QStatin® -2014

Update

Information

Revision History

Revision date	Document Version	Summary of Changes
19.08.2014	V1.0	First issue.

Contents

1 Purpose of document

This document details the update for QStatin® risk prediction algorithms derived from the QResearch® database. The update will go live on the qintervention.org on 01 September 2014. The website has details of the relevant academic publications which describe the derivation and validation of the algorithms in detail[1-3]. Suppliers are invited to synchronise their implementation as soon as practicably possible for consistency of implementation across the NHS and to minimise support calls regarding discrepancies.

2 Rationale for regular updates of QStatin®

Regular updates are required because of:

- **Changes in population characteristics** - for example, incidence of CVD is falling; incidence of diabetes is rising; obesity is rising; smoking rates are falling;
- **Changes in requirements** for how the risk prediction scores can be used eg changes in age ranges.
- **Improvements in data quality** - for example the recording of exposures and also clinical outcomes becomes more complete over time. This is especially true where outcomes are recorded on the databases which are now linked to QResearch.

These factors require us to remodel the algorithms to the latest version of the QResearch® database to ensure the algorithms keep up to date. If the algorithms are not re-calculated, then the performance would gradually decay and its clinical value would diminish as a result. We have therefore re-fitted the algorithms using a random sample of three quarters of practices contributing to the QResearch® database (version 39, 01 Aug 2014) and incorporated this into the annual update of the software. The updated algorithm was validated using the remaining one quarter of practices in the database.

3 Summary of Changes

The main changes to the algorithms are

3.1 Change in age range

The original research was based on patients aged 30-84 years. The update now includes patients aged 25-84 years.

3.2 Re-calculation of coefficients

We have updated the fractional polynomial terms and coefficients for the algorithms using the latest version of the QResearch database (version 39 from 01 Aug 2014). We have been able to link QResearch to both mortality data and hospital admissions data. The linked data has been used for identifying acute renal failure, cataracts and moderate/severe myopathy using relevant ICD10 codes. Patients with abnormal liver function tests are still identified solely from the laboratory values recorded on the GP record as before.

3.3 Extension of duration over which risk can be calculated

The original algorithms estimated risk over a 5 year period. The updated version now enables a 10 year risk to be calculated. This is then more comparable with the 10 year risk of diabetes and cardiovascular disease used in the calculation of QRisk and QDiabetes.

4 Appendix1:

The appendix shows details of the cohorts used for derivation and validation of QStatin-2014. The QResearch® database version 39 was used for the update. This version of the database was last updated on 01 Aug 2014 and contains data from 1017 general practices. We identified an open cohort of patients registered with the practices from 01 Jan 2002 until 31 July 2014. We allocated 763 practices to the derivation cohort and the remainder to the validation cohort.

There were 6,789,568 million patients in the derivation cohort and 2,133,387 million in the validation cohort which reflects the expansion of the database over the last few years. There were 730,292 new users of statins in the derivation cohort and 241,044 in the validation cohort. The comparable figures for the original study were 225,922 new users in the derivation cohort and 118,372 in the validation cohort.

Table 1 shows the number of incident cases for each outcome during the study period with age standardised rates per 10,000 person years. The addition of linked data increased the age standardised rates for acute renal failure, cataract and myopathy. For acute renal failure, only 50% of cases were identified solely using the GP records. For myopathy, approximately 80% were identified solely using the GP record. For cataract, 95% of cases were identified from the GP record.

Table 1 number of cases of cataract, moderate-severe myopathy, liver dysfunction and acute renal failure and age standard incidence rate (95% CI) per 10,000 pyrs

