Synnovis
Blood Sciences Laboratories

15th September 2023

Dear Laboratory user,

Re: Changes to lab reporting with EPIC from 5th October 2023

We are writing to inform you that from **05/10/23**, the Synnovis Blood Sciences Laboratories at Guys and St Thomas' and King's College Hospital Denmark Hill sites will be making changes to some tests with the introduction of the new Epic electronic health records system and Beaker the new LIMS**.** In all cases no changes to the analytical methodology or UKAS accreditation will occur. These changes are summarised below:

Biochemistry Changes: KCH Denmark Hill Laboratories

New reference intervals.
Following an internal review of some of our reference intervals, the below tests will have the following changes.

Test	Current Reference Interval(s)	New Reference Interval(s)
Aspartate transaminase, AST (U/L)	10-77 (<2y) 8-43 (3-6y) 7-36 (7-13y) 3-35 (14-18y) 5-38 (19y+ PRUH) 10-50 (19y+ DH)	40-175 (<15d) 28-77 (15d-1y) 24-48 (1-7y) 20-42 (7-12y) 16-36 (12-19y M) 13-29 (12-19y F) 10-50 (19y+ M) 10-35 (19y+ F)
Alanine transaminase, ALT (U/L)	5-55	7-36 (<1y) 9-26 (1-13y) 9-33 (13-19y M) 7-25 (13-19y F) 10-50 (19y+ M) 10-35 (19y+ F)
Creatine Kinase, CK (U/L)	<150 (DH) 25-175 (M) (PRUH) 25-150 (F) (PRUH)	40-320 (M) 25-200 (F)
Conjugated bilirubin (DH only) (µmol/L)	0-4	<7
Transferrin Saturation (%)	15-56 (PRUH) 20-50 (DH)	20-45
Adjusted calcium (mmol/L)	2.15-2.60	2.20-2.60

New equations for three calculated tests

The below tests will be calculated using different formula to previous and so cannot be trended pre and post EPIC go live.

Test	Current formula	New formula
Estimated Glomerular Filtration Rate (eGFR)	4v MDRD (minus ethnicity)	CKD-EPI (2009) minus ethnicity
Adjusted calcium	Calcium (mmol/L) + ((42 – albumin [g/L])/50) (PRUH) Calcium (mmol/L) + 0.02(40 – albumin [g/L]) (DH)	Ca (mmol/L) - 0.016(Alb [g/L] - 45.8)
LDL cholesterol	Friedewald	Sampson NIH2

(i) Change to eGFR calculation explained

The NICE Chronic kidney disease: assessment and management [NG203] 2021 guidelines recommend the use of the CKD Epidemiology Collaboration creatinine (CKD-EPI) equation to estimate GFR. Until now we have used the 4 variable Modification of Diet in Renal Disease (MDRD) formula (without the ethnicity factor, which was removed from the calculation in November 2021). Several studies have shown that the MDRD equation systematically underestimates the GFR, particularly in low-risk patients with a high-normal serum creatinine level. This results in the labelling of some people with CKD who do not have significant kidney disease, particularly in the earlier stages of CKD.

As a result of this change in equation please be aware of the following:

- The new equation will more accurately assess eGFR, reducing the over-diagnosis of CKD in low-risk patients and improving diagnostic performance in patients aged over 80 years.
- Serum creatinine results are not affected by this change and will continue to be comparable over time. If the creatinine has not changed significantly, then true renal function will not usually have altered and any eGFR change can be attributed to the change in equation. Likewise, a change in creatinine that is significant could be masked by a seemingly stable eGFR.

(ii) Change to adjusted calcium equation explained

The new equation was derived using inpatient data obtained from DH & PRUH sites. This was following a position paper (2015) by The Association of Clinical Biochemistry which recommends that laboratories derive equations specific to their calcium and albumin methods and analytical platforms, rather than using literature-derived equations. The new equation is therefore based on our patient population and analytical methods currently used across KCH laboratories and aligns results across KCH sites. The new equation has a small (<0.1 mmol/L) positive bias compared to the previous ones in use but this equation verifies the upper reference interval of 2.60 mmol/L i.e. our data matches the reference interval.

