Validation of QFracture compared with FRAX Analysis prepared for NICE 2011

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Revision History

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3 Purpose of document

This document presents additional information on the validation of QFracture compared with FRAX based on data presented in the original BMJ paper from 2009. It has been prepared by Professor Julia Hippisley-Cox and Dr Carol Coupland for NICE following an email from Sylvia Rabar, Senior Project Manager and Research Fellow in relation to a clinical guideline, in the UK, commissioned by the National Institute for Health and Clinical Excellence (NICE), on risk assessment for fragility fracture. See the appendix for a copy of the email.

The NICE guidance information can be found here.

http://guidance.nice.org.uk/CG/Wave25/2

4 Aims and objective

The overall aim is to examine sensitivity and specificity of FRAX and QFracture at different thresholds for osteoporotic fracture and hip fractures.

The objectives are

- to compare the ROC curve data for QFracture and FRAX when applied to the QResearch database
- To compare the sensitivity, specificity (together with True positive, true negative, false positive and false negative values) for the following thresholds:
  - Major osteoporotic fractures: 10%, 20% and 30%
  - Hip fractures: 3% and 5%

5 Background

In 2009, Hippisley-Cox and Coupland published a paper describing the development and validation of QFracture[1] – a set of risk prediction algorithms to predict 10 year risk of hip fracture and osteoporotic fracture (hip, vertebral, or distal radius fracture) in primary care. The algorithms were developed using data from a sample of two thirds of practices in the QResearch database and validated using the remaining third so that the validation sample is physically separate from the derivation sample. QResearch is a database derived from general practices using the EMIS clinical system (EMIS is the clinical system used by more than 55% of GP practices nationally). The resulting publically available web calculator and open source software can be found at www.qfracture.org . As part of the original study, we calculated FRAX scores for hip fracture using an automated call to the FRAX website in Nov

2008 so that a comparison could be made between QFracture and FRAX for hip fracture. The resulting FRAX scores were then used for the analyses reported in the BMJ paper.

In 2010, however, the authors tried to obtain FRAX scores using the same automated procedure for a second time and found that there were significant discrepancies between the FRAX scores generated by the FRAX website in 2008 (and used for the BMJ paper) and those generated by the FRAX website in 2010 for the same input data. It was not possible to determine if this was an intended change to FRAX, a bug in the underlying algorithm or a bug in the FRAX software implementing the algorithm or a combination of all three. Since the FRAX algorithm(s) is unpublished we contacted the FRAX developers. Disappointingly they have not been able to respond and have since disabled the web facility which allowed calculation of FRAX scores for large datasets. It is therefore safest to assume that the validation of FRAX reported in the 2009 BMJ paper is a historical validation of a previous version of the FRAX algorithm rather than a validation of the current FRAX algorithm[2].

In 2011, Collins, Mallet and Altman published an independent external validation of QFracture in the BMJ[3]. This validation study tested the performance of QFracture on a separate cohort of patients contributing to the THIN database. The THIN database is a primary care database derived from general practices using the Vision clinical system. The Vision clinical system is the second most commonly used GP computer system since it is used by 20% of GP practices nationally. The authors had intended to compare QFracture directly to FRAX but report they were unable to do this since the FRAX algorithm is unpublished and not available from the authors.

In this report, we summarise existing published information on the validation of QFracture and FRAX and report additional analyses using QFracture and FRAX based on the QResearch database. The FRAX scores used throughout this report are based on 2008 scores, obtained using the version that does not incorporate bone mineral density. A summary of the differences in the variables included in FRAX and QFracture can be found in the appendix.

6 Methodology

The methods have been reported in detail in the original paper[1] but are summarised here for ease of reference. Both in the original paper and the independent external validation by Collins and Altman[3], the primary measures of statistical performance are R^2(an estimate of variation in time to outcome explained by the risk score)[4] and the D statistic (a measure of discrimination where higher values indicate better discrimination)[5] as these take account of the survival nature of the data. ROC values were calculated as a rough guide and for comparison with other studies but the ROC statistic is not really appropriate for survival data since it assumes all patients have at least 10 years of follow up data (which is not always the case).

7 Results

7.1 QFracture vs. FRAX using the QResearch database

The first table shows the results from the validation of QFracture in patients aged 30-85 years using the validation cohort from the QResearch database. These are reproduced from the 2009 BMJ paper[1].

Table 1 Validation statistics for osteoporotic fracture using QFracture based on the QResearch validation cohort in patients aged 30-85.

	QFracture	*QFracture*
	Osteoporotic fracture 30-85 years	**Hip fracture 30 to 85 years**
Women		
R^2 (%)	44.87 (43.07 to 46.67)	63.94 (62.12 to 65.76)
D Statistic	1.85 (1.78 to 1.91)	2.73 (2.62 to 2.83)
ROC statistic	0.788 (0.786 to 0.790)	0.890 (0.889 to 0.892)
Men		
R^2 (%)	30.03 (22.21 to 37.84)	63.19 (60.81 to 65.57)
D statistic	1.34 (1.09 to 1.59)	2.68 (2.55 to 2.82)
ROC statistic	0.692 (0.683 to 0.701)	0.856 (0.851 to 0.860)

The next table shows the performance of QFracture for predicting hip fracture when applied to patients aged 40-85 so that it can be directly compared with FRAX (which can only be applied to patients aged 40-85 years). Overall, QFracture performed better than FRAX. For example, QFracture explained 57.3% of the variation in time to fracture for women aged 40-85 years compared with 54.8% for FRAX.

