

## Briefing on changes to lab procedures in Health Survey for England 2010-2015

Blood samples on the HSE are taken during the nurse visit, and sent to the labs at the Royal Victoria Infirmary (RVI) in Newcastle for analysis. Equipment and procedures used are kept up to date, to conform to international standards in accuracy, and both internal and external quality control procedures are used to check this. Changes to equipment, analytes, or calibration samples can have an effect on the lab results for HSE. More details on the quality control procedures are found in the methods volume of HSE reports. This paper outlines changes in 2010, 2013 and 2015, the effects they have had, and our proposed approach for data, analysis, and methods documentation.

The changes in 2010 have already been documented in the reports and user guides and flagged in the archived data, but are shown for context.

### 1. Overview of changes to total and HDL cholesterol, and HbA<sub>1c</sub>

On April 12<sup>th</sup> 2010, the cholesterol analysers were changed from Olympus to Roche, resulting in a 0.1mmol/L increase in total cholesterol, and 0.1mmol/L decrease in HDL cholesterol.

On June 16<sup>th</sup> 2015, the equipment was changed to Roche Cobas 702, and both total and HDL cholesterol decreased on average 0.1mmol/L.

For HbA<sub>1c</sub> although the equipment remained the same, a change to the calibration sample on 19<sup>th</sup> September 2013 was predicted by the manufacturer to result in a decrease of between 0.1-0.3 %HbA<sub>1c</sub> (decrease of between 1-3 mmol/mol).

The tables below summarises the difference in the lab results over time, and the variable names that have been used or are being proposed to highlight the non-equivalence:

**Table 1. Differences in unadjusted lab results for total and HDL cholesterol**

	Pre-12 <sup>th</sup> April 2010	12 <sup>th</sup> April 2010 – 16 <sup>th</sup> June 2015		Post 16 <sup>th</sup> June 2015		
	name	name	change	Name (proposed)	change	Cumulative change
Total cholesterol	Cholval	Cholval2	+0.1	Cholval3	-0.1	0.0
HDL cholesterol	hdlval	Hdlval2	-0.1	Hdlval3	-0.1	-0.2

**Table 2. Differences in unadjusted lab results for glycated haemoglobin (HbA<sub>1c</sub>)**

	Pre-19 <sup>th</sup> September 2013	Post-19 <sup>th</sup> September 2013			
	name	Name (proposed)	Change for HbA <sub>1c</sub> 3.6-6.2% 16-44 mmol/mol	Change for HbA <sub>1c</sub> 6.3-8.9% 45-74 mmol/mol	Change for HbA <sub>1c</sub> 9% + 75 mmol/mol +
Glycated haemoglobin %	glyhbval	Glyhbval2	-0.1	-0.2	-0.3
Glycated haemoglobin mmol/mol	iffcval	Glyhbval2	-1	-2	-3

## 2. Total cholesterol detail and proposal

Measurement of total cholesterol was carried out in the Biochemistry Department at the RVI using a Cholesterol Oxidase assay method throughout 2010-2015. Prior to 12<sup>th</sup> April 2010 this was on an Olympus 640 analyser, and from 12<sup>th</sup> April 2010 on a Roche Modular P analyser calibrated to the Centre for Disease Control (CDC) guidelines. The effect of this change of equipment was that measured concentrations of total cholesterol were on average 0.1mmol/L higher.

The issue was described in the 2010 Methods and Documentation. The archived data variable 'cholflag' showed whether the measurement was before or after the change in 2010, but the archived data wasn't adjusted (either forward or back), and the variable names were the same as before. From 2011, a suffix of 2 was added to the variable names to highlight the change in method.

On June 16<sup>th</sup> 2015 the analyser was changed to a Roche Cobas 702 analyser. Reference ranges were not changed, as the chemistries remained the same.

The effect of this change of equipment was that measured concentrations of total cholesterol were on average 0.1mmol/L lower. Unadjusted total cholesterol values are therefore comparable before 12<sup>th</sup> April 2010 and after 16<sup>th</sup> June 2015 (and very slightly higher in between).

- We propose to flag the date of the change in 2015 in the same way as 2010, using the variable 'cholflag3' to show whether results were before or after 16<sup>th</sup> June 2015.
- In addition, we propose to add a suffix of '3' to the post-June 2015 total cholesterol variables.
- We also propose for the first time to add adjusted variables (suffixed with an a) so that data after June 2015, and between April 2010 – June 2016, can be compared with the pre-April 2010 data for analysis of trends.
- As in 2010, the changes of 2015 will be explained in the Methods and Documentation, and data user guides.