	cases on GP data	row %	Adjusted rate (95%CI) GP data per 10,000 pyrs	cases on GP or mortality data	row %	Adjusted rate (95%CI) GP data or mortality per 10,000 pyrs	cases on GP, mortality or hospital data	Adjusted rate (95%CI) GP, mortality or hospital data per 10000 pyrs
women								
acute renal failure	4,285	50.5	2.23 (2.17 to 2.30)	5,073	59.8	2.62 (2.55 to 2.70)	8,484	4.38 (4.28 to 4.47)
cataract	95,164	95.6	52.41 (52.08 to 52.74)	95,164	95.6	52.41 (52.08 to 52.74)	99,575	54.91 (54.58 to 55.25)
abnormal LFTs	22,828	100.0	12.80 (12.64 to 12.97)	n/a	n/a	n/a	n/a	n/a
myopathy	2,058	76.8	1.13 (1.08 to 1.18)	2,078	77.6	1.14 (1.09 to 1.19)	2,679	1.47 (1.42 to 1.53)
Men								
acute renal failure	5,024	50.0	3.30 (3.21 to 3.39)	5,867	58.4	3.89 (3.79 to 3.99)	10,046	6.70 (6.57 to 6.83)
cataract	64,846	95.3	43.24 (42.91 to 43.57)	64,846	95.3	43.24 (42.91 to 43.57)	68,029	45.38 (45.04 to 45.72)
abnormal LFTs	25,660	100.0	15.46 (15.27 to 15.65)	n/a	n/a	n/a	n/a	n/a
myopathy	3,142	84.7	1.92 (1.85 to 1.99)	3,172	85.5	1.94 (1.87 to 2.01)	3,709	2.27 (2.20 to 2.35)

5 Appendix 2: updated hazard ratios

Table 3 shows the adjusted hazard ratios for each of the four outcomes. The results are also adjusted for age and body mass index. The hazard ratios are broadly similar to those reported in 2010[1].

5.1 Abnormal liver function

There are some minor changes to the input parameters for abnormal liver function tests since cardiovascular disease was no longer significant on the multivariate analysis and has therefore been removed from the model. Congestive cardiac failure reached statistical significance and has now been incorporated as a predictor.

Table 2: Adjusted hazard ratios (95% CI) for QStatin-2014 in the derivation cohort for abnormal liver function tests. Hazard ratios were adjusted for fractional polynomial terms for age & BMI

	adjusted HR (95%CI) women	adjusted HR (95%CI) men
Non-users of statins	1	1
new use of statins*	1.55 (1.48 to 1.61)	1.61 (1.55 to 1.67)
Townsend deprivation (5 unit increase)	0.95 (0.93 to 0.98)	NS
smoking status		
non smoker	1	1
ex- smoker	1.05 (1.01 to 1.09)	1.13 (1.09 to 1.17)
light smoker	1.16 (1.11 to 1.22)	1.29 (1.25 to 1.34)
moderate smoker	1.16 (1.10 to 1.23)	1.26 (1.20 to 1.33)
heavy smoker	1.41 (1.31 to 1.50)	1.55 (1.47 to 1.63)
ethnicity		
White or ethnicity not recorded		
Indian§	1.01 (0.90 to 1.14)	1.31 (1.19 to 1.44)
Pakistani§	1.46 (1.28 to 1.67)	1.66 (1.49 to 1.85)
Bangladeshi§	1.25 (1.06 to 1.48)	1.25 (1.10 to 1.42)
Other Asian§	1.28 (1.10 to 1.49)	1.94 (1.73 to 2.18)
Black Caribbean§	0.69 (0.59 to 0.80)	0.78 (0.67 to 0.91)
Black African§	0.78 (0.67 to 0.91)	0.94 (0.82 to 1.07)
Chinese§	0.97 (0.75 to 1.25)	1.33 (1.07 to 1.66)
Other ethnic group§	0.97 (0.86 to 1.09)	1.09 (0.99 to 1.21)
co-morbidity/medication		
Type 1 diabetes*	1.53 (1.25 to 1.89)	1.51 (1.26 to 1.80)
Type 2 diabetes*	1.19 (1.12 to 1.27)	1.46 (1.39 to 1.54)
congestive cardiac failure*	1.18 (1.03 to 1.36)	1.33 (1.17 to 1.50)
treated hypertension*	1.14 (1.10 to 1.19)	1.21 (1.16 to 1.26)
rheumatoid arthritis*	1.91 (1.79 to 2.05)	1.69 (1.53 to 1.87)
corticosteroids*	1.45 (1.38 to 1.52)	1.48 (1.39 to 1.57)

*compared with patient without the characteristic § compared with white/not recorded
Fractional polynomial terms women; age^2, age^2 ln(age), bmi^3, bmi^3ln(bmi), men age^{-2}, age3, bmi^{-2}, bmi^{-2} ln(bmi).

