)^{-0.219} \times (ScysC/0.80)^{-0.778} \times 0.9961^{Age}$
			SCr > 0.70	ScysC ≤ 0.80	$130 \times (SCr/0.70)^{-0.544} \times (ScysC/0.80)^{-0.323} \times 0.9961^{Age}$
			SCr > 0.70	ScysC > 0.80	$130 \times (SCr/0.70)^{-0.544} \times (ScysC/0.80)^{-0.778} \times 0.9961^{Age}$
	≥18	Male	SCr ≤ 0.90	ScysC ≤ 0.80	$135 \times (SCr/0.90)^{-0.144} \times (ScysC/0.80)^{-0.323} \times 0.9961^{Age}$
			SCr ≤ 0.90	ScysC > 0.80	$135 \times (SCr/0.90)^{-0.144} \times (ScysC/0.80)^{-0.778} \times 0.9961^{Age}$
			SCr > 0.90	ScysC ≤ 0.80	$135 \times (SCr/0.90)^{-0.544} \times (ScysC/0.80)^{-0.323} \times 0.9961^{Age}$
			SCr > 0.90	ScysC > 0.80	$135 \times (SCr/0.90)^{-0.544} \times (ScysC/0.80)^{-0.778} \times 0.9961^{Age}$
EKFC$_{Crea}$ [41]	25–40	Female	SCr/Q < 1.0		$107.3 \times (SCr/Q)^{-0.322}$
			SCr/Q ≥ 1.0		$107.3 \times (SCr/Q)^{-1.132}$
		Male	SCr/Q < 1.0		$107.3 \times (SCr/Q)^{-0.322}$
			SCr/Q ≥ 1.0		$107.3 \times (SCr/Q)^{-1.132}$
	>40	Female	SCr/Q < 1.0		$107.3 \times (SCr/Q)^{-0.322} \times 0.990^{(Age-40)}$
			SCr/Q ≥ 1.0		$107.3 \times (SCr/Q)^{-1.132} \times 0.990^{(Age-40)}$
		Male	SCr/Q < 1.0		$107.3 \times (SCr/Q)^{-0.322} \times 0.990^{(Age-40)}$
			SCr/Q ≥ 1.0		$107.3 \times (SCr/Q)^{-1.132} \times 0.990^{(Age-40)}$
EKFC$_{CysC}$ [7]	18–40		ScysC/0.83 < 1.0		$107.3 \times (SCysC/0.83)^{-0.322}$
			ScysC/0.83 ≥ 1.0		$107.3 \times (SCysC/0.83)^{-1.132}$
	>40		ScysC/0.83 < 1.0		$107.3 \times (SCysC/0.83)^{-0.322} \times 0.990^{(Age-40)}$
			ScysC/0.83 ≥ 1.0		$107.3 \times (SCysC/0.83)^{-1.132} \times 0.990^{(Age-40)}$
	>50		ScysC/Q < 1.0		$107.3 \times (SCysC/Q)^{-0.322} \times 0.990^{(Age-40)}$
			Q = 0.83 + 0.005 × (Age–50)		
			ScysC/Q ≥ 1.0		$107.3 \times (SCysC/Q)^{-1.132} \times 0.990^{(Age-40)}$
			Q = 0.83 + 0.005 × (Age–50)		
LMREV [50]		Female	<150 (in µmol/L)		X = 2.5 + 0.0121 × (150–SCr) (SCr in µmol/L)
			≥150		X = 2.5–0.926 × log(SCr/150)
		Male	<180		X = 2.56 + 0.00968 × (180–SCr)
			≥180		X = 2.56–0.926 × log(SCr/180)
					GFR = e × p(X–0.0158 × age + 0.438 × log(age))
CAPA [49]					$130 \times ScysC^{-1.069} \times age^{-0.117} - 7$

ASR, age, sex and race factors; AS, age and sex but no race factor; Q, rescaling factor for the biomarker; LMREV, Revised Lund–Malmö; SCr, serum creatinine; ScysC, serum cystatin C.
To make a more continuous transition from the pediatric EKFC$_{Crea}$ equation to the adult EKFC$_{Crea}$ equation, the Q-values for children, adolescents and young adults (up to 25 years old) can be calculated from (note that the Q-value obtained from these equations is expressed in µmol/L):
- Men, age ≤25 years: $\ln(Q) = 3.200 + 0.259 \times age - 0.543 \times \log(age) - 0.00763 \times age^2 + 0.0000790 \times age^3$
- Women, age ≤25 years: $\ln(Q) = 3.080 + 0.177 \times age - 0.223 \times \log(age) - 0.00596 \times age^2 + 0.0000686 \times age^3$

Q can be obtained in mg/dL using exp(Q)/88.4.
For white European subjects, age > 25 years, use:
- Men: Q = 0.90 mg/dL
- Women: Q = 0.70 mg/dL (see [34, 47] for Q-values in other populations).

Current equations!

Diagnostic standard: assessing glomerular filtration rate *Nephrol Dial Transplant* , 2023, **0** , 1–9
https://doi.org/10.1093/ndt/gfad241
Advance access publication date: 9 November 2023

Table 1. Q values determined in different adult populations

	Q value in women	Q value in men	Origin	Reference
White European	0.70	0.90	Big data from laboratories in Sweden and Belgium	[27, 28]
Black European	0.74	1.02	Living kidney donors in Paris	[38]
Black Africans (Central Africa)	0.72	0.96	Healthy people in Congo	[39]
White US population-specific	0.73	0.93	Big data from laboratories from University of Washington Medicine System	[51]
Black US population-specific	0.73	1.00	Big data from laboratories from University of Washington Medicine System	[51]
White US population-specific	0.70	0.94	National Health and Nutrition Examination Survey	[41]
Black US population-specific	0.72	1.03	National Health and Nutrition Examination Survey	[41]
US race-free	0.73	0.97	Big data from laboratories from University of Washington Medicine System	[51]
China	0.62	0.88	27,830 healthy people	[40]

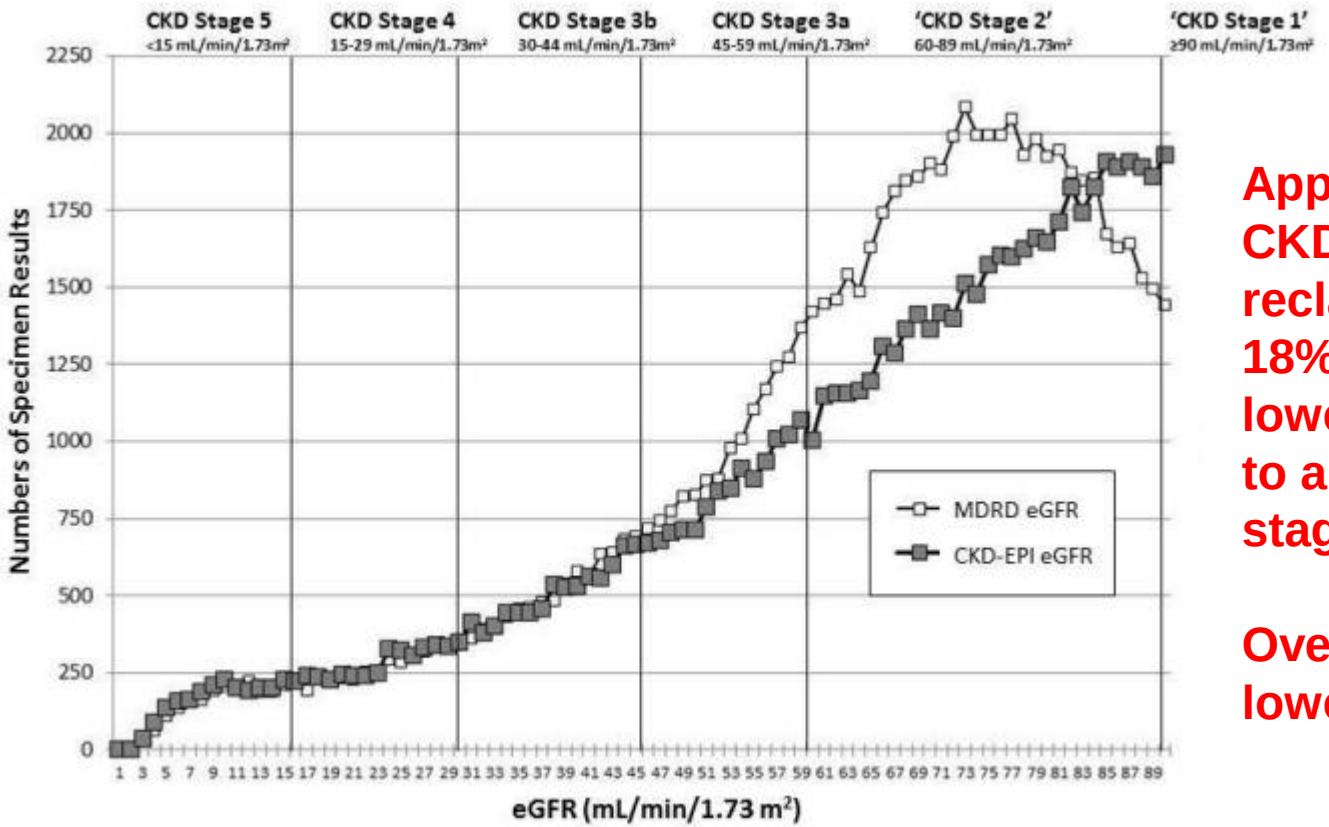
All results are expressed in mg/dL. Q values correspond to the median serum creatinine value observed either in extensive, general, and sex-specific data from laboratories or in more limited but phenotypically healthy well-defined groups. These Q values are only applicable to adult populations. Specific Q values according to age are required for populations younger than 18 years.

