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Document Version
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Statin initiations and QRISK2 scoring in UK general practice: A THIN database study.

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ABSTRACT

Background: Statin prescribing should be based on cardiovascular disease (CVD) risk, but evidence suggests overtreatment of low-risk groups and undertreatment of high-risk groups.

Aim: To investigate the relationship between CVD risk scoring in primary care and initiation of statins for the primary prevention of CVD, and the effect of national guideline change in 2014.

Design and Setting: Historical cohort study using UK electronic primary care records.

Method: We created a cohort of statin naïve patients without CVD between 01/01/2000 and 31/12/2015. We identified CVD risk scores (calculated using QRISK2 available from 2012) and statin initiations. We calculated rates of CVD risk score recording and analysed relationships between CVD risk category (low-, intermediate- and high-risk: <10%, 10-19.9% and ≥20% ten-year CVD risk) and statin initiation.

Results: We identified 1.4 million patients from 248 practices. 151,788 had a recorded CVD risk score since 2012 (10.67%) and 217,860 were initiated on a statin (15.31%). Among patients initiated on a statin after 2012, 27.1% had a documented QRISK2 score: 2.7% of low-risk, 13.8% of intermediate-risk, and 35.0% of high-risk patients were initiated on statins. Statin initiation rates halved from a peak in 2006. After the 2014 guidelines, statin initiation rates declined in high-risk patients but increased in intermediate-risk patients.

Conclusion: Most patients initiated on statins had no QRISK2 score recorded. Most patients at high CVD risk were not initiated on statins. 1 in 6 statin initiations were to low-risk patients indicating significant overtreatment. Initiations of statins in intermediate-risk patients rose after guidelines changed 2014.

How this fits in

This study confirms that there is potential under treatment of high-risk patients and, although only a

small proportion of low-risk patients are initiated on statins, low-risk patients represent a significant

proportion of all statin initiations. We have also demonstrated that the reduction in risk threshold

for recommending statins has not resulted in the massive increase in statin initiations that was

anticipated. This is the analysis to demonstrate that only a quarter of patients have evidence of

formal CVD risk assessment with QRISK2 prior to statin initiation despite the fact that this is essential

information for shared decision making and to determine treatment eligibility.

1.0 Introduction

Statins for primary prevention of CVD have been shown to be effective in reducing all-cause mortality, coronary heart disease (CHD) events and strokes. [1] CVD risk (determined from a combination of age, sex and cardiovascular risk factors) predicts benefit, therefore estimating CVD risk identifies patients who should be offered statins. [2]

Cardiovascular disease risk assessment has been a fundamental part of clinical guidance on CVD prevention in the UK and internationally for two decades. [3-5] In the UK, an absolute risk of CVD greater than a threshold was, and remains, the main criterion for offering statins. [6, 7] GPs are recommended to use QRISK2 (introduced in 2012) to estimate 10-year CVD risk. [2] Other risk calculators were used prior to this and were still available after 2012.

As estimated CVD risk is the best predictor of benefits of treatment, it is essential for effective shared decision making. [8] Evidence suggests that utilisation of risk scoring improves accuracy of perceived CVD risk and medical prescribing without causing harms. [9, 10] The use of CVD risk scoring should result in more targeted prescribing, but there is evidence both of undertreatment of high-risk patients and overtreatment of low-risk patients. [11-15] This may be because risk scores are not consistently used by clinicians [16] or because clinical information not incorporated into the risk scores is being taken into account.

In 2014, guidelines for England and Wales on lipid modification reduced the CVD risk threshold for offering statins from 20% to 10% 10-year risk. [6, 7] The benefit of lowering the threshold has been questioned. [17] The medical community and lay media raised concerns about over prescribing of statins, questioning the clinical benefit and potential for harm. [18, 19]

The aim of this study is to examine how trends in initiating statins for the primary prevention of CVD relate to QRISK2 scoring and how these have changed over recent years with particular focus on the impact of the 2014 NICE guidance. This will provide new information on the impact of, and adherence to, clinical guidelines in the UK.