5.2 Moderate or severe myopathy

Compared with the model published in 2010[1], we now have sufficient numbers to calculate an adjusted hazard ratio for all ethnic groups. Three variables which were only significant in women are now significant in both men and women so included in both models (type 1 diabetes, chronic liver disease, hypothyroidism.

One variable (Treated hypertension) was previously significant in women only but is not significant now so has been removed from the model.

Table 3 Adjusted hazard ratios (95% CI) for QStatin-2014 in the derivation cohort for moderate to severe myopathy. Hazard ratios were also adjusted for age & BMI

	adjusted HR (95%CI) women	adjusted HR (95%CI) men
Non-users of statins	1	1
new use of statins	2.53 (2.29 to 2.79)	3.48 (3.20 to 3.79)
Ethnicity		
White or ethnicity not recorded	1	1
Indian§	1.27 (0.93 to 1.73)	1.44 (1.14 to 1.82)
Pakistani§	1.19 (0.76 to 1.87)	1.16 (0.82 to 1.63)
Bangladeshi§	0.88 (0.50 to 1.55)	0.85 (0.56 to 1.30)
Other Asian§	1.33 (0.85 to 2.07)	2.20 (1.65 to 2.94)
Black Caribbean§	3.75 (3.04 to 4.63)	4.90 (4.14 to 5.81)
Black African§	3.79 (3.00 to 4.78)	4.05 (3.37 to 4.86)
Chinese§	0.72 (0.30 to 1.74)	1.60 (0.93 to 2.76)
Other ethnic group§	2.58 (2.04 to 3.25)	2.98 (2.48 to 3.58)
co-morbidity/medication		
liver disease*	2.12 (1.35 to 3.33)	2.05 (1.46 to 2.87)
Type 1 diabetes*	2.25 (1.41 to 3.59)	2.08 (1.49 to 2.92)
Type 2 diabetes*	1.15 (0.99 to 1.34)	1.16 (1.03 to 1.30)
hypothyroidism*	1.51 (1.32 to 1.72)	1.45 (1.15 to 1.84)
corticosteroids*	2.07 (1.83 to 2.34)	1.93 (1.69 to 2.21)

*compared with patient without the characteristic § compared with white/not recorded

Women and men: age and bmi linear.

5.3 Cataract

Rheumatoid arthritis was previously not significant in men. In the 2014 model, it was significant and had a hazard ratio of 1.20 so was included in as a predictor for men.

Table 4 Adjusted hazard ratios (95% CI) for QStatin-2014 in the derivation cohort for cataract. Hazard ratios were also adjusted for fractional polynomial terms for age & BMI

	adjusted HR (95%CI) women	adjusted HR (95%CI) men
Non-users of statins	1	1
New use of statins	1.31 (1.29 to 1.33)	1.33 (1.30 to 1.35)
Townsend deprivation (5 unit increase)	NS	1.02 (1.01 to 1.03)
Smoking		
non smoker	1	1
Ex-smoker	1.09 (1.08 to 1.11)	1.08 (1.06 to 1.10)
light smoker	1.06 (1.03 to 1.09)	1.10 (1.07 to 1.13)
moderate smoker	1.03 (0.99 to 1.07)	1.08 (1.03 to 1.12)
heavy smoker	1.15 (1.10 to 1.21)	1.20 (1.15 to 1.25)
Ethnicity		
White or ethnicity not recorded	1	1
Indian§	2.34 (2.23 to 2.47)	2.30 (2.17 to 2.44)
Pakistani§	2.38 (2.20 to 2.57)	2.27 (2.09 to 2.47)
Bangladeshi§	2.36 (2.16 to 2.57)	2.37 (2.16 to 2.59)
Other Asian§	2.02 (1.85 to 2.21)	2.09 (1.89 to 2.30)
Black Caribbean§	1.81 (1.71 to 1.93)	1.85 (1.73 to 1.97)
Black African§	2.50 (2.32 to 2.69)	2.80 (2.58 to 3.04)
Chinese§	1.70 (1.48 to 1.94)	1.91 (1.65 to 2.20)
Other ethnic group§	1.73 (1.62 to 1.85)	1.69 (1.56 to 1.83)
co-morbidity/medication		
cardiovascular disease*	1.12 (1.09 to 1.14)	1.13 (1.11 to 1.16)
Type 1 diabetes*	9.70 (8.86 to 10.62)	9.07 (8.30 to 9.92)
Type 2 diabetes*	1.84 (1.80 to 1.88)	2.10 (2.05 to 2.15)
rheumatoid arthritis*	1.16 (1.12 to 1.19)	1.20 (1.14 to 1.27)
corticosteroids*	1.48 (1.44 to 1.51)	1.63 (1.58 to 1.68)
atrial fibrillation*	1.20 (1.16 to 1.24)	1.24 (1.20 to 1.28)