Nephron

Clinical Practice: Mini-Review Glomerular Filtration Rate Estimation in Adults: Myths and Promises Nephron DOI: 10.1159/000536243
Published online: January 12, 2024

Observations from a teaching hospital in Ireland: changing from MDRD to CKD-EPI eGFR in routine practice

Janice Lee Veronica Reeve ,[1] Marion Davis,[1] Patrick Joseph Twomey[1,2]



Application of CKD-EPI eGFR reclassified 18%: 13.9% to a lower and 4.0% to a higher CKD stage

Overall, 10% lower

Reeve JLV, Davis M, Twomey PJ. J Clin Pathol 2021;74:608–611.

The National Clinical Programme for Pathology

EGFR PRACTICE ADVICE NOTE

Recommendations for Calculation and Reporting of eGFR in the Laboratory

Issued in conjunction with the National Renal Office

Version 1 Issued 16/11/2023
CDI/0075/1.0/2023

The Association for Clinical Biochemistry & Laboratory Medicine

Better Science, Better Testing, Better Care

March 2015

Albumin-adjusted calcium: a position paper

One commonly used equation which continues to feature widely in popular medical textbooks (and therefore familiar to clinical staff) states:[6]

Adjusted calcium = total calcium + 0.02 [40- albumin]

(Where calcium units are mmol/L and albumin units g/L)

This equation was derived for a calcium O-cresophthalein complexone methods and a bromocresol green albumin method). However this equation maybe invalid when applied to calcium and albumin results generated by alternative assays.

Br Med J. 1973 Dec 15;4(5893):643-6. doi: 10.1136/bmj.4.5893.643.

Interpretation of serum calcium in patients with abnormal serum proteins

R B Payne, A J Little, R B Williams, J R Milner

PMID: 4758544 PMCID: PMC1587636 DOI: 10.1136/bmj.4.5893.643

In 1973, Payne *et al* proposed that adjustment of serum calcium should be based on correlation with albumin

With the advent of lab computers, the equation (with 0.025 subsequently rounded down to 0.02) became extensively used in laboratories, and entrenched as a reliable universal equation for all methods despite the authors' original caveats to the contrary.

Adjusted Calcium

Recommendation 6:

Laboratories should use locally derived equations specific to their calcium/albumin methods and analytical platforms rather than unvalidated literature derived equations.

It is necessary to exclude patients in whom there are other conditions that might affect calcium homeostasis.[5,8] The following patient groups with conditions that might influence calcium metabolism should be excluded:

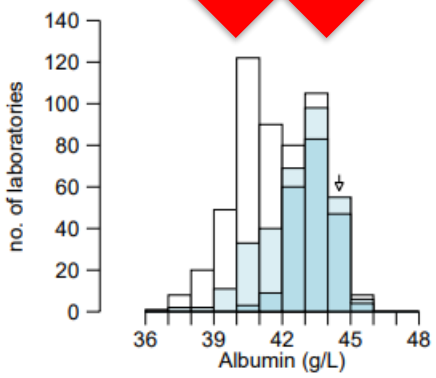
- Patients with renal impairment [creatinine > 200umol/L or urea >15mmol/L]
- Hypomagnesaemia [hypokalaemia as a surrogate marker i.e. K >3.5 and < 5.5mmol/L]
- Liver disease [ALT/ALP > upper reference limit]
- Total calcium concentration <2.0 and >2.7 mmol/L
- Hypo/hyperparathyroidism i.e. PTH outside the healthy population reference range
- Vitamin D deficiency
- Vitamin D toxicity
- Hypoadrenalism
- Patients on parenteral nutrition
- Patients with malignancy

Adjusted Calcium

Recommendation 9:

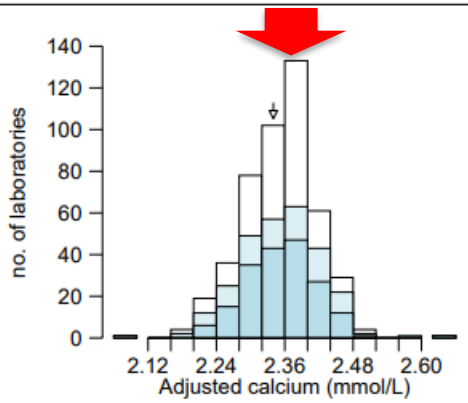
Laboratories reporting adjusted calcium should participate in an accredited External Quality Assurance scheme for adjusted calcium.

Specimen : 1105A	n	Mean	SD	CV(%)
Dry slide / Sensor	16	42.6	1.2	2.9
OCD slides [1JJ]	16	42.6	1.2	2.9
BCP	205	40.8	1.0	2.5
Abbott Alinity [12AB20]	46	41.2	0.6	1.5
Abbott Architect [12AB]	66	41.3	0.8	1.8
Roche Cobas [12BO]	55	39.8	1.0	2.6
Siemens ADVIA [12TE]	15	41.0	0.6	1.4
BCG	316	43.2	1.5	3.4
Abbott Alinity [13AB20]	9	41.1	1.0	2.3
Abbott Architect [13AB]	26	41.8	0.4	0.9
Beckman AU [13OL]	42	40.8	0.9	2.2
Roche Cobas [13BO]	206	43.8	0.9	2.1
Siemens ADVIA [13TE]	19	44.3	0.7	1.5



Your result	45
Target value (BCG)	43.2
Standard Uncertainty	0.1
Your specimen: %bias	+4.2 △
Accuracy Index	211
Method Principle mean [GLTM]	43.2
Method mean [MLTM]	43.8

Specimen : 1105A	n	Mean	SD	CV(%)
All methods [ALTM]	456	2.358	0.064	2.7
Dry slide / Sensor	13	2.349	0.032	1.4
Calculated BCP-based	174	2.357	0.056	2.4
Abbott Alinity [12AB20]	42	2.368	0.056	2.4
Abbott Architect [12AB]	52	2.323	0.062	2.6
Roche Cobas [12BO]	46	2.380	0.033	1.4
Siemens ADVIA [12TE]	13	2.353	0.082	3.5
Calculated BCG-based	278	2.358	0.069	2.9
Abbott Architect [13AB]	23	2.298	0.053	2.3
Beckman AU [13OL]	35	2.407	0.040	1.7
Roche Cobas [13BO]	188	2.358	0.063	2.7
Siemens ADVIA [13TE]	18	2.339	0.073	3.1