(iii) Change to calculated LDL equation explained

LDL cholesterol has historically been calculated using the Friedewald equation, however, this has several limitations and is not valid in samples with triglycerides >4.5 mmol/L. The Sampson-National Institutes of Health 2 equation is more accurate than the Friedewald

equation, particularly in patients with low LDL, and can also be used with triglycerides up to 9 mmol/L.

Change to HbA1c reporting

HbA1c results will no longer be accompanied by interpretative comments except for if the patient has an active pregnancy encounter in EPIC. Additionally, in the rare instances in which we are unable to report HbA1c result using our Roche c513 method, we will no longer be referring these samples for analysis by an alternative methodology. This is based on internal data which demonstrated that HbA1c is not indicated in these instances (e.g. patients with altered red cell turnover).

New tests available to order

Test
Fibrosis-4 (FIB-4) Index (calculation)

FIB-4 which uses age, AST, ALT, and platelet count is a non-invasive test for diagnosing advanced fibrosis in non-alcoholic fatty liver disease (NAFLD). It has been developed to assess the risk of cirrhosis in people with hepatitis C and non-alcoholic steatohepatitis (NASH).

Acute Kidney Injury (AKI) reporting

With the introduction of EPIC on the 5th October 2023; it will not possible for us to report an AKI status on all patients based on the first renal profile (creatinine) we process. This is due to Primary Care legacy lab data not being migrated to EPIC. You are advised to monitor AKI risk using your own historical creatinine data.

We will be able to report AKI on any subsequent samples received and, in line with the abnormal/critical telephoning limits guidance, we would notify the requester with any AKI stage 2 or 3 flags.

For Acute Kidney Injury Warning Algorithm Best Practice Guidance, please refer to; 2020-AKI-Warning-Algorithm-Best-PracticeGuidance-2018FINAL.pdf (thinkkidneys.nhs.uk)

Changes to critical phoning limits with EPIC.
The full list is available at www.synnovis.co.uk/kch.

Test	Current phone limit	New phone limit
Adjusted calcium (mmol/L)	≤ 1.80 & ≥ 3.00	≤ 1.80 & ≥ 3.40
AST (U/L)	≥ 1155 (0-2y) ≥ 645 (3-6y) ≥ 540 (7-13y) ≥ 525 (14-18y) ≥ 750 (19y+ DH) ≥ 570 (19y+ PRUH)	≥ 500 (<19y) ≥ 525 (19y+ F) ≥ 750 (19y+ M)
ALT (U/L)	≥ 825	≥ 500 (<19y) ≥ 525 (19y+ F) ≥ 750 (19y+ M)

Should you have questions related to these changes please do not hesitate to contact us.

Yours faithfully,

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Biochemistry: GSTT Laboratories

Changes to units

Test	Current Units	New Units
Total Urine Protein	g/L	mg/L
Macroprolactin	Percentage recovery (%) and bioactive monomeric prolactin (mIU/L)	Monomeric prolactin (mIU/L)

New comments

Test	Previous Comment	New Comment
Urine albumin to creatinine ratio (ACR)	NICE CG182 (2014): KDIGO ACR categories in CKD: Normal < 3 Microalbuminuria 3-30 Macroalbuminuria >30	NICE CKD Guidelines NG203: < 3 mg/mmol: normal to mildly increased 3-30 mg/mmol: moderately increased >30 mg/mmol: severely increased
AKI 2 & 3	N/A	Rise in creatinine may indicate Acute Kidney Injury stage (1, 2 or 3). This patient needs to be reviewed urgently. If AKI exists and clinically appropriate please initiate and complete the AKI Pathway (Pathway 2407) as soon as possible.