*compared with patient without the characteristic § compared with white/not recorded
Fractional polynomial terms women: age^3, age^3 ln(age), ln(bmi), $bmi^{0.5}$, men: age^3, age^3 ln(age), bmi^{-2}, bmi^{-1}.

5.4 Acute renal failure

Table 5 Adjusted hazard ratios (95% CI) for QStatin-2014 in the derivation cohort for acute renal failure. Hazard ratios were adjusted for fractional polynomial terms for age & BMI

	adjusted HR (95%CI) women	adjusted HR (95%CI) men
Non-users of statins	1	1
new use of statins	1.30 (1.23 to 1.37)	1.21 (1.16 to 1.27)
Townsend deprivation (5 unit increase)	1.30 (1.26 to 1.35)	1.34 (1.30 to 1.38)
Smoking status		
non smoker	1	1
Ex-smoker	1.13 (1.07 to 1.19)	1.05 (1.01 to 1.10)
light smoker	1.49 (1.39 to 1.61)	1.40 (1.32 to 1.49)
moderate smoker	1.45 (1.30 to 1.61)	1.43 (1.29 to 1.57)
heavy smoker	1.92 (1.71 to 2.16)	1.83 (1.66 to 2.01)
co-morbidity/medication		
Type 1 diabetes*	8.04 (6.27 to 10.32)	7.72 (6.28 to 9.49)
Type 2 diabetes*	2.37 (2.22 to 2.52)	2.10 (1.99 to 2.22)
congestive cardiac failure*	2.98 (2.74 to 3.24)	2.84 (2.63 to 3.06)
corticosteroids*	1.57 (1.48 to 1.68)	1.70 (1.59 to 1.82)
treated hypertension*	1.51 (1.44 to 1.59)	1.53 (1.46 to 1.60)
chronic renal disease*	6.14 (5.43 to 6.94)	4.68 (4.18 to 5.24)

*compared with patient without the characteristic § compared with white/not recorded
Fractional polynomial terms women: age-.5, age $^{0.5}$, bmi^{-2}, bmi^{-1}, men: age$^{-.5}$, Age$^{-.5}$ ln(age), bmi^{-2}, bmi$^{-.5}$

6 Appendix3: validation of QStatin-2014

We validated the QStatin®-2014 algorithms using a cohort of patients aged 25-84 years derived from a one quarter sample of practices in version 39 of the QResearch® database. We evaluated performance at 5 years and also 10 years. We also validated the QStatin®-2010 algorithms in patients aged 25-84 years also at 5 years for comparison.

