count below 350 cells per µL, moving away from stavudine in first-line regimens, and, where available, measuring viral load every 6 months.[7] Clearly, another WHO priority is to continue to expand antiretroviral therapy to all those in need (currently defined as those with CD4-cell count under 200 cells per µL). Countries will need help from the research community to decide on how to prioritise these developments and maximise the number of healthy lives prolonged, because few will be able to implement everything immediately, particularly against an increasingly challenging economic background.[8] For example, it is recommended to measure viral load every 6 months where available but how high a priority should programmes currently put on making viral load tests available, in view of the current lack of cheap and robust assays? The DART trial clearly shows that expansion of antiretroviral therapy to all those in need must be the very highest priority. Such expansion is logistically difficult, but we must not allow other concerns about antiretroviral delivery to detract from meeting that need.

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We declare that we have no conflicts of interest.

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Umbilical vein injection of oxytocin for retained placenta

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It is believed that uterotonics delivered into the retroplacental myometrium stimulate myometrial contraction and the eventual expulsion of a retained placenta. Many observational and experimental studies have been published on umbilical vein injection of uterotonics to obviate the need for manual removal of the placenta.[1–3]

In *The Lancet* today, Andrew Weeks and colleagues[4] present the Release trial, another attempt to answer the question of whether indeed umbilical vein injection of oxytocin is useful to manage the retained placenta. The study, which was randomised and double blind, compared 292 women with a clinical diagnosis of retained placenta who were treated with intra-umbilical vein injection of oxytocin with 285 women with retained placenta who were given placebo. The primary outcome was the need for manual removal of the placenta. The investigators concluded that they had found no clinical or statistical evidence of a difference between the two groups in the primary outcome (relative risk 0·98, 95% CI 0·87–1·12). Hence injection of oxytocin into the umbilical vein for retained placenta might well be an exercise in futility.

This conclusion, however, contrasts with the outcome of the subanalysis of a Cochrane systematic review of ten similar trials. That analysis showed a significant reduction in manual removal of placenta in the group that had umbilical vein injection of oxytocin compared with the placebo group (relative risk 0·79, 95% CI 0·69–0·91).[5] But from the same Cochrane review, the subgroup that had umbilical vein saline solution plus oxytocin compared with expectant management (a better control) showed a reduction in manual removal that was not statistically significant (0·86, 0·72–1·01). The Release investigators included in their discussion an updated systematic review and found no statistically significant difference (when looking at high-quality studies) on the need for manual removal of placenta with umbilical vein injection of oxytocin (0·92, 0·83–1·01).

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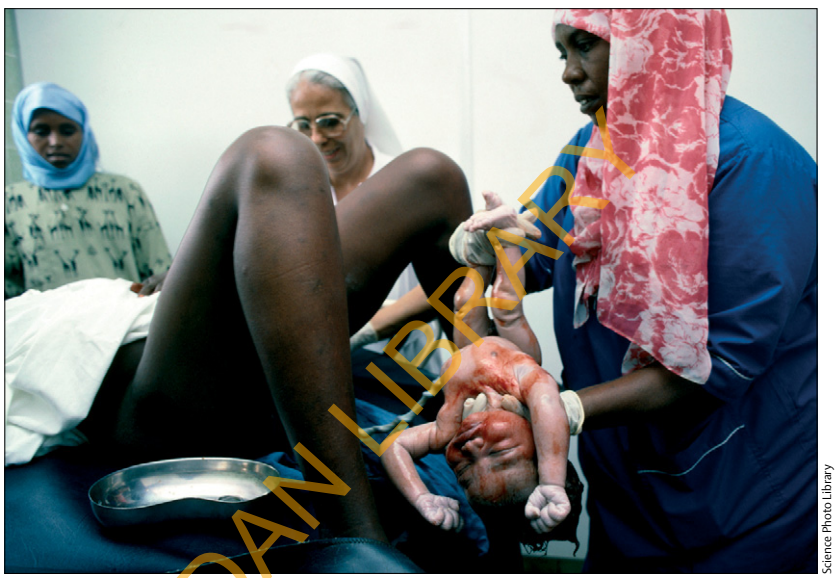
The large sample size and rigorous methodology (including the use of intention-to-treat analysis and the strict adherence to study protocol) made Release superior to many of the previous studies in terms of scientific quality. However, there are a few concerns. For instance, the use of clinical assessment alone to diagnose retained placenta without ultrasonography[6] has limitations, because it would be difficult to ascertain whether the placenta was just normally adherent, pathologically attached (accreta), or trapped in the lower uterine segment at the time of randomisation. Could there be a subtype of retained placenta in which umbilical vein injection of oxytocin might be effective? Release also did not fully record interventions that patients might have received before recruitment. Finally, it is unclear how generalisable the results will be, especially in settings with poor resources.

In developing countries, many pregnant women do not have access to skilled birth attendants and they deliver at home or outside health facilities,[7–9] where active management of the third stage of labour is hardly practised and retained placenta is not uncommon. Even when those with retained placenta are offered manual removal on admission at a health facility, the intervention is often delayed due to lack of surgical consumables, difficulty with blood transfusion, or other bureaucratic bottlenecks. It is therefore not unusual for the procedure to be delayed for days at the health facility, thus predisposing the women to other complications. In our opinion, umbilical vein injection with oxytocin might be attempted only under such circumstances of an abnormal waiting period, otherwise the evidence is no longer in support of the procedure.

The benefit of intra-umbilical oxytocin injection over manual removal of the placenta in terms of avoidable anaesthetic risks, lower chances of genital tract trauma, infection, uterine synaechia, and infertility might have informed its inclusion in the 2007 guidelines from the UK's National Institute for Health and Clinical Excellence for the treatment of retained placenta.[10] But with the strength of the evidence from Release, the guidelines might be revisited. WHO might also reconsider their recommendation that intra-umbilical vein injection of oxytocin with saline may be offered for the management of retained placenta, especially because the recommendation was classified as weak.[11]



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We do agree that the optimum period before manually removing the placenta remains to be determined.

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