Table 2 Validation statistics for hip fracture using QFracture based on the QResearch validation cohort in patients aged 40-85 years

	QFracture	*FRAX*
	Hip fracture 40-85 years	**Hip fracture 40-85 years**
Women		
R^2 (%)	57.29 (57.18 to 58.09)	54.83 (54.43 to 55.12)
D Statistic	2.37 (2.32 to 2.42)	2.26 (2.21 to 2.30)
ROC statistic	0.846 (0.841 to 0.850)	0.845 (0.840 to 0.849)
Men		
R^2 (%)	57.67 (56.78 to 58.57)	54.08 (52.10 to 53.65)
D statistic	2.39 (2.30 to 2.48)	2.22 (2.14 to 2.30)
ROC statistic	0.820 (0.809 to 0.831)	0.817 (0.806 to 0.828)

7.2 Independent external validation of QFracture on THIN

The next table summarises the performance statistics of QFracture for hip and osteoporotic fracture on THIN as reported by Collins et al in the BMJ[3]. This shows that the performance of QFracture on the external THIN dataset was comparable to that on the QResearch database. Indeed, the performance for the osteoporotic fracture outcome was better on THIN than QResearch. The authors comment that no comparison with FRAX was possible as the algorithm was unavailable[3].

Table 3 Validation statistics for hip fracture and osteoporotic fracture using QFracture based on the THIN validation cohort in patients aged 30-85.

	QFracture on THIN database	*QFracture on THIN database*
	Osteoporotic fracture	**Hip fracture**
Women		
R^2	49.24 (48.64 to 49.85)	62.82 (62.22 to 63.43)
D Statistic	2.02 (1.99 to 2.04)	2.66 (2.63 to 270)
ROC statistic	0.816	0.890
Men		
R^2	37.99 (36.64 to 39.35)	60.42 (59.22 to 61.63)
D statistic	1.60 (1.56 to 1.65)	2.53 (2.46 to 2.59)
ROC statistic	0.739	0.855

7.3 Calibration of QFracture and FRAX(2008) in patients aged 40-85 years.

As reported in the BMJ paper, for QFracture, there was close correspondence between predicted and observed 10 year risks within each model tenth. For example, in the top tenth of risk for women, the mean predicted 10 year risk of hip fracture for QFracture was 9.87% and the observed risk was 9.40%. The ratio of predicted to observed risk in this tenth was 1.05 indicating almost perfect calibration (a ratio of 1 indicates perfect calibration i.e. no under-prediction or over-prediction).

For FRAX (2008), however, there was over prediction of risk for men and women in every tenth as shown in the table.

Table 4: Predicted and observed risks for hip fracture at 10 years in patients aged 40-85 years by tenth of predicted risk using the QFracture and FRAX (2008) scores.

Women	***Hip Fracture QFracture***			***Hip Fracture FRAX®***		
tenth§	**Mean predicted risk (%)**	**observed risk (%)**	**ratio predicted/ observed**	**Mean predicted risk (%)**	**observed risk (%)**	**ratio predicted/ observed**
1	0.05	0.02	2.47	0.16	0.08	2.03
2	0.08	0.10	0.81	0.16	0.08	2.03
3	0.12	0.14	0.86	0.30	0.17	1.76
4	0.18	0.14	1.30	0.40	0.25	1.60
5	0.29	0.32	0.90	0.54	0.33	1.65
6	0.51	0.47	1.08	0.83	0.61	1.36
7	0.97	1.03	0.95	1.37	1.06	1.29
8	2.01	1.98	1.01	2.46	1.99	1.24
9	4.14	4.30	0.96	4.74	4.34	1.09
10	9.87	9.40	1.05	10.07	9.33	1.08
men		**Hip Fracture QFracture**			**Hip fracture FRAX®**	
tenth§	**Mean predicted risk (%)**	**observed risk (%)**	**ratio predicted/ observed**	**Mean predicted risk (%)**	**observed risk (%)**	**ratio predicted/ observed**
1	0.04	0.04	1.04	0.10	0.06	1.66
2	0.06	0.06	1.02	0.10	0.06	1.66
3	0.08	0.08	1.01	0.20	0.11	1.82
4	0.11	0.07	1.53	0.20	0.11	1.82
5	0.14	0.15	0.96	0.30	0.17	1.76
6	0.21	0.19	1.09	0.40	0.24	1.67
7	0.32	0.34	0.94	0.59	0.34	1.72
8	0.56	0.46	1.21	0.98	0.52	1.88
9	1.16	1.38	0.84	1.76	1.36	1.30
10	4.12	3.39	1.21	3.87	3.31	1.17

§ represents tenth of predicted risk

7.4 ROC curve for QFracture on QResearch

The receiver operator curves (ROC) for QFracture for both outcomes based on the original QResearch validation cohort are shown below. Separate curves are shown for women and men aged 30-85 years. ROC curves are also shown for FRAX for hip fracture in women and men aged 40-85.

Tables giving the sensitivity, specificity positive and negative predictive values at predefined thresholds can be found in the following section.

The ROC curves show higher areas under the curve for hip fracture than osteoporotic fracture, and higher values for women than men.