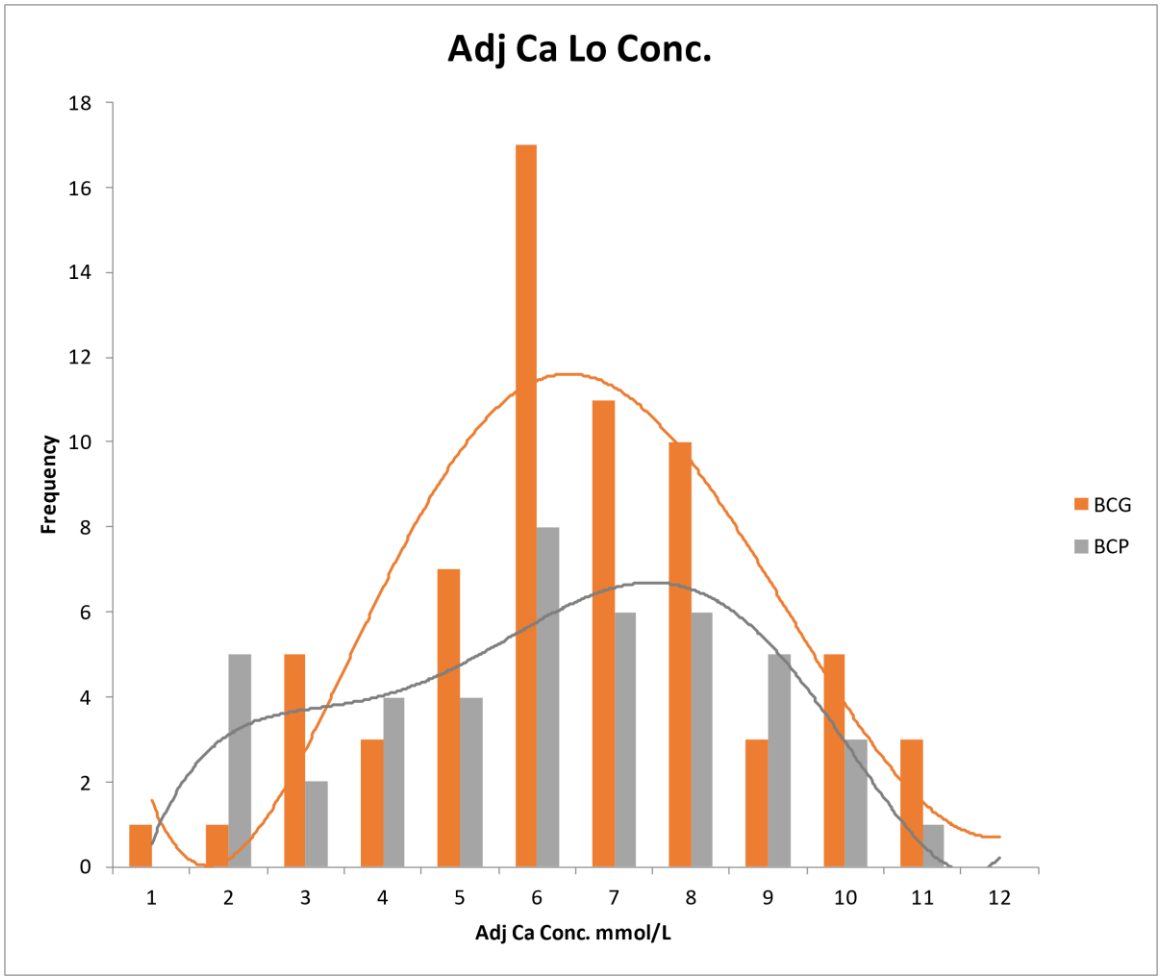


Your result	2.36
Target value (Calculated BCG-based)	2.358
Standard Uncertainty	0.005
Your specimen: %bias	+0.1 ◆
Accuracy Index	3
Method Principle mean [GLTM]	2.358
Method mean [MLTM]	2.358

Adjusted Calcium

Recommendation 9:

Laboratories reporting adjusted calcium should participate in an accredited External Quality Assurance scheme for adjusted calcium.



Adjusted Calcium

The use of online calculators will likely give different results to your labs!

Acute kidney injury programme – Think Kidneys

Acute Kidney Injury (AKI) Algorithm

Home › Acute kidney injury programme – Think Kidneys › Acute Kidney Injury (AKI) Algorithm

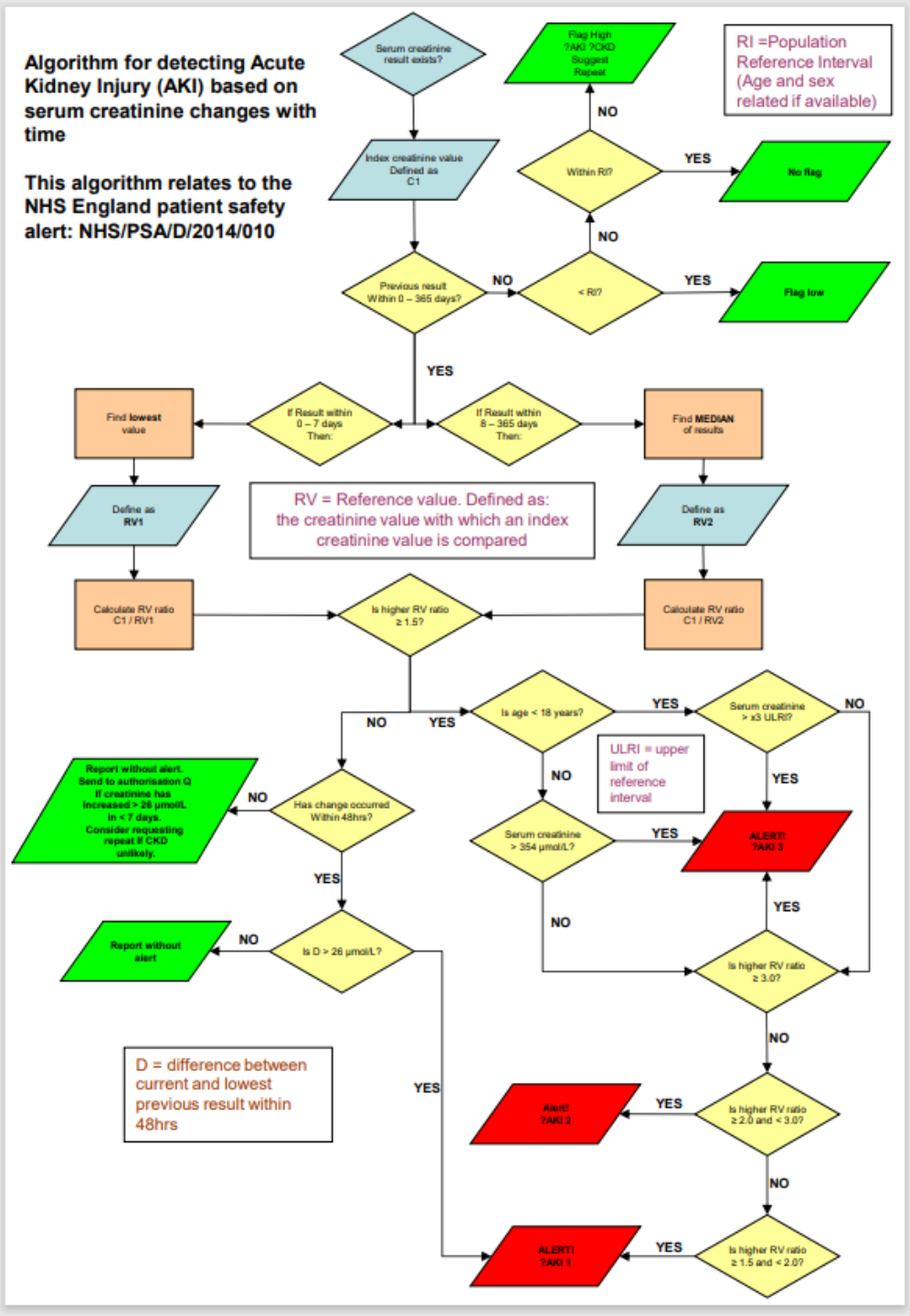
Acute Kidney Injury (AKI) Algorithm

A national algorithm, standardising the definition of AKI has now been agreed. This provides the ability to ensure that a timely and consistent approach to the detection and diagnosis of patients with AKI is taken across the NHS.

This algorithm has been endorsed by NHS England and it is recommended that the algorithm is implemented across the NHS. When integrated into a Laboratory Information Management System (LIMS) the algorithm will identify potential cases of AKI from laboratory data in real time and produce a test result. The laboratory system will then send the test result, using existing IT connections to patient management systems.

Downloads

- AKI algorithm
- AKI algorithm FAQs
- AKI patient safety alert
- Transmitting AKI warning stage data to the UK Renal Registry



-All creatinine results on the lab system irrespective of where requested or by whom

-Same alert for Primary and Secondary care

-NICE and lab computers had an incorrect version of the algorithm!

Alerting to acute kidney injury - Challenges, benefits, and strategies

Practical Laboratory Medicine 30 (2022) e00270

Josko Ivica [a,b], Geetha Sanmugalingham [c], Rajeevan Selvaratnam [d,e,*]

Table 2
Benefits and Challenges with e-alerts for AKI.