2.0 Methods

This was a historical cohort study using data from anonymised primary care records of practices in England and Wales contributing to The Health Improvement Network (THIN) database. The authors had full access to the database. THIN has been used in previous studies to validate QRISK2 and it was shown that the discrimination statistics in THIN are as good as those for the original QRISK2 cohort. [20, 21] Practices that contribute to THIN use the Vision (In Practice Systems) electronic patient records system. [22] Clinical data are coded using Read code clinical classification version 2 [23] and drug codes correspond to the British National Formulary (BNF). [24] Codes used are available in appendix 1. To maintain a stable cohort, only practices which contributed data for the whole study period (beginning of 2000 to the end of 2015) were included. Patients had to be suitable for CVD risk assessment according to NICE guidance [6] and have never been prescribed statins (or other lipid lowering therapy) in the past. Patients with CKD stages 3-5, type 1 diabetes mellitus or familial hypercholesterolaemia were excluded as risk assessment is not required for statin initiation. Patients were eligible for inclusion from the earliest of the following dates: study start date, acceptable mortality reporting date (which ensures that patient deaths and deregistrations are being recorded consistently), Vision installation date plus one year, registration date plus one year (to ensure time for baseline data to be recorded), and age 40; until the earliest of the following dates: age 85, study end date, CVD diagnosis, statin initiation, recording of a contraindication for the prescribing of statins, death, and transfer out of the practice.

All QRISK2 scores recorded during the study period were included (individuals may have had several scores recorded). Practice ID, country, ethnicity, Townsend quintile, sex, and year of birth were identified. Patients with missing gender or year of birth, or a QRISK score >99.99% were excluded. A 'missing' category was used for other missing data.

2.1 Primary analysis

Following a descriptive analysis of the cohort, the rates of statin initiations and QRISK2 recording per year were calculated. Sub-analyses were performed to establish these rates by demographic variables (sex, age and Townsend quintile). Rates were not adjusted for these variables.

2.2 Secondary analysis

2.2.1 Relationship between QRISK2 scoring and statin initiation.
QRISK2 scores were categorised into low (<10%), intermediate (10-19.9%) and high (≥20%) ten-year CVD risk. In each category, the proportion of patients initiated on statins following QRISK2 scoring was established based on the patient's latest record.

Coded CVD prevention encounters were categorised into: QRISK2 score with subsequent statin initiation, QRISK2 score without statin initiation, statin initiation without prior QRISK2 score. The proportion of initiations with/without a recorded QRISK2 score were reported by patient demographic characteristics. Statistical significance was assessed using Pearson's chi-squared tests.

2.2.2 Impact of NICE guidance
The mean recorded QRISK2 score for patients initiated on statins was calculated pre- and post-guideline publication (July 2014). The annual proportion of statin initiations in each QRISK2 category (risk scores within 60 days of prescribing) was reported from 2012 to 2015 to reveal any change in the pattern of prescribing.

3.0 Results

After excluding 3 patients who had a QRISK2 score of >99.99, the cohort comprised of 1,422,664 patients from 248 practices with a total of 9,437,754 years of follow up between 2000 and 2015. The median observation period was 5.65 years (IQR 2.50-10.50). 217,860 patients were initiated on a statin (15.31%, 95% confidence interval (CI) 15.25-15.37%) and 151,788 patients had at least one QRISK2 score recorded (10.67%, 95%CI 10.62-10.72%). Of the patients with a recorded QRISK2 score,

80.2% had just one score, 15.1% had two scores, and 4.6% had more than two scores recorded

(range 3-13). The demographic characteristics of the cohort are shown in Table 1.