Macroprolactin	• If monomeric prolactin above reference interval but prolactin recovery ≤60%: **First screen**: suggest repeat to confirm and also request immunoglobulins to exclude rare but possibly confounding effect if they are elevated **Second screen:** This confirms previous positive/equivocal screens on xx.xx.xx. Macroprolactin should be requested whenever prolactin is measured on this patient and the estimated bioactive prolactin used for interpretation.	• If monomeric prolactin above reference interval but prolactin recovery ≤60%: After removal of macroprolactin complexes the estimated monomeric prolactin is above the reference interval. Other causes for hyperprolactinaemia should be investigated.
	• If monomeric prolactin above reference interval but prolactin recovery ≥ 60%: Macroprolactin not detected. The significantly raised prolactin level therefore needs further investigation for both secondary and primary causes.	• If monomeric prolactin above reference interval but prolactin recovery ≥ 60%: No significant amount of macroprolactin complexes present thus the estimated monomeric prolactin result is elevated. Other causes for hyperprolactinaemia should be investigated.
	• Monomeric prolactin within/above reference interval: This is not elevated	• If monomeric prolactin within reference interval: After removal of macroprolactin complexes the estimated monomeric prolactin is within the reference interval. No further investigation is required.
Macroprolactin – if reflexed more than once within a 12 month period	N/A	If the previous result had no significant macroprolactin present the test will be cancelled with the following comment: Test cancelled. Macroprolactin screen not required as previously analysed within last 12 months and found to have no significant macroprolactin present.

New reference intervals

Following an internal review of some of our reference intervals, the below tests will have the following changes.

Test	Current Reference Interval(s)	New Reference Interval(s)
Transferrin saturation (%)	N/A - previously risk related comment: Please note new Abbott transferrin saturation results are not trendable compared to pre-Nov 22. This is a calculated test that now uses direct measurement of transferrin compared to previous use of total iron binding capacity. Transferrin saturation (>45% females, >50% male) with a raised ferritin (>200 mg/L in females, >300 mg/L in males) suggests iron overload (EASL 2010 HFE Hemochromatosis).	20-45
High sensitive Troponin I (ng/L)	No previous paediatric reference ranges Male >19 years: <35 Female >19 years: <16	0 to <6 months: <55.8 6 months to <19 years:<5.5 Male >19 years: <35 Female >19 years: <16
NT pro BNP (ng/L)	No previous paediatric reference ranges	0 to < 1 year: 29.6-1594.0 1 to < 19 years: 11.0-214.0

New equations for three calculated tests

The below tests will be calculated using different formula to previous and so cannot be trended pre and post EPIC go live.

Test	Current formula	New formula
Estimated Glomerular Filtration Rate (eGFR)	4v MDRD	CKD-EPI (2009) minus ethnicity [NG203]
Adjusted calcium	Payne	James
LDL cholesterol	Friedewald	Sampson NIH2

(iv) *Change to eGFR calculation explained*

The NICE Chronic kidney disease: assessment and management [NG203] 2021 guidelines recommend the use of the CKD Epidemiology Collaboration creatinine (CKD-EPI) equation to estimate GFR. We will use the 2009 CKD-EPI and not 2021 as this has not been validated in a UK population. Until now we have used the 4 variable Modification of Diet in Renal Disease (MDRD) formula. Several studies have shown that the MDRD equation systematically underestimates the GFR, particularly in low-risk patients with a high-normal serum creatinine level. This results in the labelling of some people with CKD who do not have significant kidney disease, particularly in the earlier stages of CKD.

As a result of this change in equation please be aware of the following:

- The new equation will more accurately assess eGFR, reducing the over-diagnosis of CKD in low-risk patients and improving diagnostic performance in patients aged over 80 years.
- Serum creatinine results are not affected by this change and will continue to be comparable over time. If the creatinine has not changed significantly, then true renal function will not usually have altered and any eGFR change can be attributed to the change in equation. Likewise, a change in creatinine that is significant could be masked by a seemingly stable eGFR.

(v) Change to adjusted calcium equation explained

The Payne equation used to calculate adjusted calcium was derived using a bromocresol green (BCG) method for albumin measurement. A clinical review was prompted when the albumin method changed to bromocresol purple (BCP) following the introduction of the Abbott Allinity analysers (November 2022). This review showed that the BCG Payne based formula is not suitable for use with BCP-based albumin methods unlike the James equation which has been externally validated on BCP-based albumin methods as well as on internal GSTT patient data.