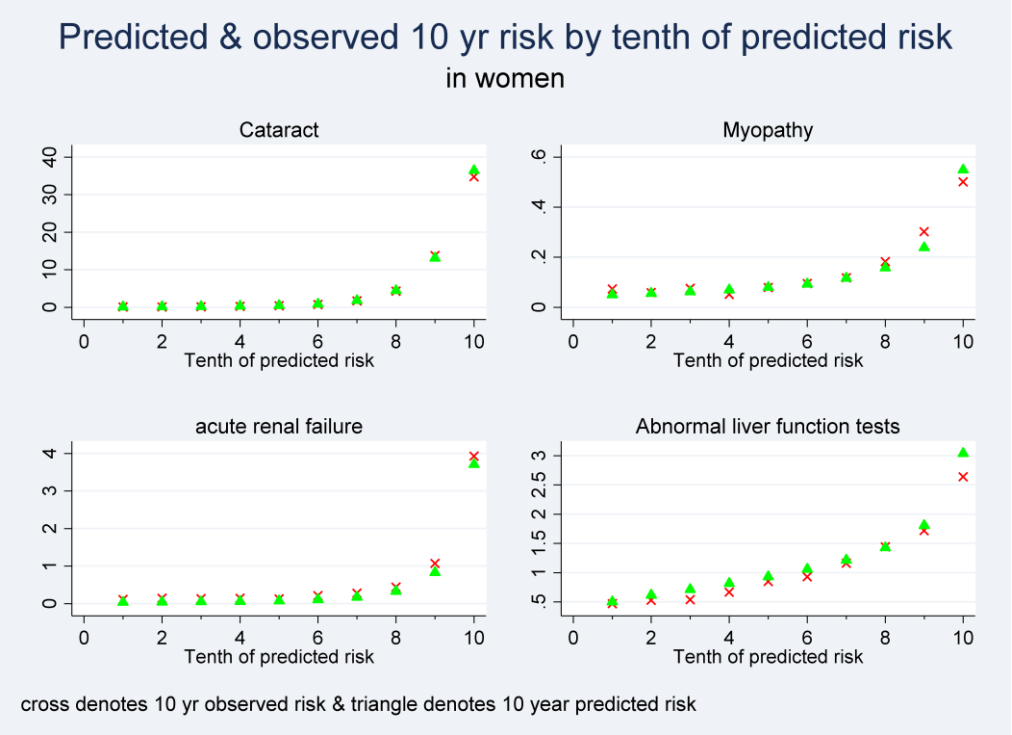
Table 6 shows results of the performance of the scores i.e. how accurate the scores are at identifying patients who have an event and distinguishing them from patients who don't and how much of the 'variation' in risk is explained by the scores themselves. High values for these measures are better than low values. The 5 year and 10 year version of QStatin-2014 showed comparable performance and both show improvement on the ROC values, D statistic and R^2 values obtained using QStatin-2010. The QStatin-2010 algorithms applied to version 39 QResearch (August 2014) generally showed slightly lower performance compared with the values previously published using version 24 of QResearch (June 2008). Figure 1 shows good calibration of each of the four algorithms with a close correspondence between observed and predicted risks.

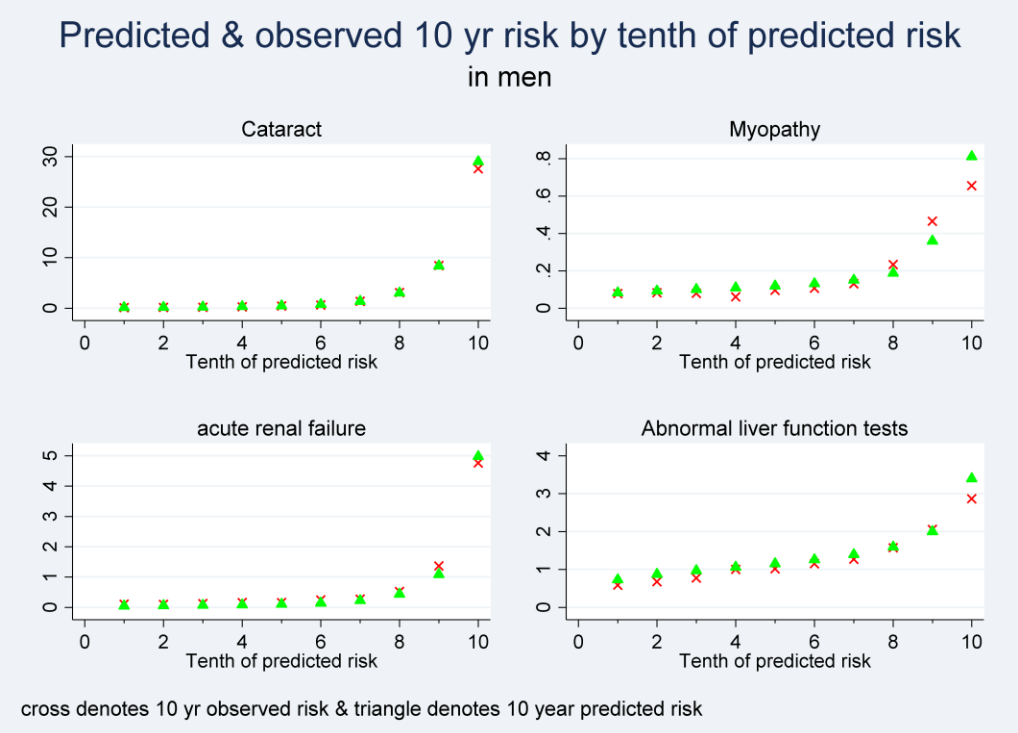
Table 6: Validation statistics for QStatin-2014 evaluated over 5 years and 10 years compared with QStatin-2010 evaluated over 5 years for patients aged 25-84 years