		N (%)	Statin initiation rate (95% CI) (initiations/1000 ptyrs)*	QRISK recording rate (95% CI) (scores/1000 ptyrs)*
Sex	Male	693403 (48.7)	25.5 (25.4-25.7)	51.7 (51.3-52.1)
	Female	729261 (51.3)	20.9 (20.8-21.0)	61.4 (61.0-61.8)
Age group (on entering cohort)	40-59	779,566 (54.8)	8.3 (8.2-8.4)	43.3 (42.9-43.7)
	50-59	304,440 (21.4)	21.7 (21.5-21.8)	61.8 (61.3-62.4)
	60-69	186,641 (13.1)	42.1 (41.8-42.4)	81.2 (80.4-82.0)
	≥70	152,017 (10.7)	41.7 (41.4-42.1)	51.8 (51.0-62.6)
Townsend deprivation quintile	1st (least)	397,251 (27.9)	20.6 (20.5-20.8)	56.4 (55.9-57.0)
	2nd	321,663 (22.6)	22.5 (22.3-23.2)	59.3 (58.7-59.9)
	3rd	299,183 (21.0)	23.4 (23.2-23.7)	57.7 (57.0-58.3)
	4th	239,649 (16.9)	25.6 (25.4-25.9)	53.8 (53.1-54.5)
	5th (most)	143,353 (10.1)	27.8 (27.4-28.1)	55.2 (54.2-56.2)
	Missing	21,565 (1.5)	22.8 (21.8-23.8)	58.1 (55.7-60.6)
Ethnicity	Asian	21,993 (1.6)	33.8 (32.7-34.9)	87.0 (84.2-89.9)
	Black	18,361 (1.3)	20.7 (19.7-21.6)	64.4 (61.9-67.0)
	Chinese	2,668 (0.2)	18.7 (16.6-21.2)	64.2 (57.8-71.3)
	Mixed	3,929 (0.3)	19.0 (17.1-21.1)	77.6 (71.7-84.0)
	Other	6,389 (0.5)	22.3 (20.6-24.1)	73.5 (68.9-78.4)
	White	516,436 (36.3)	25.6 (25.4-25.8)	72.0 (71.5-72.5)
	Missing	852,888 (60.0)	21.4 (21.3-21.5)	43.8 (43.4-44.1)

* From 2012-2015 inclusive
Table 1: Cohort characteristics

3.1 Statin initiation trends

From 2000 to 2006 there was an increase in the rate of statin initiations from 9.05 (95%CI 8.66-9.45) initiations/1000 patient-years (ptyrs) to 34.41 (33.95-34.87) initiations/1000ptyrs. The rate then declined to 17.26 (95%CI 16.95-17.57) initiations/1000ptyrs in 2015 (Figure 1). Males had a higher overall annual initiation rate than females (25.5 vs 20.9, p<0.001) (not adjusted for other characteristics).

