and VIA was the option recommended for immediate introduction into district cancer control programmes (5). By 2005, the WHO /Government of India committee to which the authors refer had drafted guidelines for the incorporation of both VIA (at the primary health centre level) and the Pap smear (at the district hospital level) into the existing health system, starting with a demonstration programme (7).

4. The authors state: "The choice of no screening for the control arm was discussed with several experts at the national level prior to starting the trial."

   This statement does not throw any light on whether the ethics of a no screening control was discussed by these national experts, and what the conclusions were. Nor is there any mention, in the three documents cited by the authors, of a no screening control, let alone the ethics of this methodology.

   Further, while ethical clearance would not have rendered the trials ethical, the authors offer no evidence to suggest that the no screening arm was even discussed by the ethics committees reviewing the trials.

5. The authors describe the editorial as a "show of moral outrage" that vitiates the "healthy tension between ethics and the scientific process." For a healthy tension between ethics and the scientific process, there must be evidence that the scientific process has considered ethics and that the scientists have met their ethical responsibility towards the research participants.

I thank Ruth Macklin for her comment (8) in support of my argument and for providing clarity to the issues raised in the editorial. Regarding my reference to the use of cluster randomisation, I did not mean to imply that all cluster randomised trials are unethical. My intention was only to underline the consequences for the women in the control arm of these trials.

Macklin's conclusion is that the placebo-controlled VIA trials were not ethical, not necessary and not appropriate research. The question we must, therefore, ask is: why were they conducted? The response by Pramesh and colleagues does not shed any light on this question.

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Ethical issues in adapting new technologies for rapid diagnosis

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The Xpert® MTB/RIF (hereafter Xpert) is a recent technology that has "demonstrated sensitive detection of tuberculosis (TB) and rifampicin resistance directly from untreated sputum in less than two hours" (1). Many are in favour of the widespread implementation of this technology in India. In a recent article in the *IJME*, Singh, Bhan and Upshur state that "India is ethically obliged to phase in the nationwide deployment of Xpert…as soon as reasonably possible" and "is ethically obliged to provide those diagnosed with first-line drug resistance universal access to second-line TB drugs" to treat multiple drug-resistant tuberculosis (MDR-TB) (1).

The prevalence of MDR-TB in India is estimated to be about 2%. In their review of the Xpert technology, A Trebucq and colleagues make the point that the question is not whether to treat MDR-TB, but rather, when, where and how to treat it (2). Besides the limitations related to cost (~$10 per test), the environment required (the need for a stable, regular electric supply for an air conditioner to be able to maintain the room temperature at 15–30 °C), the shelf life of the test cartridges (18 months), and supply and maintenance issues, there are other questions as well regarding the reliability of the test at different levels of prevalence of MDR-TB. When the prevalence is 1% or less, the positive predictive value (ppv) is 32%; when the

prevalence is 2%, the ppv is 49%; and when the prevalence is greater than 15%, the ppv is above 90%. Any specimen testing positive for rifampicin resistance in a low-prevalence area will have to be verified by culture and antibiotic testing.

To control clinical TB and reduce the rate of infection, a well-run national TB programme must be in place (2). This translates into the following: 70% of cases must be identified and 85% of sputum-positive cases should be treated successfully with Directly Observed Treatment, Short-course (DOTS). Second-line drugs (SLDs) used to treat MDR-TB cost at least 100–200 times more than those used in a standard DOTS programme. The patient must take the SLDs for 18–24 months and usually has to spend the first six months in hospital. The success rate is about 60%. In general, DOTS requires six months of treatment with no hospitalisation.

Scaling up treatment of MDR-TB poses its own special problems. At the moment, SLDs are not being produced in adequate amounts and the prices of these drugs have been increasing year by year. Some who advocate the widespread treatment of MDR-TB cite the example of HIV/AIDS, for which the initial cost of treatment was high and prices were slashed subsequently, following intensive lobbying. However, MDR-TB is much less common than HIV/AIDS (though the number of patients is growing), there has been much less advocacy for widespread treatment of cases, and there has been a significant delay in the development of effective SLDs. Singh et al note that South Africa has rolled out the treatment of MDR-TB nationally, even though it may not be affordable, and say India could do the same (1). South Africa has a purchasing power parity per capita that is three times that of India: $11,375 vs $3830 (3), and has a much more developed and efficient healthcare delivery system.

Why is the incidence of MDR-TB increasing? A high dropout rate from DOTS programmes, limited follow-up of patients on therapy, inappropriate and incomplete treatment regimens (especially in the private sector), and counterfeit drugs have all contributed to the rise in incidence. Without an excellent DOTS programme at the point of care, backed by a multi-drug resistance treatment programme which has trained staff, adequate drugs in stock and a laboratory capable of carrying out cultures for drug resistance, testing for MDR-TB will present an ethical dilemma for the caregiver, since up to 10% of those who test positive for drug resistance will respond to first-line drugs.

Two other issues raised by Singh et al deserve comment. The authors state that the government is ethically bound to continue administering SLDs once the treatment has been started in the private sector. This makes sense if the original diagnosis is confirmed. If a few days of inappropriate treatment for MDR-TB are extended for another two years, it could place the patient at great inconvenience and risk. This would also be at a high cost to society. According to the definition of autonomy, a patient has a right to choose among treatment options (1). However, what if the patient chooses not to be treated? Does the public have a right not to be exposed to a disease that is spread by air – a common public good?

In reviewing the when, where and how to use Xpert, India would be well advised to move cautiously in rolling out this technology to diagnose rifampicin resistance. The use of Xpert should be restricted to those centres where a positive test can be confirmed in the laboratory, and where complete uninterrupted treatment can be assured. Without this basic infrastructure, the widespread use of Xpert could lead to over-diagnosis and inadequate treatment, which could lead to more cases of XDR-TB, an essentially untreatable disease within the Indian context. When it comes to the community, the most effective intervention and the most ethical approach would be for the country to continue to improve its DOTS programme to ensure effective treatment to the vast majority of TB patients, as this itself will reduce the incidence of MDR-TB. Technology does have its limits.

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