CRD summary
This review found that the concordance between fractional flow reserve and quantitative coronary imaging or noninvasive imaging is modest to low. There was substantial variation in the results. The authors’ conclusions appear to be largely based on summary measures and so are unlikely to be reliable.

Authors’ objectives
To compare fractional flow reserve (FFR) with quantitative coronary angiography (QCA) and/or noninvasive imaging for the evaluation of myocardial ischemia.

Searching
PubMed was searched to February 2006 using the terms 'fractional flow reserve' and 'FFR'. Reference lists of retrieved studies and relevant review articles were screened for additional relevant studies. Only English language studies were eligible for inclusion.

Study selection
Study designs of evaluations included in the review
Studies of any design that included at least 5 patients were eligible for inclusion.

Specific interventions included in the review
Studies that assessed FFR measurements or QCA were eligible for inclusion. Studies that assessed native coronary arteries or arteries that had undergone percutaneous coronary interventions (not bypass grafts) were eligible for inclusion. Evaluations of the extent of coronary stenosis through visual examination were excluded.

Reference standard test against which the new test was compared
Studies of QCA had to include FFR as the reference standard to be eligible for inclusion. Studies of FFR had to include noninvasive imaging for the same coronary lesions as the reference standard to be eligible for inclusion. Noninvasive imaging techniques eligible for inclusion as the reference standard were various nuclear medicine applications using thallium-201 (Tl-201) or technetium-99m (Tc-99m) with or without single-photon emission computed tomography (SPECT) and dobutamine stress echocardiography. Studies with overt verification bias (different application of the reference standard based on the results of the index test) were excluded. The specific imaging techniques evaluated were SPECT (using Tl-201 or Tc-99m) and dobutamine stress echocardiography.

Participants included in the review
Studies of patients in any clinical setting were eligible for inclusion. The patients in the included studies were symptomatic; asymptomatic; had experienced a myocardial infarction; had left main coronary artery disease; had undergone (angiographic) restenosis; or had side branch post-stenting. The mean age ranged from 54 to 68 years and the proportion of men ranged from 42 to 93%. The majority of studies focused on moderate stenoses.

Outcomes assessed in the review
Studies had to report sufficient data to construct a 2x2 table of test performance. The outcomes reported in the review were sensitivity and specificity as an indication of the concordance between the imaging techniques evaluated.

How were decisions on the relevance of primary studies made?
Two reviewers assessed studies for relevance. A third reviewer resolved any disagreements.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
Two reviewers independently extracted the data as 2x2 tables of test performance for the concordance of FFR with each of the comparator tests. A third reviewer resolved any disagreements. FFR was considered positive for values less than 0.75 in the main analysis, but data were also extracted for the 0.80 threshold. QCA was considered positive for diameter stenosis of at least 50%. For imaging techniques, the thresholds reported by each study for inducing ischaemia were accepted. Sensitivity and specificity were calculated for each set of 2x2 data.

Methods of synthesis
How were the studies combined?
The pooled sensitivity and specificity, together with their 95% confidence intervals (CIs), were estimated independently across studies using a random-effects model. A summary receiver operating characteristic (SROC) analysis based on the Moses-Littenberg model was also conducted.

How were differences between studies investigated?
Heterogeneity was assessed using Fisher's exact test (p<0.10 considered statistically significant). Sensitivity analyses were conducted to exclude studies that exclusively or predominantly enrolled patients after myocardial infarction, that included only patients with restenosis, or that measured hyperemia differently to other studies.

Results of the review
Thirty-one studies (2,092 patients, 2,368 vessels) were included.

All values for ranges in sensitivity and specificity were read from SROC plots and so are approximate.

For QCA compared with FFR, threshold 0.75 (18 studies), there was substantial heterogeneity. The sensitivity ranged from 30 to 100% and the specificity from 0 to 90%. The pooled sensitivity and specificity were 78% (95% CI: 67, 86) and 51% (95% CI: 40, 61), respectively.

For QCA compared with FFR, threshold 0.80 (16 studies), there was substantial heterogeneity. The sensitivity ranged from 30 to 100% and the specificity from 0 to 88%. The pooled sensitivity and specificity were 76% (95% CI: 64, 85) and 54% (95% CI: 40, 68), respectively.

For FFR (threshold 0.75) compared with noninvasive imaging (17 studies), there was substantial heterogeneity although less than for the comparisons of QCA with FFR. The sensitivity ranged from 40 to 100% and the specificity from 36 to 100%. The pooled sensitivity and specificity were 76% (95% CI: 69, 82) and 76% (95% CI: 71, 81), respectively.

Studies that compared FFR with SPECT (15 studies) showed a pooled sensitivity of 75% (95% CI: 66, 82) and pooled specificity of 77% (95% CI: 70, 83). Concordance was greater for studies that compared FFR with dobutamine echocardiography (6 studies): the pooled sensitivity and specificity were 82% (95% CI: 62, 92) and 74% (95% CI: 66, 81), respectively.

The exclusion of three studies that enrolled patients exclusively or predominantly following myocardial infarction, two studies that included patients with restenosis, or one study that measured hyperemia differently to the other studies, did not alter the results.

Authors’ conclusions
FFR and QCA show extensive lack of concordance, suggesting that they provide largely independent information. FFR shows greater although still modest concordance with noninvasive imaging tests.

CRD commentary
This review addressed a focused question that was supported by defined inclusion criteria. The literature search was limited to one electronic database but the search terms were appropriate. The review was restricted to English language studies and there were no attempts to locate unpublished studies, thus the review may be subject to language and publication bias. A formal quality assessment was not carried out, so the validity of the included studies remains
unclear. Appropriate steps were taken to minimise bias and errors in the review process.

The methods of analysis were acceptable, although the use of more sophisticated models would have been preferable. The use of FR as the reference standard in one analysis and that of noninvasive imaging in the other was somewhat confusing but, given the lack of a reference standard in this area and the authors' objective of assessing concordance between the different techniques evaluated, this was acceptable. The inclusion of SROC plots greatly helped the interpretation of the results and illustrated the substantial variation between the studies. Some attempts were made to investigate the observed heterogeneity, but further investigation would have been helpful. The authors' conclusions, which appear based largely on summary measures, are unlikely to be reliable given the heterogeneity between the studies.

Implications of the review for practice and research
Practice: The authors stated that none of the single tests evaluated can act as a single measure of the haemodynamic significance of coronary lesions.

Research: The authors stated that the prognostic implications for the discordant FFR and imaging results seen needs further study.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.