The potential usefulness of stem-cell therapy was first shown in animal models with large infarctions. The benefits were profound.[6,7] However, we have not yet observed this profound benefit in clinical populations. Whether these initial disappointments relate to the failure to focus on high-risk patients or whether the strategy will not translate well to clinical populations remains unknown. We may find that true myocardial regeneration with this strategy is difficult to achieve.[8] How will this field move forward? No doubt larger well-controlled clinical trials will be undertaken, but these studies should focus on patients at high risk for morbidity and mortality after acute myocardial infarction and must be powered to detect modest benefits. Clinical studies must be done in collaboration with basic science investigators who are trying to unravel and optimise the biology underlying this therapeutic approach. Obviously, the road ahead is challenging, but well worth the effort. Until now, regenerative therapy for acute infarct has represented an unattainable dream, but I remain confident that such an approach will eventually transform treatment after myocardial infarction for these compromised and vulnerable patients.

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I declare that I have no conflict of interest.

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Thin-layer cervical cytology: a new meta-analysis

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In today's *Lancet*, the landmark study by Elizabeth Davey and colleagues[1] will help clear the air on thin-layer cytology. The two messages that come to mind first after reading this paper are that peer review does not automatically indicate high quality, and enthusiasm for new technology should not replace proper study design.

Consider this: of 147 articles originally culled from the literature, only 56 fulfilled the inclusion criteria for the study by Davey and colleagues. Of those 56 papers, none was of ideal quality; only five were of high quality, 32 of medium quality, and 19 of low quality. This indicates not that Davey had unrealistic expectations about study quality, but that our peers are recommending papers that do not meet basic requirements. The standards for study quality set by Davey were not excessively high: an "independent randomised sample study, with verification by a masked reference standard, of at least all positive slides" (see table 2 in the article). Yet not a single study fulfilled these requirements. The authors did not even ask that negative slides were referenced, which would have been unrealistic in a screening situation. Interestingly, a study by Lee and colleagues,[2] which led the US Food and Drug Administration (FDA) to approve a commercial product of thin-layer cytology, was classified by the authors as being of poor quality. This raises questions about the validity of such regulatory procedures, particularly because FDA approval is heralded as a sign of high quality. The most common problems with study design were deficiencies in randomisation and blinding, and, most importantly, deficiencies in referencing of positive results.[3–8] For

	Our laboratory	US laboratory
Within normal limits	462	429
Low squamous intraepithelial lesion (LSIL)	21	11
High squamous intraepithelial lesion (HSIL)	6	10
ASCUS/AGUS	4	33
Unsatisfactory	4	14
Total	497	497

ASCUS =atypical squamous cells of underdetermined significance; AGUS=atypical glandular cells of underdetermined significance.

Table: **Results of rescreening 50% ThinPrep Slides**

example, a recent study,[9] in which almost a third of positive cases in the thin-layer arm had negative biopsies, claimed greater sensitivity than the conventional method on the basis of three more cases detected by thin-layer cytology.[10]

Even though few of the studies were of a high standard, Davey and colleagues did not find an advantage of thin-layer cytology over the conventional method. Overall, Davey included more than 1·25 million slides in the review. There was no significant difference between thin-layer cytology and conventional cytology, either for satisfactory rate, or in the detection rate of preinvasive lesions. Thus, Davey's study lends support to previous independent reviews in Australia, New Zealand, Canada, the USA, France, and Germany, that all came to the conclusion that there is no significant difference between the two methods.[3-8]

Why then is liquid-based cytology being introduced in some countries? To answer this question, differences between different countries' health-care systems must be taken into account. Clearly, in the USA the incentive is partly monetary. After FDA approval, insurance companies were ready to pay considerably higher fees for liquid-based smears than for conventional smears. That led, understandably, to a rapid conversion to this new technology in a market-driven health-care system. In addition, the remaining liquid of thin-layer cytology provides an ideal platform for additional tests—whether or not they are necessary. In England and Scotland, with a nationalised health-care system, the central decision-makers were convinced that this technique would improve their problem of a very high unsatisfactory rate.[11,12]

In continental Europe funding agencies were much more restrictive, and tended not to provide additional funding for thin-layer cytology, because the methods are considered equal in their accuracy. Therefore, in Switzerland and France for example, it is left to the pathologist to decide which method is used, with the same fee for both methods.

Besides quality of study design, other factors, such as health-care system, reimbursement pattern, and legal background, will influence the diagnostic approach. A striking example is illustrated in the table. A rescreening of 50% of the liquid-based slides of our comparison study was done on request,[13] showing marked differences between the Swiss and US laboratories.

It appears that new technology will not be the answer to the remaining incidence and mortality rates of cervical cancer. Increasing the coverage rate, as done in England since 1988, has been shown to be the key to success.

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