Figure 1
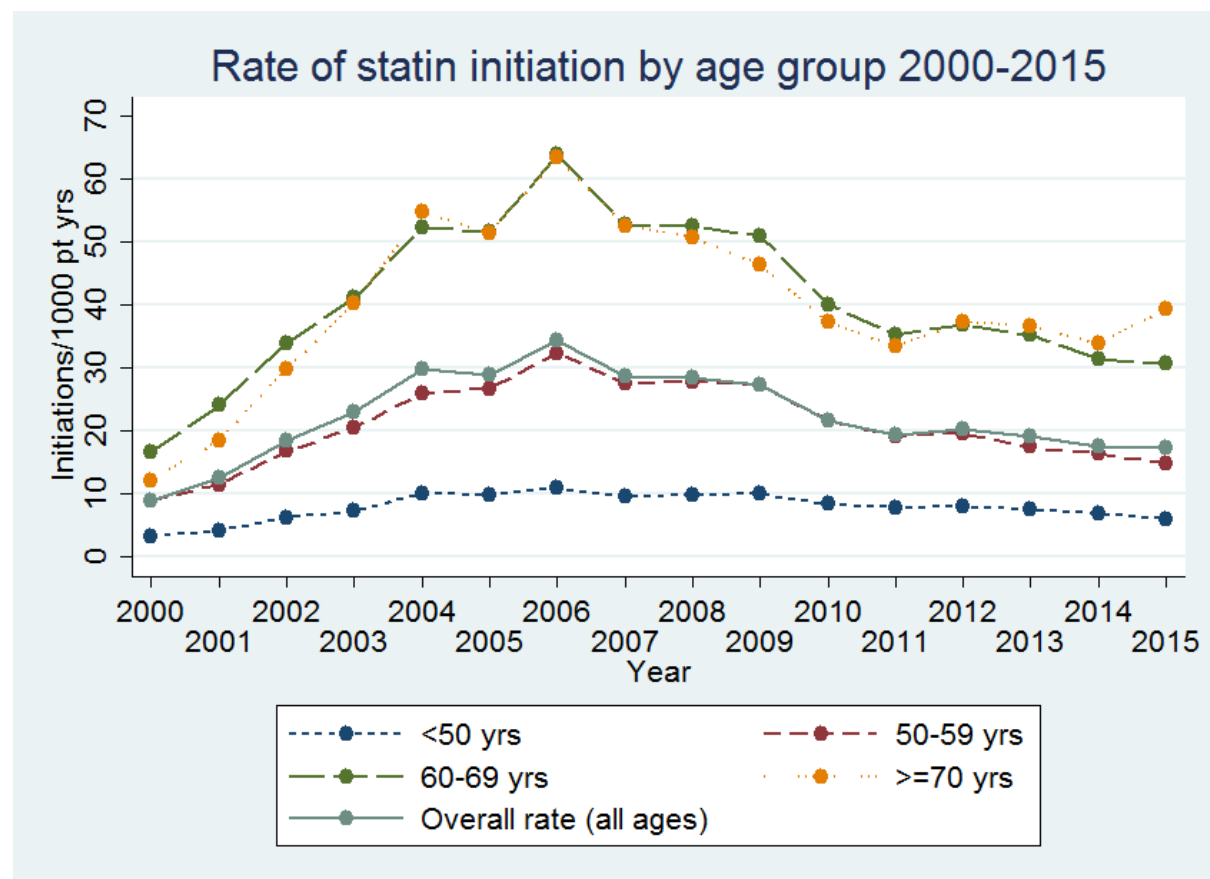
3.2 Trends in the recording of QRISK scores

From the introduction of the QRISK2 code (2012) until 2015, there was a steady increase in the recording of QRISK2 scores from 31.6 (30.2-33.1) to 99.1 (95%CI 96.6-101.7) per 1000ptyrs. Women had an overall unadjusted rate of QRISK2 recording of 61.4 (95%CI 61.0-61.8) scores/1000ptyrs compared with 51.7 (51.3-52.1) QRISK2 scores/1000ptyrs for men.

3.3 Association between QRISK2 scores and statin initiation

The majority of patients who had a QRISK2 score documented did not subsequently have a statin prescribed (90.2%, 95%CI 90.0-90.3%). Table 2 shows the number of patients in each QRISK2 category and the proportion initiated on a statin. Low, intermediate and high-risk patients accounted for 16.6%, 37.1% and 46.3% of all patients prescribed a statin following recorded QRISK2 assessment.

Period	QRISK2 Category	Patients initiated on statin (%)	Total patients in category	Guideline congruent initiations (%)
2012 - 2015	≥20%	6,923 (35.0)	19,781	
	10-19.9%	5,545 (13.8)	40,272	
	0-9.9%	2,481 (2.7)	91,735	
	Total	14,949 (9.8)	151,788	NA
Pre-guideline change (01/2012-06/2014)	≥20%	3,862 (36.7)	10,531	
	10-19.9%	2,198 (12.8)	17,117	
	0-9.9%	1,381 (3.6)	38,258	
	Total	7,441 (11.3)	65,906	3,862 (51.9)
Post guideline change (07/2014-12/2015)	≥20%	3,061 (33.1)	9,250	
	10-19.9%	3,347 (14.4)	23,155	
	0-9.9%	1,100 (2.1)	53,477	
	Total	7,508 (8.7)	85,882	6,408 (85.3)

Table 2: Proportion of patients with previous CVD risk assessment initiated on statins by QRISK2 category and time period.