Figure 1 ROC curve for QFracture for osteoporotic fracture in women aged 30-85

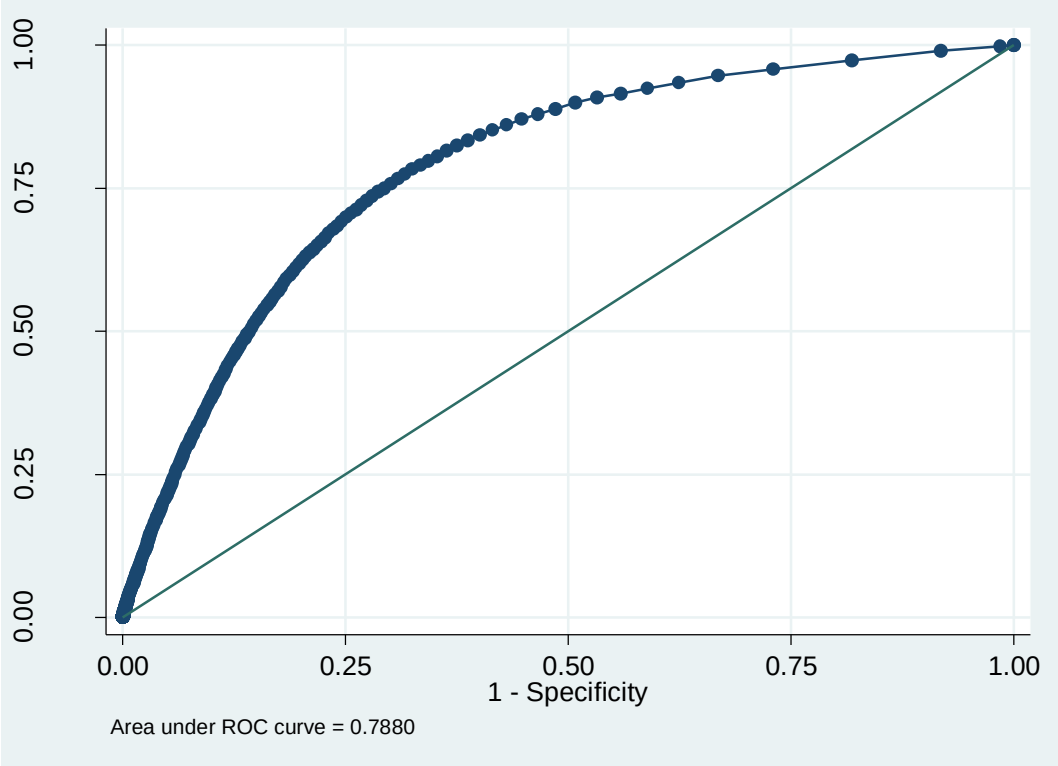


Figure 2 ROC curve for QFracture for hip fracture in women aged 30-85