## 3. HDL-cholesterol detail and proposal

HDL-cholesterol analysis was carried out in the Biochemistry Department at the RVI using a direct method (no precipitation) throughout 2010-2015. Prior to 12<sup>th</sup> April 2010 an Olympus 640 analyser was used, and from 12<sup>th</sup> April 2010 a Roche Modular P analyser. The effect of this change of equipment was that measured concentrations of HDL-cholesterol were on average 0.1mmol/L lower.

The variable 'cholflag' showed whether the measurement was before or after the change, but the archived data wasn't adjusted (either forward or back), and the variable names were the same as before. From 2011, a suffix of 2 was added to the variable names to show the change in method.

On June 16<sup>th</sup> 2015 this was changed to a Roche Cobas 702 analyser. Error! Bookmark not defined. The effect of this change of equipment was that measured concentrations of HDL cholesterol were on average 0.1mmol/L lower. Unadjusted HDL cholesterol is therefore on average 0.2mmol/L lower after June 16<sup>th</sup> 2015 than before April 12<sup>th</sup> 2010.

- We propose to flag the date of the change in 2015 in the same way as 2010, using the variable 'cholflag3' to show whether results were before or after 16<sup>th</sup> June 2015.
- In addition, we propose to add a suffix of '3' to the post-June 2015 HDL cholesterol variables.
- We also propose to add adjusted variables (suffixed with an a) so that data after June 2015, and between April 2010 – June 2016, can be compared with the pre-April 2010 data for analysis of trends.
- As in 2010, the changes of 2015 will be explained in the Methods and Documentation, and data user guides.

The following table shows the variable names for total and HDL cholesterol.

**Table 3. Variable names for total and HDL cholesterol**

	Before 12 April 2010	12 April 2010 – 16 June 2015	After June 2015
(D) Flag variable, whether blood sample received at lab before or after 12 April 2010	Cholflag		
(D) Flag variable, whether blood sample received at lab before or after 16 June 2015			Cholflag3
(D) Valid Total Cholesterol Result mmol/L	Cholval	cholval2	Cholval3
(D) Valid Total Cholesterol Result mmol/L (incl those on LLD)	cholval1	cholval12	cholval13
(D) Whether Total Cholesterol < 4 (incl those on LLD) {revised}		cholfour2	Cholfour3
(D) Whether Total Cholesterol < 5 (incl those on LLD) {revised}		cholfive2	Cholfive3
(D) Valid HDL Cholesterol Result mmol/L	Hdlval	hdlval2	Hdlval3
(D) Valid HDL Cholesterol Result mmol/L (incl those on LLD)	hdlval1	hdlval12	hdlval13
(D) Whether HDL Cholesterol result <1 (incl those on LLD) {revised}		hdlone2	Hdlone3
(D) Valid Total Cholesterol Result mmol/L (later results adjusted to be comparable with pre-2010 results)	Cholvala		
(D) Valid Total Cholesterol Result mmol/L (incl those on LLD) (later results adjusted to be comparable with pre-2010 results)	Cholval1a		
(D) Whether Total Cholesterol < 4 (incl those on LLD) {revised} (later results adjusted to be comparable with pre-2010 results)	Cholfoura		
(D) Whether Total Cholesterol < 5 (incl those on LLD) {revised} (later results adjusted to be comparable with pre-2010 results)	Cholfivea		
(D) Valid HDL Cholesterol Result mmol/L (later results adjusted to be comparable with pre-2010 results)	Hdlvala		
(D) Valid HDL Cholesterol Result mmol/L (later results adjusted to be comparable with pre-2010 results)	hdlval1a		
(D) Whether HDL Cholesterol result <1 (incl those on LLD) {revised} (later results adjusted to be comparable with pre-2010 results)	hdlonea		

#### 4. Glycated haemoglobin

Glycated haemoglobin (HbA<sub>1c</sub>) analysis was carried out in the Blood Sciences Department at the RVI using the Tosoh G-series analysers. A Tosoh G7 analyser was used until 26<sup>th</sup> August 2010; when it was replaced with the Tosoh G8 analyser and the change made no impact on measured concentrations, therefore was not flagged in the data. Both Tosoh G7 and Tosoh G8 were calibrated using Diabetes Control and Complications Trial (DCCT) standards until 3rd October 2011, when International Federation of Clinical Chemistry (IFCC) standardisation was introduced. The effect was to change the main reporting units from %HbA<sub>1c</sub>, to mmol/mol HbA<sub>1c</sub>. Both units are now included in the HSE reports and archived data.