Since 2012, 72.9% (95%CI 72.5-73.3%) of patients initiated on a statin did not have a QRISK score recorded at any time. The outcomes of clinical encounters involving the initiation of statins or recording of QRISK2 score are illustrated in Figure 2. Table 3 demonstrates the variations in these outcomes for different demographic groups. The proportion of statin initiations that occur without a recorded QRISK2 score was relatively consistent, with the notable exception that younger patients seemed to have a higher proportion of initiations without a recorded risk assessment.

Figure 2

3.4 Impact of NICE guidance on QRISK2 scoring and statin prescribing

When examining risk scores that were calculated within 60 days of statin initiation, the mean QRISK2 score before the 2014 guidance was 23.06 , dropping to 19.28 after July 2014 (p=<0.001). Figure 3 shows that an increasing proportion of statin initiations occur in the 10-19% QRISK2 category in 2014/15 whilst initiations in the high-risk category (>20%) continue on a declining trajectory.

For patients with a recorded QRISK2 score (at any time), the proportion of statin initiations that were consistent with prevailing NICE guidelines increased from 51.9% (2008 guideline) to 85.3% (2014 guideline). This change is mostly accounted for by the patients with a QRISK2 score of 10-19.9% (Table 2).

Characteristic		QRISK2 score, no statin (%)	QRISK2 score, subsequent statin (%)	Statin initiated without QRISK2 (%)	Proportion of initiations without QRISK*
Gender	Male	54,874 (67.5)	7,134 (8.8)	19,281 (23.7)	0.73
	Female	79,438 (76.3)	6,691 (6.4)	17,934 (17.2)	0.73
Age group (years)	40-49	42,913 (84.7)	1,347 (2.7)	6,396 (12.6)	**0.83**
	50-59	43,924 (75.6)	3,255 (5.6)	10,943 (18.8)	**0.77**
	60-59	33,007 (65.0)	5,542 (10.9)	12,201 (24.0)	**0.69**
	≥70	11,468 (50.2)	3,681 (16.1)	7,675 (33.6)	**0.68**
Townsend deprivation quintile	1st	40,004 (74.4)	3,669 (6.8)	10,080 (18.8)	0.73
	2nd	31,760 (73.4)	3,425 (7.9)	8,087 (18.7)	0.70
	3rd	27,546 (72.0)	2,896 (7.6)	7,804 (20.4)	0.73
	4th	19,185 (68.2)	2,272 (8.1)	6,654 (23.7)	0.75
	5th	10,829 (66.5)	1,380 (8.5)	4,072 (25.0)	0.75
	Missing	49,88 (87.7)	183 (3.2)	518 (9.1)	0.74
Total		134,312 (72.5)	13,825 (7.5)	37,215 (20.1)	0.73

* Proportions in bold show significant trend (p<0.001) by Pearson's chi squared test
Table 3: Breakdown of outcomes from clinical encounters 2012-2015

4.0 Discussion

4.1 Summary

The rate of statin initiations has halved since 2006. The initial peak in statin initiations may have

been influenced by a dramatic reduction in the cost of prescribing when simvastatin came off patent

in 2003. In addition, there were major publications on CVD prevention around this time including the

Joint British Societies' guidelines and a NICE technological appraisal recommending the use of

statins. [25, 26] This may have resulted in saturation the population of patients who were eligible and

willing to take statins over the next few years. This could explain the decline in initiations from 2006

to 2015, as patients who could potentially be prescribed statins would be the newly eligible (lower