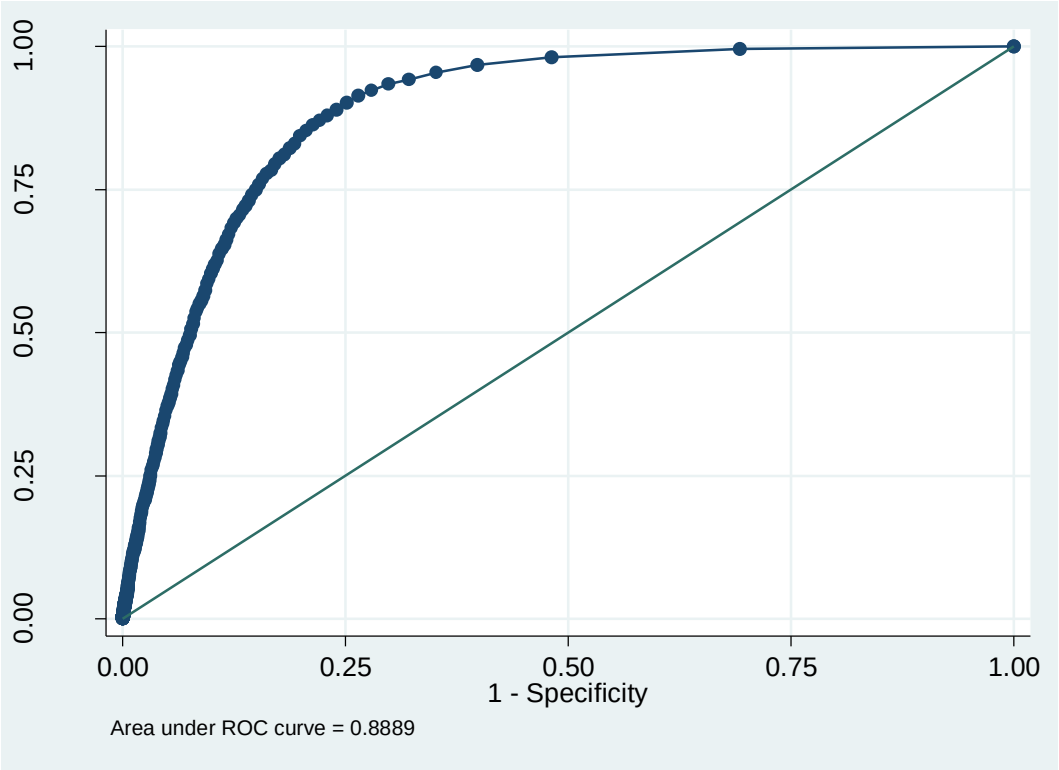


Figure 3 ROC curve for QFracture for osteoporotic fracture in men aged 30-85

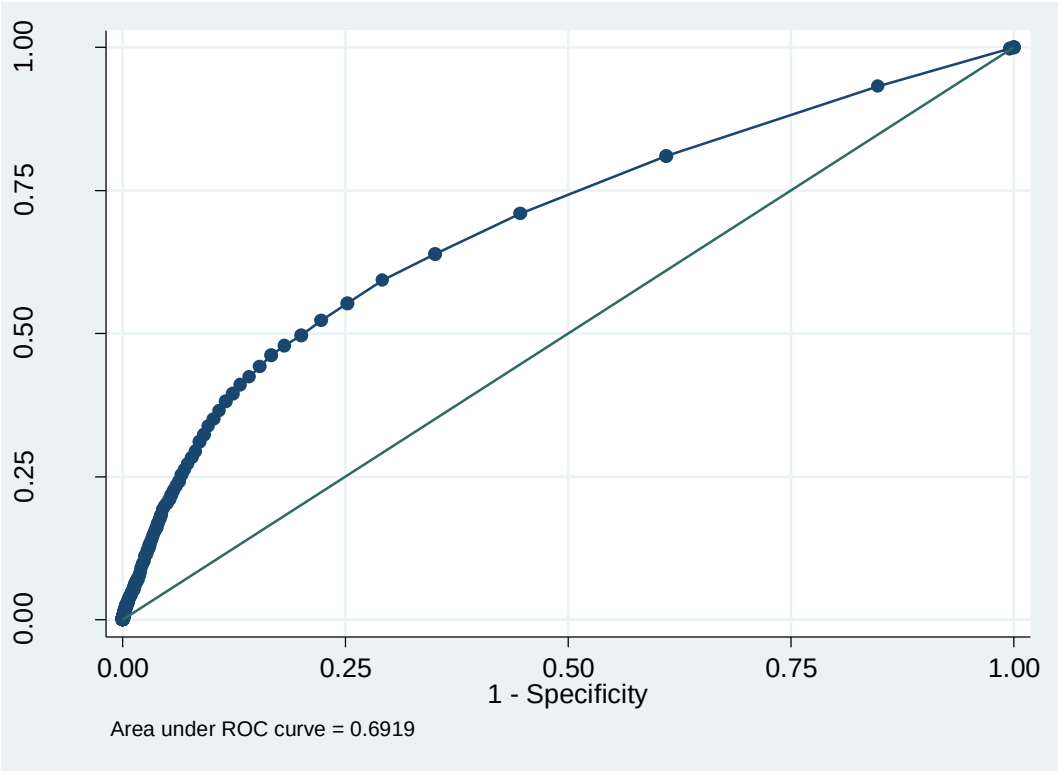


Figure 4 ROC curve for QFracture for hip fracture in men aged 30-85