Benefits	Challenges
● Enables early detection and opportunities for intervention when uptake and response to alerts is timely. ● Some alerts systems (e.g. relying on simple sCr changes) are unsophisticated and easily deployable than others. ● Complex alert models enable physicians to harness siloed information from multiple databases such as lab and pharmacy for integrated decision making. ● Alerts enables data collection and surveillance of AKI, allowing analysis of alert triggers for the heterogeneous population of AKI. ● Potential for use as a quality metric when alert triggers are known to improve clinical outcomes or show impact on patient management.	● Alert fatigue (increased with lack of specificity or false positives). ● Ensuring assay precision within acceptable limits (i.e. $\leq$ 3.4%). ● Appropriate or necessary baseline measurement of sCr may not be available. ● Ensuring applicability by location specific delivery (e.g. consider dialysis or pregnancy related changes). ● Setup and/or maintenance cost in terms of human capital and other resources. ● Variable approaches to trigger e-alert, leading to lack of standardization in design of algorithms or models. ● Transferability of workflow design and processes across institutions (e.g. due to interoperability or resources). ● Dependence on retesting intervals or frequency of testing necessary biomarkers of interest. ● Some alert models are only informational. Unless tied to specific therapies or subsequent actionable items, this pasive nature may have little or no impact on patient care. ● Unproven clinical benefits or outcome measures in the US when using the KIDGO definition of AKI. ● Financial implications and return on investment after e-alert implementations remains unclear. ● Monitoring dismiss rates or acknowledgement rates may not be feasible with all approaches; However this information could be vital in understanding uptake and improving outcome.

AKI Alert UK algorithm

Beyond the algorithm for AKI detection, a consistent nationwide alert system seems like a challenge in North America and the studies published from the UK have generally shown to be beneficial from a detection and alerting standpoint [43,65,73,79–81]. Some studies as discussed below have also reported improved clinical outcomes [65,80,81].

Thu 02/12/2021 14:26

Feeney Eoin (Consultant)

Negative cholesterol

To McManus, Eimear (Senior Pharmacist)

Cc Twomey, Patrick (Biochemistry)

Follow up. Completed on 27 January 2022.
You forwarded this message on 27/01/2022 10:00.

Action Items

Hi Eimear

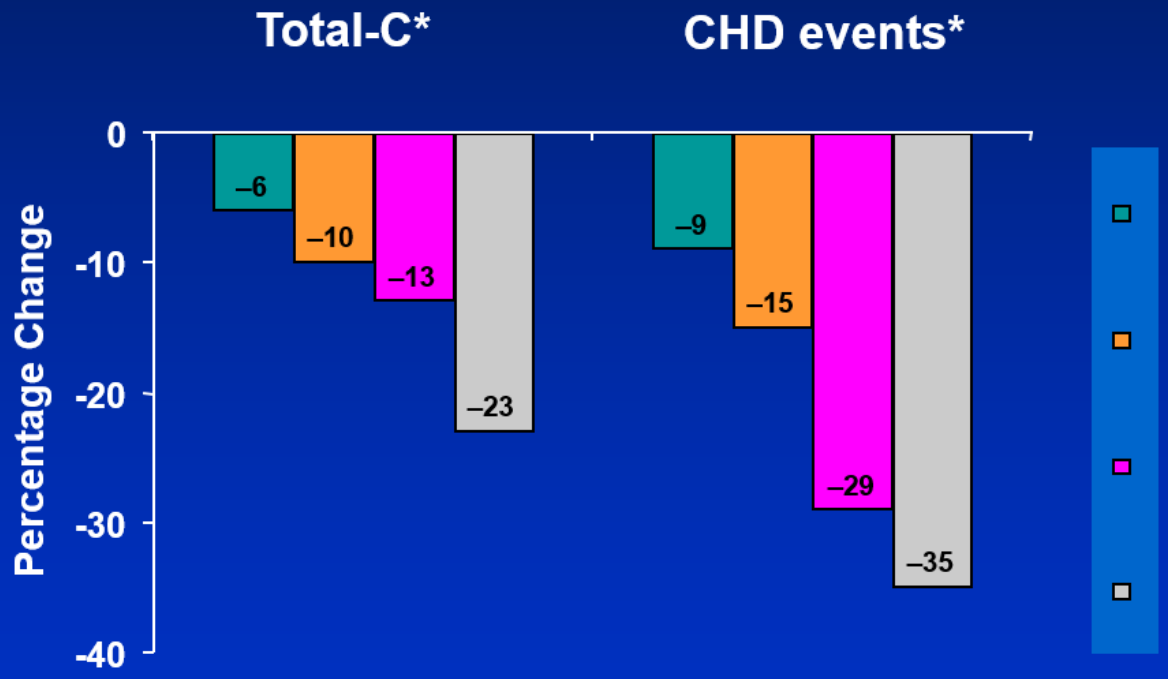
Can you email Pat Twomey and I back with the MRN of the patient with LDL -0.1?

Thanks

Eoin

The Friedewald equation for the calculation of LDL-C was developed in 1972!

Overview of Early Secondary Prevention Trials



CDP: clofibrate
n=8341; *P*=NS

CDP: niacin
n =8341; *P*=NS

Stockholm: clofibrate + niacin
n =555; *P*=NS

POSCH: partial ileal bypass
n =838; P<0.001

CDP, Coronary Drug Projects; NS, not significant; POSCH, Program on Surgical Control of the Hyperlipidaemias. *Net difference between treatment and control groups (*P* values are for events). Kwiterovich PO. *Am J Cardiol* 1998;**82**(12A):3U–17U.

Secondary Prevention Case

Date	TC	Trigs	HDL-C	cLDL-C	Ratio	Non HDL-C		Date	TC	Trigs	HDL-C	cLDL-C	Ratio	Non HDL-C
01/11/2022	3.73	1.02	1.64	1.62	2.3	2.09		**01/11/2022**	144	90	63		2.3	81
29/11/2022	4.14	2.2	1.62	1.51	2.6	2.52		**29/11/2022**	160	195	63		2.6	97
27/06/2023	3.88	1.02	1.58	1.83	2.5	2.3		**27/06/2023**	150	90	61		2.5	89

- Treatment to Target important
- Non HDL-C > LDL-C
  - Europe constant 0.8 mmol/L (30 mg/dL)
  - CCS 0.6-0.8 mmol/L proportional to concentration

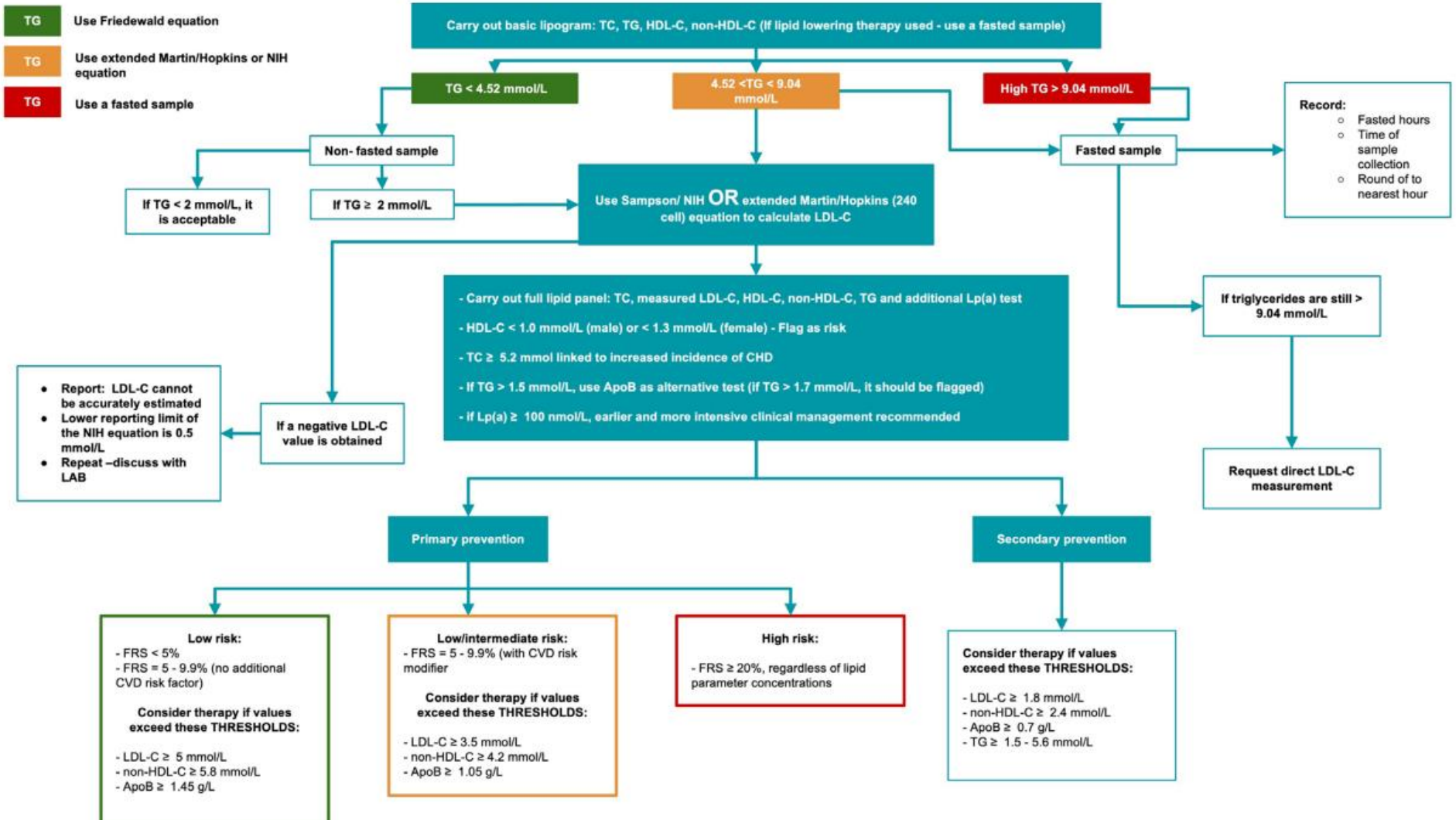
- Looking out for the discrepancies between cLDL-C and Non HDL-C give an insight into the effect of Triglycerides on the Friedewald equation
- 0.47, 1.01 and 0.47
- Trigs >1.5 mmol/L – 2021 CCS