		2014	2014	2010
		women 10 year risk (95% CI)	women 5 year risk (95% CI)	women 5 year risk (95% CI)
acute renal failure	D	2.26 (2.2 to 2.32)	2.04 (1.97 to 2.12)	1.59 (1.5 to 1.68)
	R^2	54.98 (53.65 to 56.31)	49.94 (48.03 to 51.86)	37.66 (35.01 to 40.31)
	ROC	0.827 (0.82 to 0.835)	0.801 (0.79 to 0.813)	0.745 (0.731 to 0.758)
cataract	D	2.67 (2.65 to 2.69)	2.65 (2.62 to 2.67)	2.32 (2.29 to 2.35)
	R^2	62.99 (62.65 to 63.33)	62.62 (62.19 to 63.05)	56.24 (55.67 to 56.82)
	ROC	0.906 (0.904 to 0.907)	0.916 (0.914 to 0.917)	0.861 (0.857 to 0.865)
Myopathy	D	1.3 (1.18 to 1.42)	1.25 (1.11 to 1.4)	1.23 (1.38 to 1.09)
	R^2	28.7 (24.99 to 32.4)	27.27 (22.65 to 31.9)	26.55 (31.16 to 21.94)
	ROC	0.694 (0.676 to 0.712)	0.7 (0.677 to 0.723)	0.682 (0.706 to 0.659)
abnormal LFTs	D	0.94 (0.89 to 0.99)	1 (0.95 to 1.06)	0.84 (0.77 to 0.9)
	R^2	17.41 (15.96 to 18.86)	19.39 (17.58 to 21.2)	14.28 (12.49 to 16.06)
	ROC	0.686 (0.679 to 0.693)	0.695 (0.685 to 0.704)	0.667 (0.656 to 0.678)
Men		**men 10 year risk (95% CI)**	**men 5 year risk (95% CI)**	**men 5 year risk (95% CI)**
acute renal failure	D	2.41 (2.35 to 2.46)	2.31 (2.23 to 2.38)	1.99 (1.91 to 2.07)
	R^2	58.01 (56.84 to 59.17)	55.96 (54.38 to 57.53)	48.61 (46.71 to 50.51)
	ROC	0.841 (0.834 to 0.848)	0.835 (0.825 to 0.845)	0.803 (0.792 to 0.814)
cataract	D	2.72 (2.7 to 2.75)	2.68 (2.65 to 2.71)	2.52 (2.48 to 2.55)
	R^2	63.91 (63.51 to 64.31)	63.18 (62.67 to 63.7)	60.17 (59.58 to 60.76)
	ROC	0.901 (0.899 to 0.903)	0.91 (0.907 to 0.912)	0.881 (0.877 to 0.885)
Myopathy	D	1.44 (1.34 to 1.55)	1.53 (1.41 to 1.65)	1.38 (1.26 to 1.51)
	R^2	33.26 (30.19 to 36.34)	35.84 (32.19 to 39.49)	31.35 (27.52 to 35.18)
	ROC	0.723 (0.707 to 0.739)	0.73 (0.71 to 0.749)	0.726 (0.705 to 0.747)
abnormal LFTs	D	0.85 (0.81 to 0.89)	0.93 (0.88 to 0.98)	0.83 (0.78 to 0.88)
	R^2	14.7 (13.52 to 15.88)	17.01 (15.52 to 18.49)	14.09 (12.64 to 15.53)
	ROC	0.654 (0.647 to 0.66)	0.671 (0.662 to 0.679)	0.657 (0.648 to 0.666)

Figure 1 Calibration graphs for QStatins-2014 10 year risk.

The graphs show that QStatin-2014 is well calibrated with close correspondence between the observed and predicted values in men and women.





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