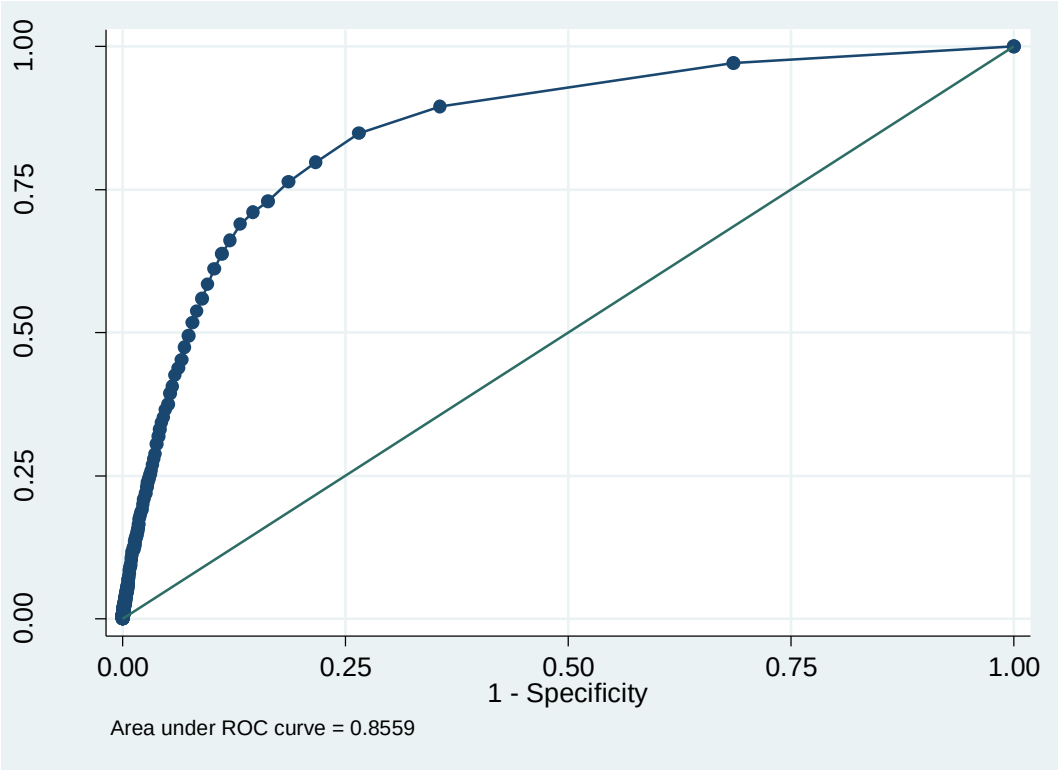


Figure 5 ROC curve for FRAX for hip fracture in women aged 40-85

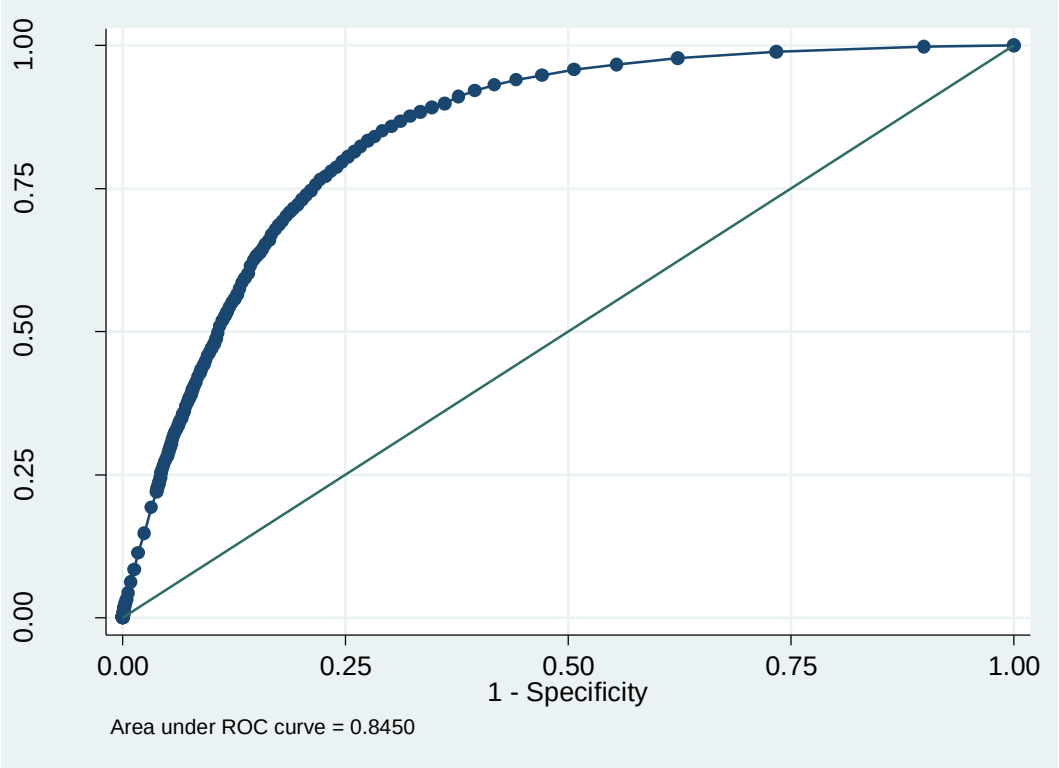
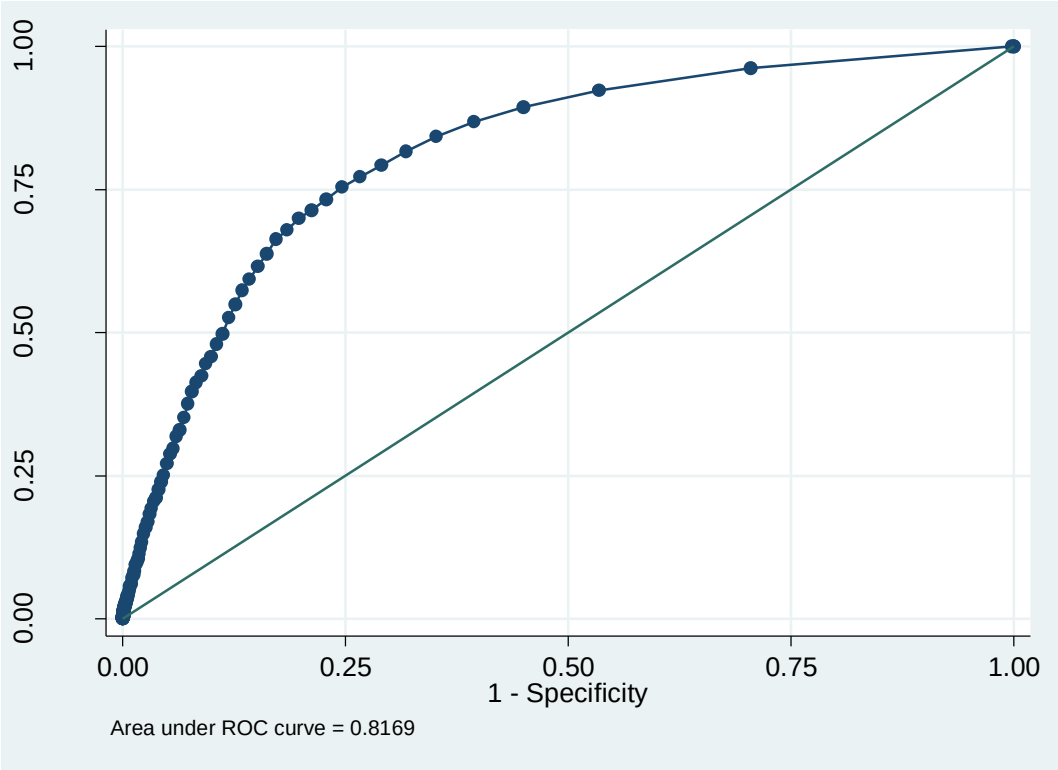