2019 ESC/EAS Guidelines for the management of dyslipidaemia: lipid modification to reduce cardiovascular risk. Eur Heart J 41 (2020) 111-188.
https://doi.org/10.1093/eurheart/ehz455
Canadian Cardiovascular Society guideline for the management of dyslipidaemia for the prevention of cardiovascular disease in the adult. Can J Cardiol 37 (2021) 1129-1150.
https://doi.org/10.1016/j.cjca.2021.03.016

Best practice for LDL-cholesterol: when and how to calculate

Martins J, *et al. J Clin Pathol* 2023;**0**:1–8. doi:10.1136/jcp-2022-208480

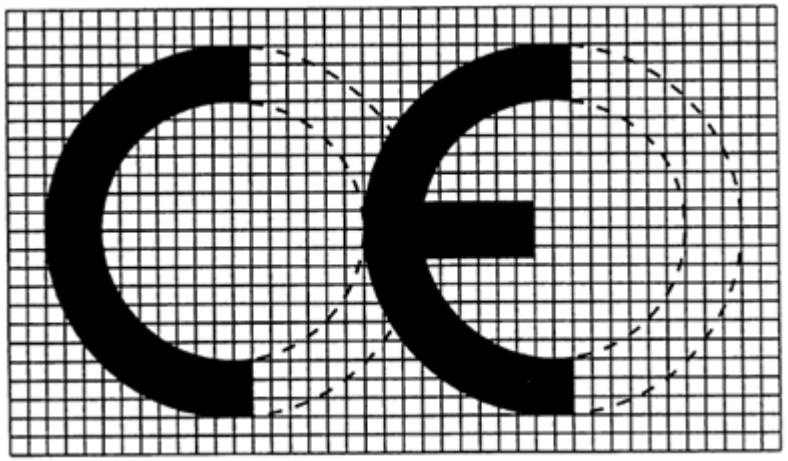
Janine Martins [1], Nicolene Steyn [1], H Muller Rossouw,[1] Tahir S Pillay [1,2]



Policy on calculated methods PS36

1. Purpose

The purpose of this document is to clarify INAB policy in the area of the accreditation of calculated methods.
The policy applies to all applicant and accredited testing laboratories (ISO/IEC 17025 and ISO 15189).



2. Statement

2.1. Calculated methods are considered a separate test method for the purposes of accreditation. A laboratory shall apply for accreditation for these types of tests in the same manner as with other test methods on their scope of accreditation.

2.2. Assessment of these test methods shall be completed in the same manner as the normal assessment processes in place (on site during surveillance visits, by correspondence, or added on using a flexible scope system if the laboratory is accredited for flexible scope).

2.3. The validation or verification of the method itself shall be fit for purpose.

2.4. In order for a calculated method to be reported as accredited all the constituent results used in the calculation shall also be accredited. This is to preserve the accreditation/traceability chain.

2.5. The laboratory may subcontract one or more of the constituent tests to another laboratory. If this is the case, the subcontracted laboratory shall also be accredited for the test in question.

2.6. In reporting a calculated method, the laboratory shall report the results of all of the constituent tests on the same report. This will include stating whether any of the constituent tests have been subcontracted and their accreditation status. This is to ensure transparency to the user of the results/report.

2.7. If it is not practical to report all constituent tests (due to the large numbers of tests involved) the report shall detail, at minimum, the list of tests that are subcontracted and also refer the user back to the laboratory for full details of all tests, if so required.

Uses of Tests/Calculations

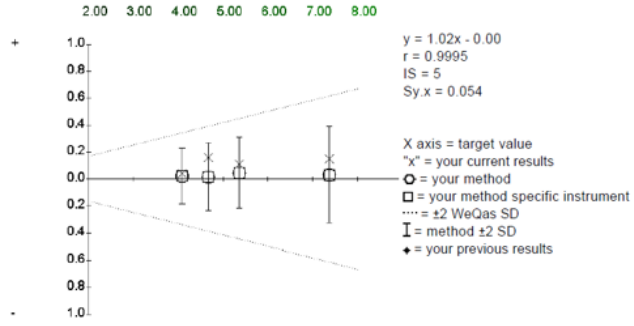
- (Targeted) Screening
- Case finding
- Diagnosis
- Prognosis
- Monitoring/Management

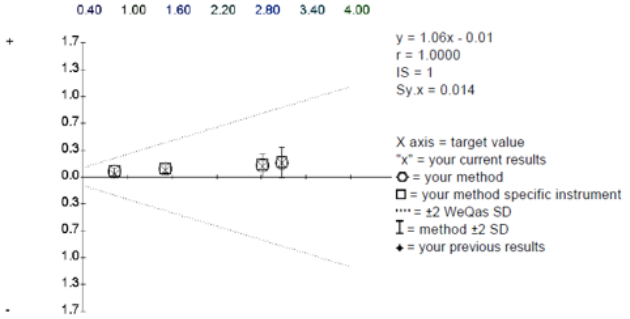
Calculations

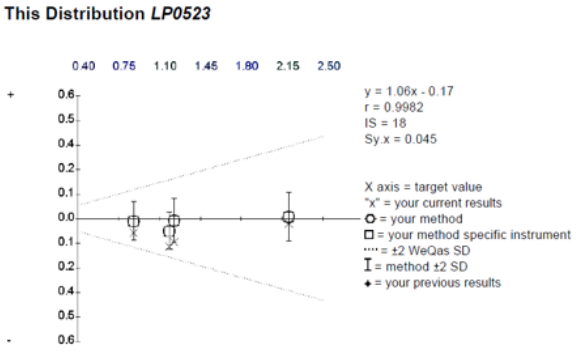
Even though IVD producers sells A & B assays, they sell 2 separate assays and issues relating to the calculation of the ratio is often not their responsibility

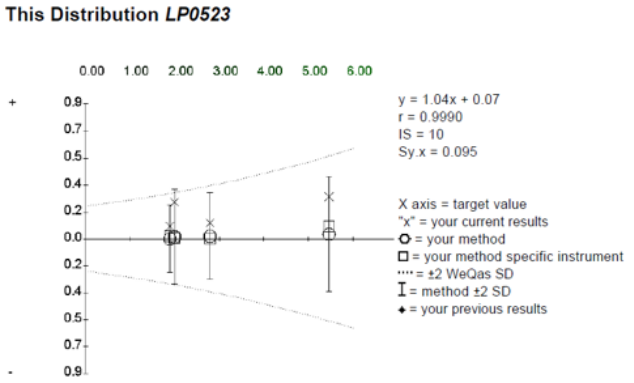
Change	10%	5%		5%	10%
Method A	11	10.5	10	9.5	9
Method B	0.9	0.95	1	1.05	1.1
A/B	12.22	11.05	10.00	9.05	8.18