risk) or those less active in seeking treatment. Additionally, over this period there was increased focus on the adverse effects of statins as data from observational studies differed from trial findings [27] which may have influenced both the clinicians' decision to prescribe, and the patients' decision to accept, treatment.
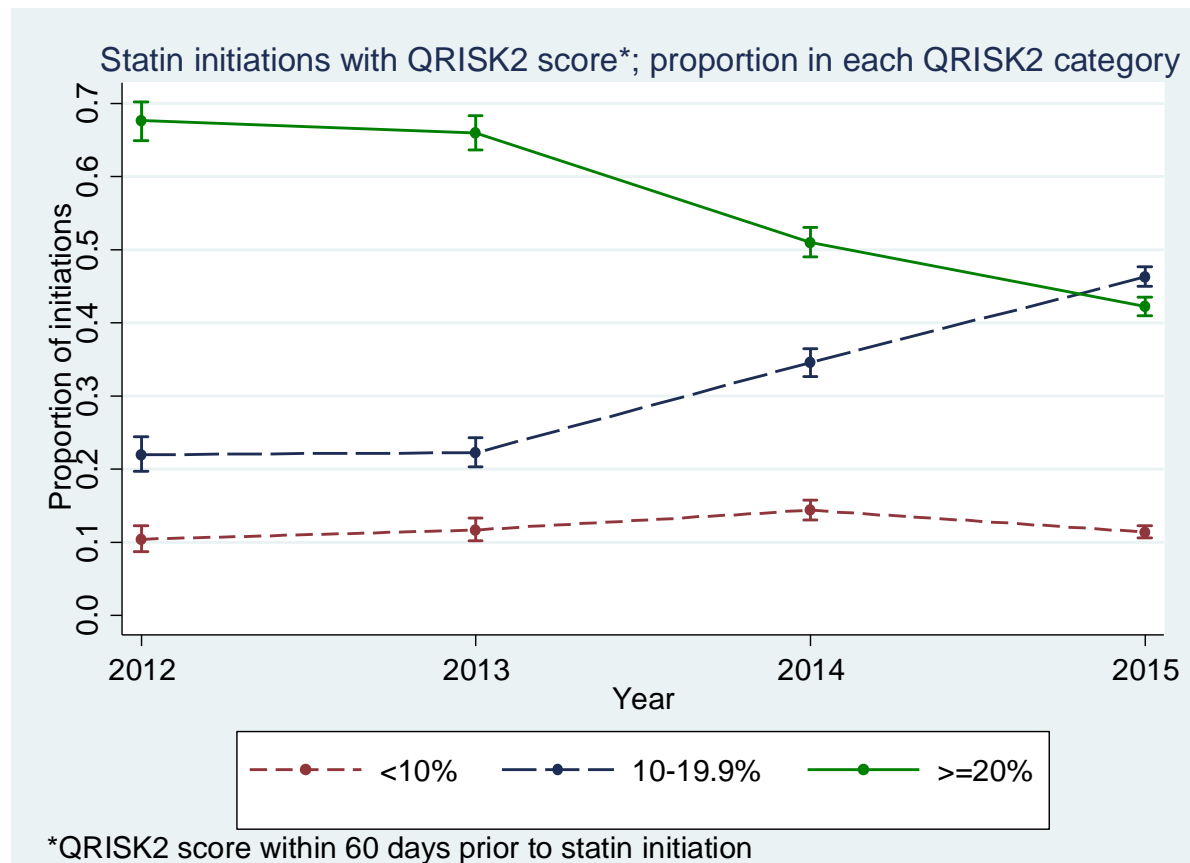

Figure 3

The rate of QRISK2 coding has showed a steady increase since it became the recommended risk calculator in 2012. Most patients who had a QRISK2 score calculated were not prescribed a statin in the following 60 days, even those found to be in the high-risk category. It is not possible to establish whether those patients who were above the threshold to be prescribed a statin did not receive treatment because they were not offered it, or because they declined an offer. Older patients (aged ≥70 years) were less likely to have a QRISK2 score recorded than patients aged 50-69 years. Younger patients were more likely to be initiated on statins without recorded QRISK2 assessment than older patients.

Most patients initiated on statins since 2012 did not have a prior QRISK2 score recorded. Of those that did, one in six patients were in the low-risk category and should not have been offered a statin according to NICE guidance. These findings indicate that factors other than risk score were being considered when initiating statins. It is possible that clinicians were responding to individual patient preference when prescribing to low-risk patients, but without a discussion about risk (informed by a risk estimate) these preferences cannot be fully informed. It appears that the latest NICE guidance changed clinicians' behaviour; the rate of statin initiation amongst patients in the intermediate-risk category (10-19%) increased whilst the high-risk initiation rate continued to decrease.