Figure 6 ROC curve for FRAX for hip fracture in men aged 40-85



7.5 Sensitivity and specificity of QFracture ages 30-85 years

The next table show the sensitivity, specificity, positive and negative predictive values at pre-selected thresholds of 10 year risk for QFracture for hip fracture and major fractures (comprising hip, vertebral, and distal radius fractures) It includes all patients (even if censored before 10 years).

For example, if a cut off of a 10 year risk of 3% for hip fracture in women is used, then it will identify 13.1% of women aged 30-85 as high risk. This will then contain 64.1% of all cases of hip fracture in the next 10 years will be identified (i.e. sensitivity of 64.1%). The positive predictive value is 4% meaning that for every 100 women selected in this high risk group, then 4 are likely to have a hip fracture over the next 10 years. If the threshold is increased to 5%, then the sensitivity will fall to 46.8% but the positive predictive value will increase to 4.6% and the specificity will increase to 92%.

Table 5 sensitivity, specificity, positive predictive value and negative predictive value of QFracture for hip fracture and major fracture at selected thresholds of 10 year risk. Analysis of all patients 30-85 years.

	cut off (%)*	*Total % identified as high risk*	*true negative*	*false negative*	*false positive*	*True positive*	*sensitivity*	*specificity*	*PPV*	*NPV*
Women										
hip fracture	3%	13.3	562,941	1,948	83,463	3,476	64.1	87.1	4.0	99.7
hip fracture	5%	8.4	593,975	2,887	52,429	2,537	46.8	91.9	4.6	99.5
major fracture	10%	7.7	582,257	10191	45,567	3,761	27.0	92.7	7.6	98.3
major fracture	20%	0.5	624,773	13640	3,051	312	2.2	99.5	9.3	97.9
major fracture	30%	0.1	627,500	13916	324	36	0.3	99.9	10.0	97.8
Men										
hip fracture	3%	3.6	615,500	1325	22787	413	23.8	96.4	1.8	99.8
hip fracture	5%	1.6	628,457	1529	9830	209	12.0	98.5	2.1	99.8
major fracture	10%	0.2	627,723	4464	1445	55	1.2	99.8	3.7	99.3
major fracture	20%	0.0	629,102	4515	66	4	0.1	100.0	5.7	99.3
major fracture	30%	0.0	629,163	4518	5	1	0.0	100.0	16.7	99.3
All										
hip fracture	3%	8.5	1,178,441	3,273	106,250	3,889	54.3	91.7	3.5	99.7
hip fracture	5%	5.0	1,222,432	4,416	62,259	2,746	38.3	95.2	4.2	99.6
major fracture	10%	4.0	1,209,980	14,655	47,012	3,816	20.7	96.3	7.5	98.8
major fracture	20%	**0.3**	1,253,875	18,155	3,117	316	1.7	99.8	9.2	98.6
major fracture	30%	**0.03**	1,256,663	18,434	329	37	0.2	100.0	10.1	98.6

*10 year risk of outcome calculated using QFracture(%)

Note that caution must be taken when interpreting the statistics in these tables, since they do not differentiate patients who were censored before 10 years (eg because of death or the end of the study) and so we do not know the eventual outcome for these patients. The effect of this is to under-estimate the positive predictive values.

7.6 Sensitivity and specificity of QFracture ages 40-85 years

The next QFracture table is similar to the previous table in what it reports except it applies to patients aged 40-85 years.

Table 6 sensitivity, specificity, positive predictive value and negative predictive value of QFracture for hip fracture and major fracture at selected thresholds of 10 year risk. Analysis includes all patients 40-85 years.

	*cut off *(%)*	*% high risk*	*true negative*	*false negative*	*false positive*	*True positive*	*sensitivity*	*specificity*	*PPV*	*NPV*
Women										
hip fracture	3	19.1	365,682	1,918	83,463	3,476	64.4	81.4	4.0	99.5
hip fracture	5	12.1	396,716	2,857	52,429	2,537	47.0	88.3	4.6	99.3
major fracture	10	11.1	386906	9513	45567	3761	28.3	89.5	7.6	97.6
major fracture	20	0.8	429422	12962	3051	312	2.4	99.3	9.3	97.1
major fracture	30	0.1	432149	13238	324	36	0.3	99.9	10.0	97.0
Men										
hip fracture	3	5.5	399875	1261	22787	413	24.7	94.6	1.8	99.7
hip fracture	5	2.4	412832	1465	9830	209	12.5	97.7	2.1	99.6
major fracture	10	0.4	415053	3766	1445	55	1.4	99.7	3.7	99.1
major fracture	20	0.0	416432	3817	66	4	0.1	100.0	5.7	99.1
major fracture	30	0.0	416493	3820	5	1	0.0	100.0	16.7	99.1
All										
hip fracture	3	12.5	765,557	3,179	106,250	3,889	55.0	87.8	3.5	99.6
hip fracture	5	7.4	809,548	4,322	62,259	2,746	38.9	92.9	4.2	99.5
major fracture	10	5.9	801,959	13,279	47,012	3,816	22.3	94.5	7.5	98.4
major fracture	20	0.4	845,854	16,779	3,117	316	1.8	99.6	9.2	98.1
major fracture	30	0.04	848,642	17,058	329	37	0.2	100.0	10.1	98.0