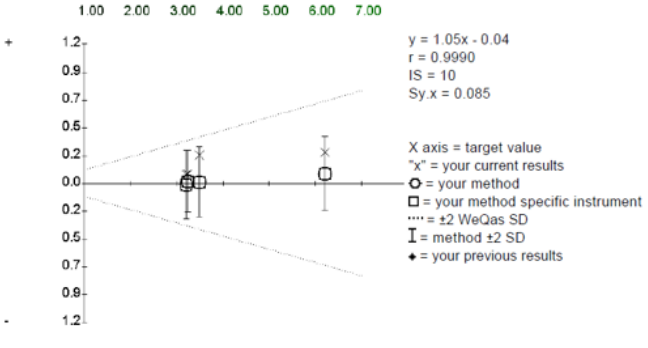
External Quality Assurance











Weqas

Unit 6, Parc Ty Glas
Llanishen, Cardiff
CF14 5DU
office@weqas.com
Scheme Organiser:
Annette Thomas

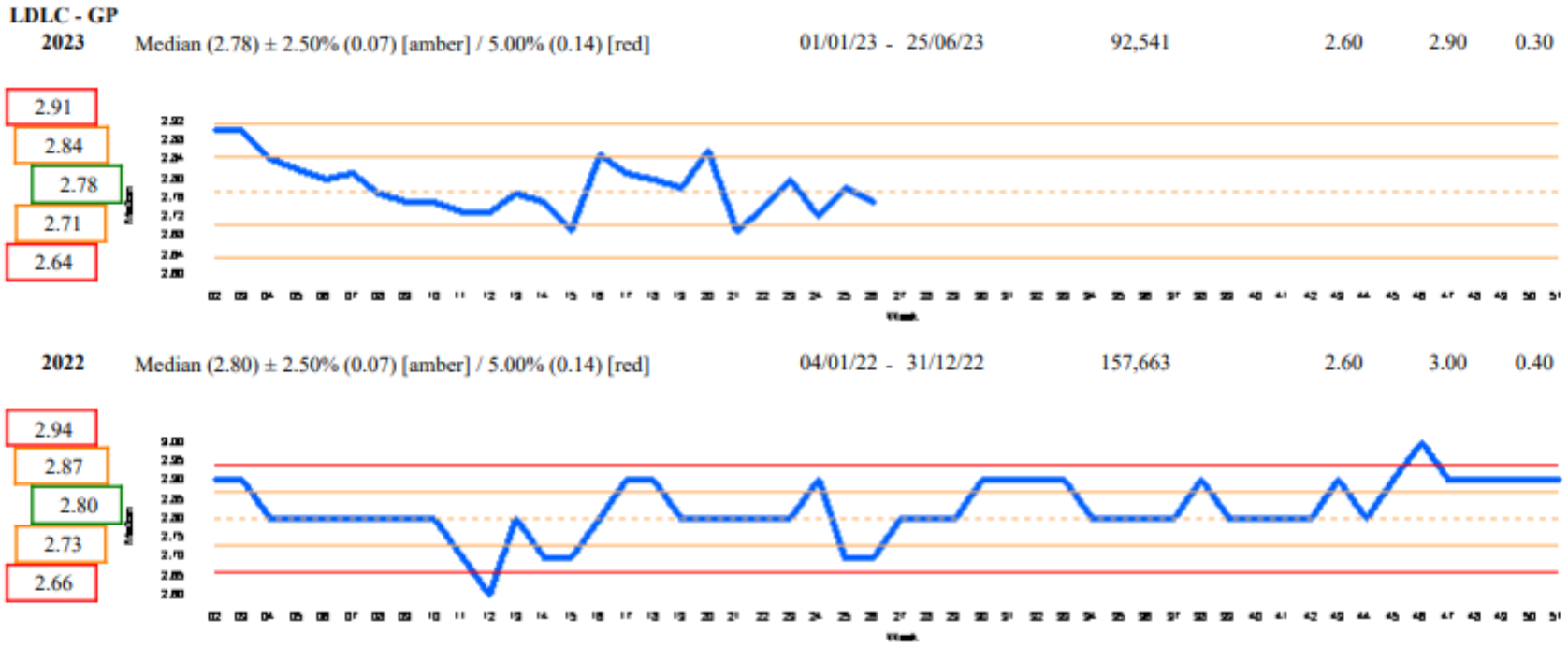
External Quality Assurance

Section SDI scores for this distribution

Section	Line 2 (7788)	Line 3 (788)	Line 4 (78)
Overall	**0.61**	**0.97**	**0.58**
Cholesterol	0.50	0.95	0.38
Triglyceride	0.32	0.47	0.45
HDL Cholesterol	0.72	0.86	0.82
LDL Cholesterol	0.87	1.40	0.71
Non-HDL Cholesterol	0.63	1.17	0.56

All SDI Ranges	
< 1	Good
1 - 2	Acceptable
> 2	Poor

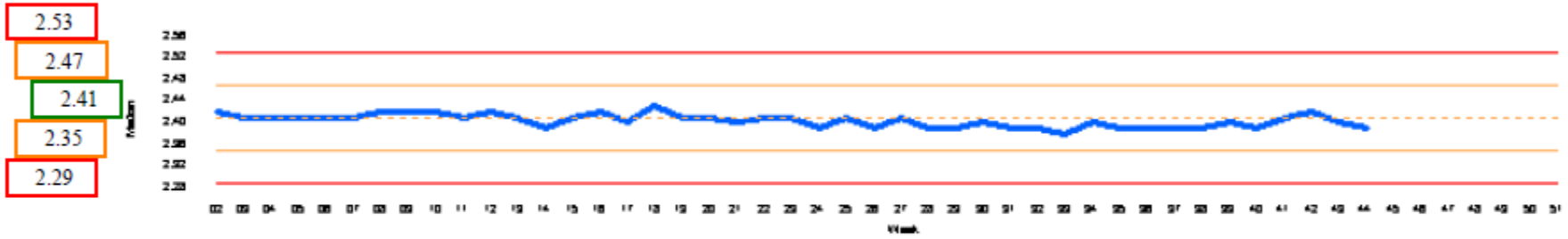
Primary care data for calculated LDL-C



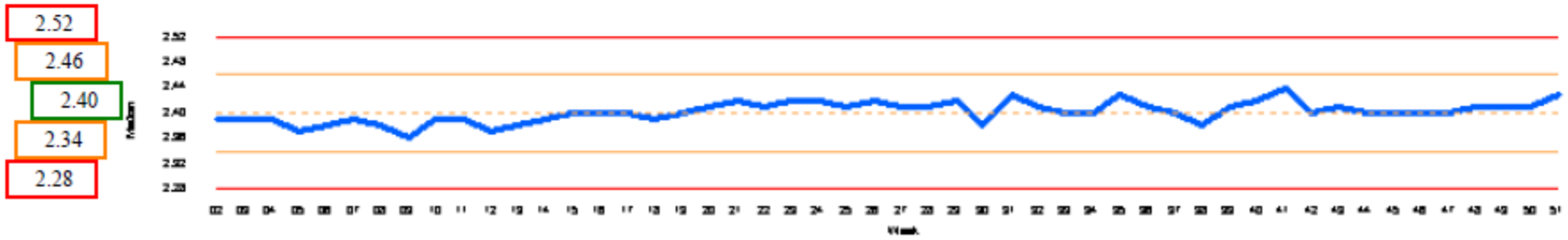
Primary care data for adjusted Calcium

Weekly Median Data

Code	Metric and Limit Span	Data Range		Results	Min	Max	Range
3 - Calcs							
ACA - GP							
2024	Median (2.41) ± 2.50% (0.06) [amber] / 5.00% (0.12) [red]	08/01/24 - 02/11/24	Patient	115,337		4.24	
			Median		2.38	2.43	0.05



2023	Median (2.40) ± 2.50% (0.06) [amber] / 5.00% (0.12) [red]	02/01/23 - 17/12/23	Patient	122,788		3.13	
			Median		2.36	2.44	0.08



Uses of Tests/Calculations

- (Targeted) Screening
- Case finding
- Diagnosis
- Prognosis
- Monitoring/Management
- Variation
  - Between hospitals
  - Over time - ? What is a significant change

The Future

Even more calculations!

	2023
Analysed	10,195,670
Calculated	2,813,200
Indices	1,868,757
Total	14,877,627

-FIB-4 Index since added

-updated calculated LDL-C (but hopefully users will not notice this change)

- KFRE to be looked at

Fibrosis-4 (FIB-4) Index for Liver Fibrosis ☆

Noninvasive estimate of liver scarring in HCV and HBV patients, to assess need for biopsy.