4.2 Strengths and limitations

THIN includes a large number of practices which are generalizable to the UK population. [28] This permits identification of prescribing trends across large numbers of patients over a 16-year period. This period included 18 months of data following the publication of the latest NICE guidance which is sufficient time to identify changes in prescribing and coding behaviour. Prescribing data is well recorded as prescriptions are generated and recorded by the clinical system.

We could only identify QRISK2 scores that were entered automatically or manually as coded data in the electronic patient record. It is possible that clinicians calculated a QRISK2 score but did not enter it as coded data. This would result in an underestimate of the rate of QRISK2 scoring and the proportion of patients being prescribed a statin following QRISK2 score. Additionally, some clinicians may have used alternative risk calculators in their decision making. Risk scores calculated using an alternative calculator were not identified and this may lead to us underestimating the use of risk estimation in decision making.

We have assumed that a QRISK2 score within 60 days of statin initiation was likely to be taken into consideration when deciding if a statin should be initiated. It is possible the QRISK2 score was not considered, or that scores older than 60 days featured in the decision. The latter would lead to an underestimate of the proportion of patients initiating statins on the basis of QRISK2 score.

Importantly, the decision to prescribe statins is a clinical decision and should not be based on QRISK2 score alone. Patient preferences, co-morbidities and individual patient circumstances will all inform the shared decision to prescribe statins. Some guideline incongruent decisions will have been clinically justifiable but we are not able to identify this from the data.

4.3 Comparisons with existing literature

The peak in statin initiation in 2006 has previously been reported by O'Keefe et al who used the same database so the initiation patterns are identical. [29] However, this study ended in 2013 so any effects of the 2014 NICE guidance were not observed.

Matthews et al observed a steady increase in statin initiations for primary prevention between January 2011 and October 2013 rather than the decline in initiations we observed. [30] This may be explained by the fact that Matthews et al only identified statin initiations for primary prevention in patients with a preceding CVD risk score. Our results would suggest that this definition would exclude up to 75% of initiations.

Other studies considering the relationship between risk score and statin prescribing have used *post hoc* risk calculations [12, 14] or risk scores that were collected for the purpose of research [15] so it is difficult to imply that prescribing decisions were based on risk scores. Homer et al did use routinely collected risk scores, but their data was limited to a specific geographical area [13] and they found that nearly 60% of patients suitable for risk assessment had a risk score documented. We found that only 10% of our population had a coded risk score suggesting that Homer's results may not be generalizable to the rest of England and Wales.

Balder et al. considered whether statin prescriptions were consistent with guidelines in the Netherlands. [15] They classified 66% of prescriptions as guideline-inconsistent. In the UK, previous studies have found that 58.3% [12] and 58.1% [13] of prescriptions were guideline-inconsistent. We found lower rates of guideline-inconsistent prescribing (48.1%) under the 2008 guidance. Guideline-inconsistent prescribing decreased to 14.7% from July 2014, but this is as a result of the guidelines

changing to be more in keeping with practice rather than the other way around. Guidelines consistently recommend that patients with a risk of <10% should not be prescribed statins. We found that 2.7% of patients in this category were prescribed a statin, which is lower than other studies (2.9% [15], 3.7% [13], 5.0% [14]) suggesting improved concordance with guidelines.

5.0 Implications for research and practice

As CVD risk estimation is instrumental in the decision to initiate statins, we feel that all patients should have a documented CVD risk score prior to statin initiation. It is possible that a higher proportion statin initiations are based on patients' individual risk than our data indicates, but we feel that the medical record should routinely reflect the incorporation of risk score in this decision. Further research needs to be done to understand why some patients do not undergo risk assessment prior to statin initiation and on what basis the decision to prescribe is founded if risk assessment is not used. We also need to investigate why low-risk patients are initiated on statins and whether high-risk patients who are not initiated on statins represent missed opportunities to lower CVD risk or an appropriate informed and shared decision.

Data Sharing: List of codes used to search the database is available in the appendices

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