*10 year risk of outcome calculated using QFracture(%)

7.7 Sensitivity and specificity of FRAX (2008) ages 40-85 years

The next table is similar to the previous table but is based on FRAX (2008) instead of QFracture and only includes hip fracture (the FRAX risk score for fracture was not included in the original BMJ paper as the outcome definition was different).

Using a cut off for women of 3% for the FRAX score, would identify 21.6% of women aged 40-85 at risk compared with 19.1% for QFracture. Using the 5% threshold would identify 13.9% at risk using FRAX but 12.1% using QFracture. In other words if pre-defined thresholds are used then this will identify large number of patients with FRAX compared with QFracture

Table 7 sensitivity, specificity, positive predictive value and negative predictive value of FRAX (2008) for hip fracture at selected thresholds of 10 year risk. Analysis includes all patients 40-85 years.

	*cut off *(%)*	*% high risk*	*true negative*	*false negative*	*false positive*	*True positive*	*sensitivity*	*specificity*	*PPV*	*NPV*
Women										
hip fracture	3	21.6	354,655	1,652	94,451	3,741	69.4	79.0	3.8	99.5
hip fracture	5	13.9	388,921	2,570	60,185	2,823	52.3	86.6	4.5	99.3
Men										
hip fracture	3	6.9	393717	1166	28945	508	30.3	93.2	1.7	99.7
hip fracture	5	1.6	416108	1540	6554	134	8.0	98.4	2.0	99.6
All										
hip fracture	3	14.5	748,372	2,818	123,396	4,249	60.1	85.8	3.3	99.6
hip fracture	5	7.9	805,029	4,110	66,739	2,957	41.8	92.3	4.2	99.5

*10 year risk of outcome calculated using FRAX(%)

7.8 Sensitivity and specificity using deciles of predicted risks

Given that FRAX (2008) over predicts risk of hip fracture compared with observed risks (as shown by the ratio of predicted to observed risks in the previous section), the use of pre-defined thresholds does not give a direct comparison between the two scores. To make a direct comparison, we have therefore repeated the analysis based on the top 10% and top 20% of predicted risk for each score, to give equivalent numbers of people in high risk groups.

The next table shows the results of the direct comparison between QFracture and FRAX and shows that the sensitivity of QFracture is similar or slightly higher than that for FRAX for men and women when comparison high risk groups of the same size. For example, for men the cut off for the top decile was a 10 year risk of 1.8% using QFracture and 2.4% for FRAX. The sensitivity at this threshold for men using QFracture was 41.1% compared with 39.0% for FRAX.

Table 8 Direct comparison between QFracture and FRAX (2008) for patients in the top 10% and 20% of predicted risk of hip fracture using each algorithm for men and women.

QFracture	***cut off *(%)***	***true negative***	***false negative***	***false positive***	***True positive***	***sensitivity***	***specificity***
		TN	FN	FP	TP		
Women							
top 20%	2.8%	361,775	1,826	87,331	3,567	66.1	80.6
top 10%	5.8%	405,823	3,228	43,283	2,165	40.1	90.4
Men							
top 20%	0.8%	338,915	555	83747	1119	66.8	80.2
top 10%	1.8%	380,918	986	41744	688	41.1	90.1

FRAX	***cut off *(%)***	***true negative***	***false negative***	***false positive***	***True positive***	***sensitivity***	***specificity***
		TN	FN	FP	TP		
Women							
top 20%	3.3%	363,222	1,841	85,884	3,552	65.9	80.9
top 10%	6.4%	406,496	3,233	42,610	2,160	40.1	90.5
Men							
top 20%	1.2%	339,346	567	83316	1107	66.1	80.3
top 10%	2.4%	383,263	1021	39399	653	39.0	90.7

8 Re-classification statistics

For the next analysis, we define high risk a 10 year risk of hip fracture in the top tenth for each risk score. We then looked at how many patients would be re-classified using QFracture compared with FRAX. The results are shown in the table below.

For example, for women, then using the top decile for each score, then 88.9% are classified classifed as low risk by both scores and 8.8% are classified as high risk by both scores. 1.2% of women would be classified as high risk on QFracture and low risk on FRAX and the observed 10 year risk in these women was 7.69%. Conversely, 1.1% of women would be classified as low risk on QFracture but high risk on FRAX. The observed 10 year risk in these women was 7.15%. In other words, women who would be missed' as high risk if FRAX were used, had a higher observed risk than women who would be 'missed' as high risk if QFracture were used. There were similar findings in men