Part of the process involves regular calibration of the analyser with samples of known value supplied by the manufacturer Tosoh. Calibration lot ZS2002 was used up til the 19th September 2013, when ZS3001 was used as ZS2002 was no longer available. Comparisons made by the manufacturer Tosoh indicated that the change caused variations of 1.4-2.2 mmol/mol, which is deemed acceptable<sup>1,2</sup>. The calibrator used from 19<sup>th</sup> September 2013 produced lower glycated haemoglobin results compared to the previous one.<sup>3</sup>

- We propose to flag the date of the change in 2013 using the variable 'glyflag' to show whether results were obtained before or after 19<sup>th</sup> September 2013.
- We also propose to add a suffix of 2 to the to the post-September 2013 glycated haemoglobin variables.
- We also propose to add adjusted variables (suffixed with an a) that can be compared with the pre- September 2013 glycated haemoglobin variables for analysis of trends.
- The changes in 2013 will be explained in an amendment to the Methods and Documentation, and data user guides.
- The UK Data Service will contact users of the 2013 and 2014 data to advise them of the change, and instruct them how to adjust the HbA<sub>1c</sub> data (if they are using it).

**Table 4 Variable names for glycated haemoglobin**

	Before 19 <sup>th</sup> September 2013	19 <sup>th</sup> September 2013 onwards
(D) Flag variable, whether blood sample received at lab before or after 19 September 2013	Glyflag	Glyflag
(D) Valid Glycated HB Result	Glyhbval	Glyhbval2
(D) Glycated haemoglobin 3 groups	Glyhb3g	Glyhb3g2
(D) Raised glycated haemoglobin	Glyhbhi	Glyhbhi2
(D) Valid Glycated haemoglobin Result in mmol per ml (IFCC)	Iffcval	Iffcval2
(D) Valid Glycated HB Result (later results adjusted to be comparable with pre-September 2013)	Glyhbvala	
(D) Glycated haemoglobin 3 groups (later results adjusted to be comparable with pre-September 2013)	Glyhb3ga	
(D) Raised glycated haemoglobin (later results adjusted to be comparable with pre-September 2013)	Glyhbhia	
(D) Valid Glycated haemoglobin Result in mmol per ml (IFCC) (later results adjusted to be comparable with pre-September 2013)	Iffcvala	

<sup>1</sup> Sacks DB, et al. *Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus*. Diabetes Care, 34:e61-e99, 2011

<sup>2</sup> Little et al. *Status of HbA<sub>1c</sub> measurement and goals for improvement: from chaos to order for improving diabetes care*. Clin Chem 2011;57:205–14

<sup>3</sup> In the HSE 2013 dataset, a variable glyflag shows whether the sample was analysed pre or post change. Variables from HSE 2013 onwards are suffixed with 'o' or 'a' to indicate whether they are the original results from the lab, or adjusted so that post-change matches pre-change.

## 5. Method for producing adjusted variables, for comparable trends over time

The more recent results are amended to be comparable with the earlier results in the following way:

### Total cholesterol and HDL cholesterol

For samples analysed before 12<sup>th</sup> April 2010

Compute cholvala = cholval.

Compute hdlvala = hdlval.

For samples analysed 12<sup>th</sup> April 2010 to 16<sup>th</sup> June 2015

Compute cholvala = cholval -0.1.

Compute hdlvala = hdlval+0.1.

For samples analysed after 16<sup>th</sup> June 2015

Compute cholvala = cholval.

Compute hdlvala = hdlval+0.2.

Other variables based on total cholesterol and hdl cholesterol (such as whether total cholesterol is 5 or above) are then also derived from the adjusted variables.

### Glycated haemoglobin reported in units of %HbA<sub>1c</sub> and mmol/mol

For samples analysed up to 19<sup>th</sup> September 2013

Compute glyhbvala=glyhbval.

Compute iffcvala=glyhbval.

For samples analysed after 19<sup>th</sup> September 2013

compute glyhbvala= glyhbval.

if glyhbval>3.5 and glyhbval<6.3 glyhbvala = glyhbval+0.1.

if glyhbval>6.2 and glyhbval<9 glyhbvala = glyhbval+0.2.

if glyhbval>8.9 glyhbvala = glyhbval+0.3.

compute iffcvala= iffcval.

if iffcval>15 and iffcval<45 iffcvala = iffcval+1.

if iffcval>44 and iffcval<75 iffcvala = iffcval+2.

if iffcval>74 iffcvala = iffcval+3.

Other variables based on glycated haemoglobin (such as undiagnosed diabetes) are then also derived from the adjusted variables.