patients with a baseline LDL-cholesterol concentration less than 2·6 mmol/L (26% of the study population) had a 26% reduction in major cardiovascular events with atorvastatin. Thus, there is consistency of the size of treatment effect across the subgroup with low LDL cholesterol in different trials. Since the treatment effect is almost independent from baseline total and LDL cholesterol, the current data do not justify a particular threshold concentration of LDL cholesterol for the initiation of statin treatment in patients with type 2 diabetes.

The CARDS data, together with the fact that patients with diabetes without previous myocardial infarction have as high a risk of major cardiovascular events as patients without diabetes with previous myocardial infarction, provide a strong rationale for treating individuals with diabetes as aggressively (including statins) as those without who have had a myocardial infarction.[3] On the basis of available clinical trial evidence, guidelines have included patients with diabetes in the high risk category and confirmed the benefits of LDL-lowering therapy in these individuals.[4]

Based on this robust evidence, we disagree with Abhimanyu Garg (Aug 21, p 641)[5] who concludes in his Comment that "for patients with type 2 diabetes at moderate to low risk of coronary artery disease, lifestyle changes must be attempted before considering lipid-lowering drugs". We agree, that therapeutic lifestyle changes, including diet, exercise, and weight loss, remain an essential modality in clinical management of high risk patients, but several landmark trials, including the Heart Protection Study and CARDS, have convincingly shown a clinically relevant treatment effect with the addition of statins to therapeutic lifestyle changes. Since patients with diabetes are at high risk of major cardiovascular events, an approach of withholding statins in these individuals seems not to be justified.

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Cervical cerclage for prevention of preterm delivery in women with short cervix

Meekai To and colleagues' findings (June 5, p 1849)[1] indicate that cervical competence should be defined in terms of both the diameter of the cervical internal os and the cervical length. Hitherto, emphasis was only on internal os diameter.

However, more information is needed about some aspects of the trial. How many sonologists at each centre, for example, were involved in the ultrasound scans at 22–24 weeks? How was interobserver variation minimised if more than one sonologist did the scan at each centre? Additionally, for how long, if at all, were patients admitted to hospital for insertion of a Shirodkar cervical suture?

To and colleagues conclude that insertion of a suture in women with a short cervix does not substantially reduce the risk of early preterm delivery. This finding is good news, especially for those of us that practice in low-resource settings. Theoretically, we can now allow such women to go home and continue their normal activities. However, normal activities in some communities include farming, fetching firewood, pounding yam, etc. When the extent of normal activities is unknown, should we not, therefore, advise bed rest just in case?

Finally, we postulate that expectant management with suspension of sexual intercourse would have a better outcome than one in which normal coital activity was allowed to continue.

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1 To MS, Alfirevic Z, Heath VCF, et al. Cervical cerclage for prevention of preterm delivery in women with short cervix: randomised controlled trial. *Lancet* 2004; **363:** 1849–53.

Meekai To and colleagues[1] report that the insertion of a Shirodkar suture in women with a short cervix, at between 22 and 24 weeks, does not substantially reduce the risk of early preterm labour. This finding may be correct when low-risk women are screened once, and cerclage done at 15 mm cervical length. Evidence for the optimum management of women with a previous poor obstetric history and a short cervix detected by transvaginal ultrasound is, however, conflicting.[2,3] We caution against extrapolation of the findings of this trial to women who have a history of previous midtrimester or preterm delivery. Despite the large numbers in this trial, only 46 women had such a history and no conclusions can be drawn as to possible benefit or otherwise in this group from the data (relative risk of preterm delivery 1, 95% CI 0·38–2·60); the CIs are consistent with either a substantial risk or with benefit.

As To and colleagues state, the absence of benefit in randomised trials of cervical cerclage could be a result of suboptimum selection of patients. The pathophysiology of cervical shortening could be very different in women with

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Still Pictures

recurrent loss, compared with women with no risk factors. In this trial, the cut off for cerclage was fairly short at 15 mm or less. One rationale for cerclage is to minimise ascending infection by preventing membrane exposure. Cerclage at a cervical length of 15 mm might therefore be too late. The risk of preterm delivery increases exponentially with cervical lengths shorter than 15 mm. We have shown[4] that outcome in women with a cervical length of 15 mm or less, is not dependent upon cervical length, but on membrane exposure. At cervical lengths of longer than 15 mm no membranes are visible in asymptomatic women. This finding lends support to the notion of offering cerclage before cervical length reaches 15 mm, and could be another reason why there was no apparent difference in outcome between the cerclage group and the expectant management group in To and colleagues' study. We suggest that earlier, or longitudinal screening of cervical length, would allow cerclage to be undertaken sufficiently early to be beneficial.

To and colleagues have shown that screening of a low risk population late in the second trimester and undertaking cervical cerclage when the cervix is very short does not affect preterm delivery rates. This data should not be extrapolated to patients at higher risk. Many patients at high risk will have aborted before 22–24 weeks, and such late intervention at such short cervical lengths will probably not benefit those who have not. Longitudinal screening in women at high risk with early intervention has gradually crept into clinical practice in some centres but has not yet been proven to be of benefit. Despite the results of this study, further work is needed.

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Authors' reply

We did not attempt to define cervical competence, as suggested by Bissallah Ekele and Lydia Airede, but purely tested the effect of cervical cerclage in women with a short cervical length. As stated in table 1 of the article, 93–95% of patients had funnelling, which we have defined previously as dilatation of the internal os of 5 mm or more.[1] All sonographers held the Fetal Medicine Foundation Certificate of Competence in Cervical Assessment and regular audit of images was done in each participating centre to ensure consistency. Patients were admitted for the day for insertion of the cervical cerclage and we encouraged all women to continue their daily activities, since there is no evidence that bed rest is beneficial in the prevention of preterm delivery in such patients. We advised all women with a short cervix against sexual intercourse.

We acknowledge the comments of R Simcox and colleagues, and agree that we did not test the benefit of a cervical suture in women with a history of preterm birth. While the authors hypothesise that the pathophysiology of cervical shortening could be different in women with recurrent loss, it is interesting to note that the rate of preterm delivery in the expectantly managed group of women with such a history did not differ from those without. With respect to the cervical length threshold for cerclage, we have previously shown[2] that the risk of preterm delivery increases from 1·1% at 25 mm to 4% at 15 mm and 78% at 5 mm, and that about 1% of the population have a cervical length of 15 mm or less. Decreasing the threshold for cerclage to 20 mm or 25 mm would result in a three-fold and seven-fold increase, respectively, in the screen-positive rate, and subject many women with a very low risk of preterm delivery to a surgical procedure.

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Stem-cell therapy: what dose should we use?

Kai Wollert and colleagues (July 10, p 141)[1] have provided further evidence of the benefit of autologous stem-cell transplantation for myocardial infarction. However, the optimum dose of CD34+ cells for stem-cell therapy in this area remains undefined. Studies[1,2] have used doses ranging from 10^6 to 10^8 cells (compared with the optimum dose for stem-cell therapy in haematological cancers, which is $\geqslant 2{\cdot}0 \times 10^6$ CD34+ cells per kg bodyweight[3]).

The dose requirement in myocardial infarction will probably not be as high as that needed in haematological cancer, because of the treatment territory involved (heart *vs* bone marrow) and direct intracoronary injection or infusion to the targeted ischaemic or infarcted myocardium. This assumption is of practical importance. If the optimum dose of CD34+ cells needed is proven to be much less than 10^6, proce-