for drug-susceptible tuberculosis is expected[7,8] to increase treatment completion rates, decrease burden on delivery systems, and therefore help treat more patients—decreasing selection and spread of drug-resistant tuberculosis. Bayer Healthcare's cooperation with the TB Alliance in the clinical development of a moxifloxacin-containing combination therapy is evidence of Bayer's commitment to making an effective new drug available in countries with a high tuberculosis burden. Bayer Healthcare will work towards making moxifloxacin available to patients with tuberculosis at affordable prices if the present studies are successful. Novel regimens that quickly and safely treat both drug-susceptible and drug-resistant tuberculosis and are delivered in a context of appropriate controls including widespread drug susceptibility testing are the only long-term solution.

MS is an employee of Bayer Healthcare Pharma, the manufacturer of moxifloxacin. CM declares that he has no conflicts of interest.

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Authors' reply

We thank Kasha Singh and Carl Mendel and their coauthors for engaging in this important discussion. The need to shorten first-line tuberculosis treatment is a pressing priority. Tuberculosis is overwhelmingly a disease of the poor, and 6 months of daily treatment is understandably difficult for many patients. These demands are even more substantial for patients with multidrug-resistant tuberculosis, who are expected to undergo over 18 months of daily observed treatment with drugs that are often associated with debilitating side-effects. Unsurprisingly, on average over 10% of these patients default from care, rising to over 50% in some settings.[1]

For decades, the global strategy to tackle multidrug-resistant tuberculosis has been to reinforce the treatment of simple tuberculosis. This strategy has not worked and is no longer relevant to today's epidemiological reality where most multidrug-resistant cases arise through direct transmission.[2] Improving first-line treatment while ignoring multidrug-resistant tuberculosis will not curtail the epidemic of drug-resistant tuberculosis.

We advocate that moxifloxacin, at present, is reserved preferentially for treatment of multidrug-resistant tuberculosis. Because access to resistance testing is limited and cross-resistance between older and newer generation fluoroquinolones is not complete,[3] the addition of moxifloxacin as a single new drug to a first-line regimen will probably increase resistance pressure worldwide, further curtailing our ability to treat multidrug-resistant and extensively drug-resistant tuberculosis effectively. Inappropriate use of tuberculosis drugs has led to dramatic second-line resistance,[4] but restricting the use of fluoroquinolones or indeed any tuberculosis drugs is a persistently challenging issue; this practical difficulty needs to be addressed and should not, in itself, justify a recommendation for widespread moxifloxacin use.

We agree that the evidence base for multidrug-resistant tuberculosis treatment needs to improve. Further research is needed on optimum dosing, not just for the newer-generation fluoroquinolones but also for many existing second-line drugs. This research should be a priority for the TB Alliance. In the meantime, although treatment outcomes for extensively drug-resistant tuberculosis are poor overall, they are not non-existent.[5] The existence of extensively drug-resistant tuberculosis highlights the need for better second-line regimens, and patients with extensively drug-resistant tuberculosis should not be denied the best available treatment.

A choice needs to be made when new drugs become available: do we hold off using promising new drugs until we have enough for an entirely new regimen? Or do we incorporate new drugs into the current armamentarium as they arise, according to public health need and potential effect on tuberculosis control? We believe that a balance needs to be made between long-term ideals and present realities.

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MDR tuberculosis and non-compliance with therapy

Suheir Ereqat and colleagues[1] described a patient with multidrug-resistant (MDR) tuberculosis who has defaulted after 2 years of treatment and is untraceable. They lament the absence of legal means by which this patient might be forced to return to Palestine and continue treatment.

We believe this approach puts a mistaken emphasis on legal coercion that is neither effective nor humane. If this patient failed treatment, as it would seem, an understanding of the reasons for treatment failure would be important. Did the patient have a history of defaulting treatment previously and, if so, what counselling did this patient receive? Aside from directly observed treatment, what support was offered to empower him to continue his treatment? What further treatment do the authors suggest should be prescribed? Forcing a patient to continue an ineffective, toxic regimen that results in no clear benefit is clearly difficult. For patients like these, attention could be more usefully directed at exploring possible regimens with better chances of cure; and securing an appropriate environment, such as supportive accommodation with access to counselling and palliative care when required, that might reduce the risk of transmission to others, as is being attempted in South Africa.[2]

As case detection and treatment for MDR tuberculosis is scaled up internationally,[3] how to care for patients who have exhausted all treatment options with existing second-line drugs will become increasingly important. Currently, no third-line treatment for tuberculosis exists. Until newer drugs become available, we will need to care for such patients in a manner that balances the risk of ongoing transmission with individual human rights. The health system must still support patients in whom treatment has failed. The provision of home-based palliative care, for example, is likely to be more humane and less costly to health services compared with involuntary detention.[4]

Although a small proportion of patients might realistically be classified as recalcitrant, and legal means may be necessary to restrict transmission, we feel that every effort should be made to support patients, either to continue treatment if they so wish, or to live out the remainder of their lives in a manner that minimises the risk of transmission to others.[5] In this case, the threat of incarceration is also likely to further reduce the chances that this patient will be located. We feel that such patients should not be managed by an automatic resort to legal coercion.

We declare that we have no conflicts of interest.

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Authors' Reply

We thank Helen Cox and colleagues for their comments, but point out that we do not disagree with them. Health is a human right that should be guaranteed through legal and social policies. We endeavoured in our letter[1] to ask questions, not to propose an answer. Naturally the Palestinian Health Authority made all efforts to keep the patient in therapy. Our letter was directed at a recalcitrant patient, one who has had all counselling suggested and who then disappeared and thus refused further therapy. What are our obligations as doctors in this case and what do we do if the patient goes to a different country? As multidrug-resistant microbes are becoming an increasing health and community problem, should thought be given to making some such infections notifiable diseases, as is done in Australia for various other diseases?[2] Such a move could solve many problems and allow some control of patients.

Cox and colleagues state that no new third-line treatment for tuberculosis exists, but happily the situation is not quite that bleak.[3,4] We would pose the question: if this individual were a teacher of young children, would he be allowed to work? And if he moved and left treatment, what are the legal obligations and constraints on his physicians or the relevant health authority to notify people at his destination or issue a general warning? We too believe that any form of control should not affect the patient's dignity, but the question of compulsory isolation for