Table 9: reallocation of patients based on using top decile of risk for each score. Figures are counts(%) and 10 year observed risks calculated using Kaplan Meier plots

	numbers	*% of total*	*10 yr observed risk*
women			
low on both QFracture and FRAX	404105	88.9	0.88
low on FRAX high on QFracture	5624	1.2	7.69
high on FRAX low on QFracture	4946	1.1	7.15
high on both QFracture and FRAX	39824	8.8	9.66
total	**454499**	**100.0**	
Men			
low on both QFracture and FRAX	377954	89.1	0.09
low on FRAX high on QFracture	6330	1.5	2.24
high on FRAX low on QFracture	3950	0.9	1.45
high on both QFracture and FRAX	36102	8.5	3.63
total	**424336**	**100.0**	

9 Summary of main findings

We have presented a direct comparison between QFracture and FRAX based on the same population with the following conclusions:

- QFracture performs better than FRAX (2008) with better discrimination.
- QFracture is well calibrated whereas FRAX (2008) over-predicts risk in every tenth of risk.
- QFracture has similar sensitivity compared with FRAX(2008) for men and women when the top decile of risk is identified.
- QFracture also performed well on an independent external dataset using data from the THIN database. Some of the performance statistics were better on the THIN dataset than the separate sample of practices used for the validation from QResearch.
- The current version of FRAX (2011) does not match the version of FRAX from 2008, so the comparisons made in this paper are with a historical version of FRAX and it is not possible to determine comparisons with a current version of FRAX.

9.1 Scientific and Ethical Approval

The project was approved by the QResearch Scientific board and is therefore approved by the Trent Multi Centre Research Ethics Committee.

9.2 Funding and acknowledgements

This original study was funded by Dr David Stables (medical director of EMIS).We acknowledge the contribution of EMIS and EMIS practices contributing to the QResearch database.

9.3 Competing Interests

JHC is co-director of QResearch – a not-for-profit organisation which is a joint partnership between the University of Nottingham and EMIS (leading supplier of IT for 60% of general practices in the UK). EMIS may implement the QFracture within its clinical system. JHC is also director of ClinRisk Ltd and CC is a consultant statistician for ClinRisk Ltd. ClinRisk Ltd produces software to ensure the reliable and updatable implementation of clinical risk algorithms within clinical computer systems to help improve patient care. JHC is also GP and professor of clinical epidemiology at the University of Nottingham.

10 References

1. Hippisley-Cox J, Coupland C. Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of QFractureScores. BMJ 2009;339:b4229-.
2. Hippisley-Cox J, Coupland C. QFracture - authors reponse. BMJ: BMJ, 2011.
3. Collins GS, Mallett S, Altman DG. Predicting risk of osteoporotic and hip fracture in the United Kingdom: prospective independent and external validation of QFractureScores. BMJ 2011;342:d3651.

11 Appendix 1- variables included in QFracture compared with FRAX

	Included in QFracture	*Included in FRAX*
Age range	30-85	40-90
Sex	Yes, separate models men and women	Yes as variable in one model
Smoking status	5 levels - non, ex smoker, light, moderate, heavy smoker	Yes as binary variable
Alcohol	Yes 5 categories	Yes as binary variable
Body mass index	Yes	Yes
Family history of osteoporosis	yes	Yes
Rheumatoid arthritis	Yes	Yes
Type 2 diabetes	Yes	Type 1 included within secondary osteoporosis
Regular steroids	Yes	Yes
Chronic liver disease	Yes	Included within secondary osteoporosis
Malabsorption (crohn's, ulcerative colitis, coeliac disease, blind loop)	Yes	Included within secondary osteoporosis
Other endocrine disorders (thyrotoxicosm, cushing's hyperparathyroidism,)	Yes	Hyperthyroidism included within secondary osteoporosis
HRT	Yes (women only)	no
Cardiovascular disease	Yes	no
History of falls	Yes	No
Menopausal symptoms (flushes or vaginal dryness)	yes	No
Asthma	Yes	no
Tricyclic antidepressants	Yes	No
Previous fracture	No	yes

12 Appendix 2- request from NICE

From: Silvia Rabar [mailto:Silvia.Rabar@rcplondon.ac.uk]
Sent: 02 November 2011 10:01
To: julia.hippisley-cox@nottingham.ac.uk
Subject: Information request

Dear Dr Hippisley-Cox,

I am writing to ask you for more information related to your publication in BMJ 2009; 339:b4229, entitled "Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of QFracture scores"".

We are currently developing a clinical guideline, in the UK, commissioned by the National Institute for Health and Clinical Excellence (NICE), on risk assessment for fragility fracture

http://guidance.nice.org.uk/CG/Wave25/2

I understand from your paper you have performed a subgroup analysis to compare FRAX (I believe you used the version FRAX without BMD, as opposed to FRAX with BMD) to QFracture, and you have reported the ROC value for the FRAX algorithm. One of our aim is to compare sensitivity and specificity of FRAX (both with and without BMD, where available) and QFracture at different thresholds for osteoporotic fractures and hip fractures. Therefore, it would be very helpful for our purposes if you could send me the ROC curve data, point by point, for both FRAX (without BMD?) and QFracture, applied to the same population. If this is not possible, would you be able to send me at least sensitivity, specificity (together with True positive, true negative, false positive and false negative values) for the following thresholds:

- Major osteoporotic fractures: 10%, 20% and 30%

- Hip fractures: 3% and 5%

Should you require any further information, please do not hesitate to contact me. I look forward to hearing from you soon.

Regards,

Silvia

Dr Silvia Rabar

Senior Project Manager and Research Fellow

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