When to Use ⌄ | Pearls/Pitfalls ⌄ | Why Use ⌄

Age
Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients

[ ] years

AST
Aspartate aminotransferase

Norm: 15 - 41 U/L

ALT
Alanine aminotransferase

Norm: 1 - 35 U/L

Platelet count

Norm: 150 - 350 × 10^3/µL ⇆

Result:

Please fill out required fields.

» Next Steps | Evidence | Creator Insights

FIB 4

St Elsewhere

FIB-4 SCORE

FIB-4 Score	6.0

FIB-4 Calculation is for patients with NAFLD/NASH (fatty liver) where other causes of chronic liver disease have been excluded with liver screen.
Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients.
Advise refer to Hepatology for Fibroscan if patient with NASH have FIB-4 >1.3 (age 35-64) or >2.0 (age >65).
If FIB-4 score does not require referral please monitor 3 yearly and manage life-style risk factors for NASH.

To be decided

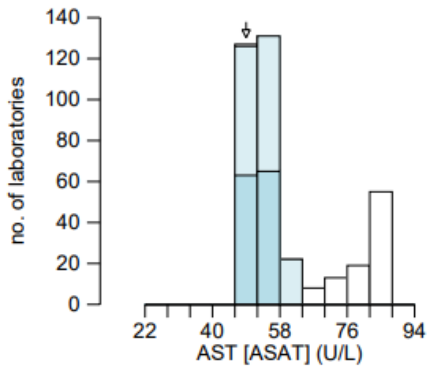
What age range?

Limit on ALT or AST level?

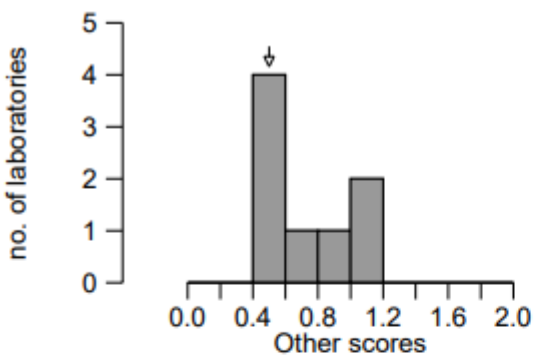
Limit on Platelet level?

Pathway

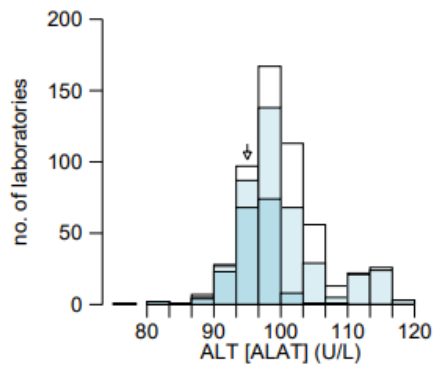
FIB 4 – site differences



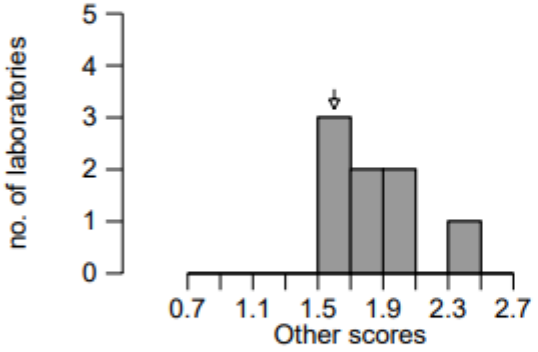
Your result	51
Target value (Roche Cobas [4BO])	52
Standard Uncertainty	0
Your specimen: %bias	-2.7
Accuracy Index	77
Method Principle mean [GLTM]	53
Method mean [MLTM]	52



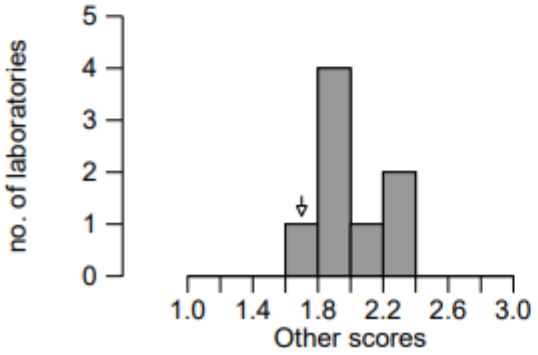
Your result	0.44
Your target	0.7
Your deviation (%)	-32.8
Standard Uncertainty	0.18



Your result	95
Target value (Roche Cobas [4BO])	96
Standard Uncertainty	0
Your specimen: %bias	-1.1
Accuracy Index	25
Method Principle mean [GLTM]	100
Method mean [MLTM]	96



Your result	1.57
Your target	1.8
Your deviation (%)	-11.5
Standard Uncertainty	0.14

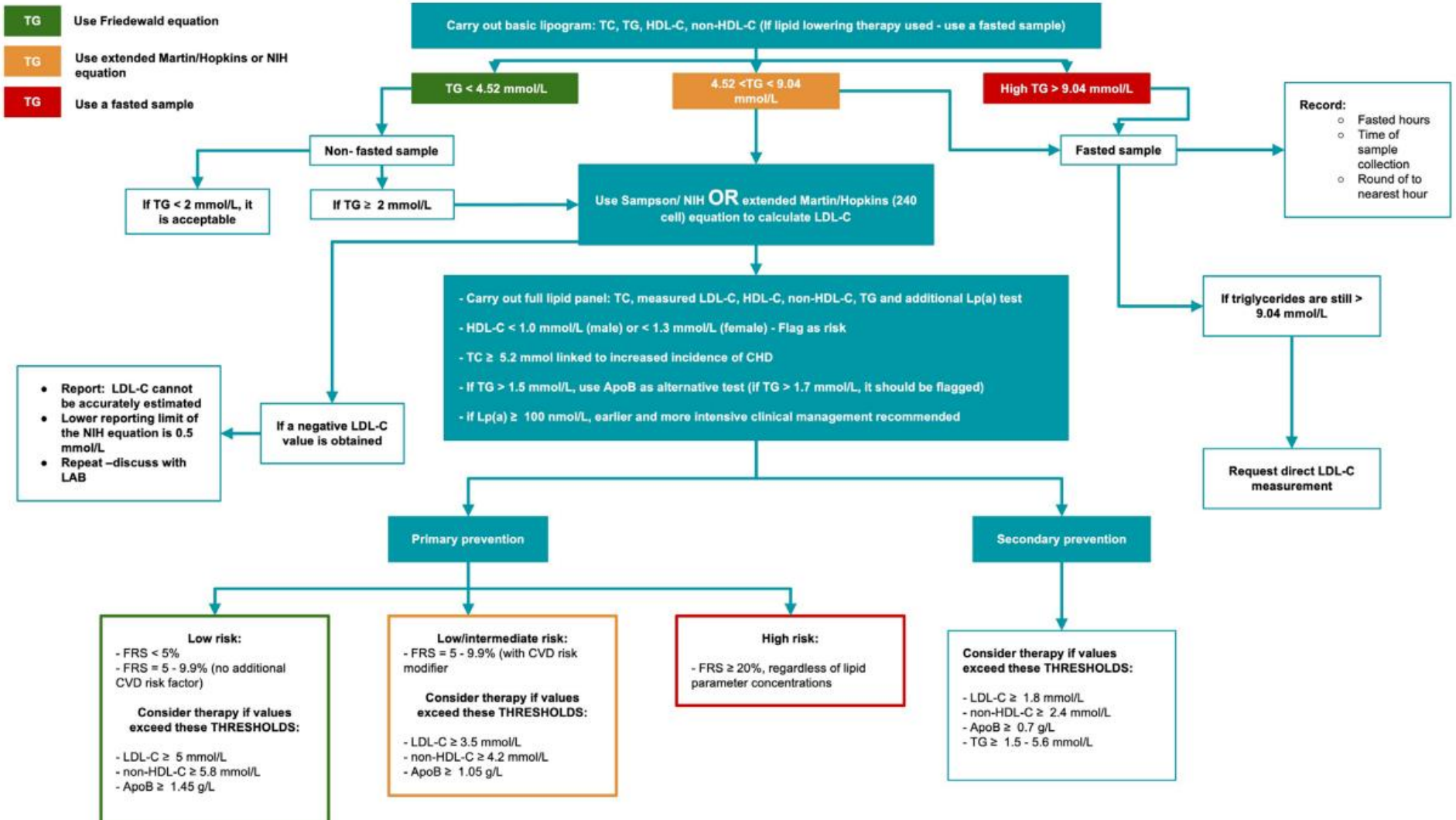


Your result	1.72
Your target	2.0
Your deviation (%)	-14.2
Standard Uncertainty	0.13