(vi) Change to calculated LDL equation explained

LDL cholesterol has historically been calculated using the Friedewald equation, however, this has several limitations and is not valid in samples with triglycerides >4.5 mmol/L. The Sampson-National Institutes of Health 2 equation is more accurate than the Friedewald equation, particularly in patients with low LDL, and can also be used with triglycerides up to 9 mmol/L.

Changes to critical phoning limits

Test	Previous limits	New limits
AKI alerts 2 & 3	N/A	All AKI alerts 2 & 3 will be phoned

Just as a reminder the following reference ranges were changed November 2022 when we went live with the Abbott Alinity analysers and will not be changing.

Test	Reference range
Albumin (g/L)	0 to 4 days: 28-44 4days to 14 years: 38-54 15-59 years: 35-50 60-90 years: 32-46 >90 years: 29-45
Alanine transaminase (U/L)	0-55

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FBC Haematology Changes: GSTT Laboratories

What is happening and when?

New full bood count (FBC) analytical instruments are being installed in Guy's and St Thomas' hospitals.

The service will swap to the new FBC analysers on 5 October 2023 alongside the introduction of Epic, the new Electronic Health Record (EHR). While the project has been carefully planned to cause minimal disruption, there are some minor planned delays during the swap out.

Will there be any disruption to services?

There will be a disruption to the service overnight on 4 October which we anticipate will be up to 5 hours, resulting in a delay in issuing results of up to 1 hour. The laboratory team will prioritise all urgent samples during this period. Following this planned disruption, the service will return to business as usual although there may be some disruption to the service while the new instruments are fully embedded. We will continue to communicate with you throughout the transition.

How have the new reference ranges been generated?

The new paediatric full blood count reference ranges (<12 years old), including the age groups have been extracted from Dacie and Lewis Practical Haematology (12th edition) By B. J. Bain, I. Bates and M. A. Laffan, Elsevier, London, 2017.

The adult reference ranges (>12 Years old), were obtained by testing more than five hundred GP patient samples in the new haematology analysers. Samples were collected in the phlebotomy department at St Thomas' Hospital and tested within 2 hours from collection. The aim was to assess a "near normal" population using specific criteria based on the patient's clinical details. The new reference ranges have also embedded the feedback from the Haematology Clinical Leads from GSTT, KCH and PRUH and reflect the clinical requirements for adequate patient management.

Table of changes	Current GSTT	Changes GSTT
Haemoglobin (Adult Male)	130 - 170 g/L	125 – 170 g/L
Haemoglobin (Adult Female)	120 – 150 g/L	115 – 148 g/L
Lymphocyte counts (Adults Male & Female)	1.2 - 3.5 x 10^9 /L	0.80 - 3.50 x 10^9
White Blood Cell (WBC)		White Blood Cell (WBC) differential count reported with 2 decimal places
Eosinophil count high resolution test		Eosinophil count high resolution test will not be available any more as the FBC will report the Eosinophil count with 2 decimal places.
Neutrophil Counts		Neutrophil counts below 1.5x 10^9/L will trigger the following message: *Normal neutrophil counts in healthy people with family origins from Africa may be lower than 1.5 x 10^9 /L.* This will act as a reminder for the ethnic differences of Neutrophil counts.
Paediatric reference range changes		With enhanced age group stratification, this will allow more comprehensive and adequate reference ranges for patients under 12 years old.
Age group parameters	• 1 Day • 3 Months • 6 Months • 1 Year • 6 Years • 13 Years >13 years *For some FBC parameters, the age groups differ slightly.	• Birth (0 days) • Day 3 • Day 7 • Day 14 • 1 Month • 2 Months • 3 – 6 Months • 1 Year • 2 – 6 Years • 6 – 12 Years • >12 Years
Other new parameters		• MCHC (Mean Corpuscular haemoglobin concentration) • PDW (Platelet distribution width)
Changes to compatible sample tubes		Yellow top K_3EDTA tubes and Large (wide) EDTA tubes will no longer be accepted and should not be used beyond 4 October. Compatible tube types are on page three.
Location of sample analysis	Priority samples processed at the Guy's laboratory and other samples processed at St Thomas'.	All samples taken at Guy's Hospital will be processed at Guy's laboratory. Clinicians at Guy's will see improved turnaround times after the new analysers are embedded.