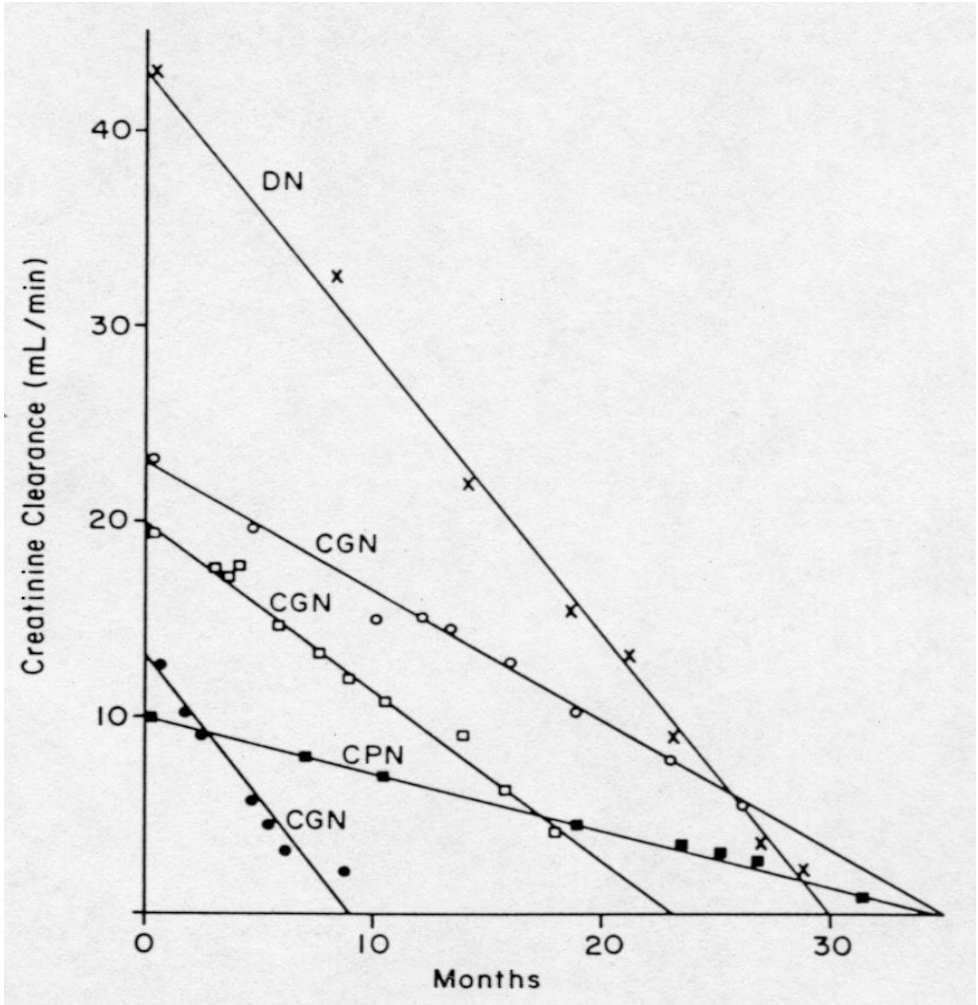
Best practice for LDL-cholesterol: when and how to calculate

Martins J, *et al. J Clin Pathol* 2023;**0**:1–8. doi:10.1136/jcp-2022-208480

Janine Martins [1], Nicolene Steyn [1], H Muller Rossouw,[1] Tahir S Pillay [1,2]



Importance of Serial Monitoring



Diabetic Nephropathy (DN)

Chronic Glomerulonephritis CGN)

Chronic Pyelonephritis (CPN)

Kidney Failure and the Kidney Failure Risk Equations (KFRE): What You Need to Know

What is kidney failure?

Kidney failure happens when your kidneys stop working. At this point, you need to choose a treatment that replaces lost kidney function, such as dialysis or kidney transplant. Or, you may choose medical care alone, without dialysis or transplant. You may also choose no treatment.

What are the Kidney Failure Risk Equations (KFRE)?

The KFRE are math equations that can predict how high or low your chance (risk) is for reaching kidney failure within the next 2-year and 5-year points in time. Results are given as a percent (%) on a scale of less than 1% to 99.99%. For example, a result of 1% chance of reaching kidney failure within 2 years, with a 5% chance at 5 years, is considered low.

The KFRE use specific information about you and your health called **variables**. Some variables such as **age** and **gender** can't be changed, so they're called *non-modifiable* variables.

However, other variables such as **phosphorus** and **urine albumin-to-creatinine ratio (UACR)** *can* be improved to lower your chances of reaching kidney failure, or to prolong the time it takes to reach kidney failure. These variables are *modifiable* because they can improve with the right care.

By studying the health information of more than 700,000 patients with **chronic kidney disease (CKD)** in 30 countries around the world, experts found which variables increase a person's chances for reaching kidney failure. These variables are listed below. By clicking a variable, you'll be taken to a page with more information about how it fits into the KFRE and how it might be improved to lower your chances of reaching kidney failure, or at least prolong the time it takes to reach kidney failure.

The Future

Even more calculations!

-Specialist external tests such as urine steroid panels will have more calculations (formally or informally) to help pick up rare diseases

-Mass Specs produce more data

-AI will add to this

CONCLUSION

Calculations have their limitations

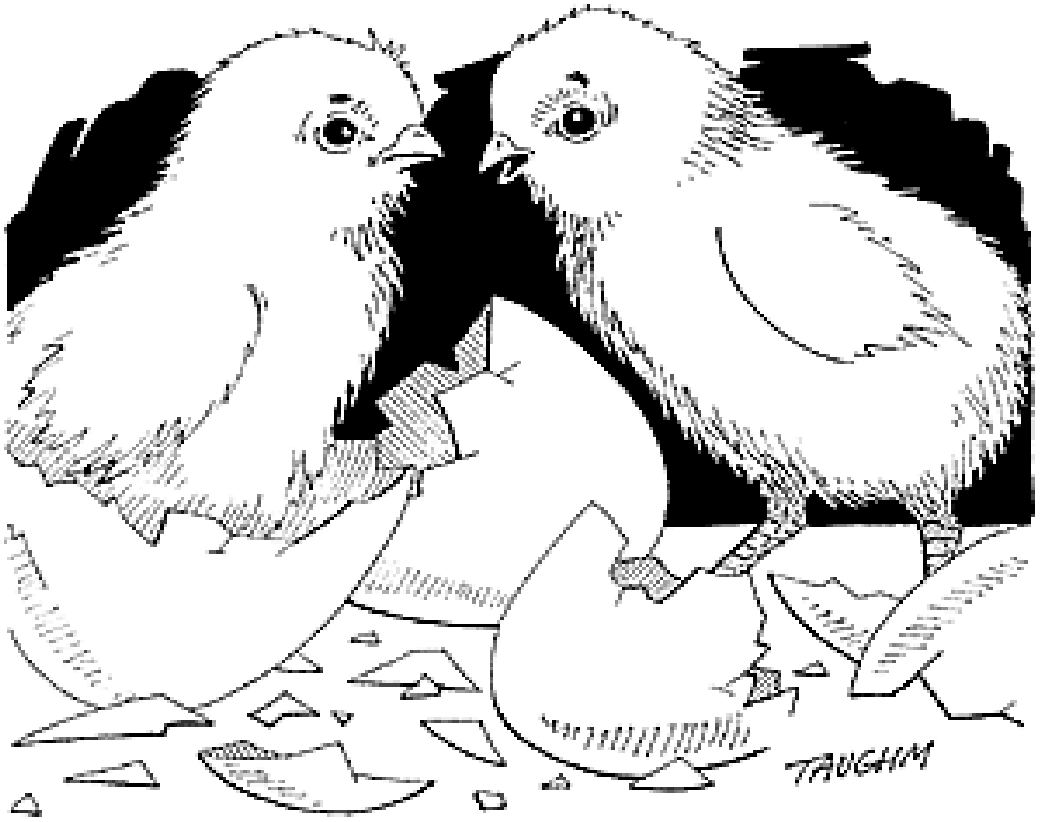
The correct equations need to be used

Results will differ due to method associated differences

The laboratory computer system ideally should be employed for calculations that use lab data

Working with colleagues at the coal face is essential to minimise unintended consequences

THANK YOU



"Whew! I'm glad that's over - all that cholesterol was killing me!"