Better treatment of XDR tuberculosis needed in South Africa

Elize Pietersen and colleagues (April 5, p 1230) show the very poor outcomes for treatment of extensively drug-resistant (XDR) tuberculosis in South Africa. The study suggests that large numbers of patients, for whom treatment was ineffective, pose a risk of ongoing community transmission.

Although we support the provision of community-based care minimising transmission risk after treatment failure, we would also like to put these numbers into context. More than 1500 XDR tuberculosis cases are diagnosed in South Africa annually, likely representing a fraction of the actual burden. In view of that less than half of people diagnosed receive treatment, the combination of undiagnosed and untreated XDR-tuberculosis poses a much larger risk in our communities than the small number of patients discharged with treatment failure Pietersen and colleagues describe.

Rather than emphasising the risk from these few patients, the focus should be directed towards early diagnosis and rapid initiation of effective treatment for all drug-resistant tuberculosis cases, including individuals unfortunate enough to have contracted XDR-tuberculosis. South African guidelines describe individualised XDR-tuberculosis treatment, including the use of linezolid and clofazamine. Unfortunately, access to both these drugs is restricted; clofazamine due to supply issues and linezolid due to high costs charged by Pfizer in the absence of a registered generic alternative. Early XDR-tuberculosis diagnosis, treatment with more drugs (including linezolid and new drugs via expanded access), and particularly timely initiation of antiretroviral HIV

Authors’ reply

We thank Aurélien Dupré and colleagues for their interest in our Article. So far, most research into adhesions has focused on the consequences and prevention of small bowel obstruction, which is shown by the results presented in our meta-analysis. However, there is growing evidence suggesting that difficulties and subsequent iatrogenic injuries in reoperations are an even larger health problem in terms of morbidity and costs.

Dupré and colleagues justly remark that the burden of adhesiolysis is only expected to rise further with the increasing number of reoperations in oncological surgery.

Although somewhat outside the scope of our systematic review, these new epidemiological data warrant a change in the understanding of adhesion-related morbidity and strategies for adhesion prevention. Previous cost-effectiveness models for adhesion barriers that focused on prevention of adhesive small bowel obstruction demonstrated that these agents might be cost effective for only selected patients. A more complete cost-effectiveness model would also account for the additional costs made in reoperations and fertility and chronic visceral pain treatments. A more comprehensive model is expected to show that barriers are cost effective in most patients who undergo abdominal surgery because reduction of adhesion formation would already provide a benefit.

For explanation, the difficulty in prevention of adhesive small bowel obstruction is that small bowel obstruction can be caused by just one adhesive band and prevention of small bowel obstruction therefore requires total adhesion prevention in the whole peritoneal cavity, which is relatively difficult to achieve. The complications of adhesiolysis during reoperation are correlated to the extent and severity of adhesion formation. Thus, although the use of adhesion reducing agents might not completely prevent adhesion formation in operations with extensive peritoneal damage and have only a modest effect on the incidence of small bowel obstruction, reducing the extent and severity of adhesions is likely to have a beneficial effect on the outcomes of future operations.

These new data have consequences for the design of future trials on adhesion prevention. Dupré and colleagues were one of the first to study the effect of adhesion barriers on adhesiolysis time in two-stage oncological liver surgery. Whether this reduction of adhesiolysis time is indeed correlated to a reduction in iatrogenic bowel injury and serious adverse events of the reoperation needs validation in larger trials.

We declare no competing interests.

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treatment, would all be expected to improve treatment outcomes over what is described. Preventive treatment failure saves lives and is the best infection control.

We declare no competing interests.

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**Author’s reply**

We agree entirely that the focus of the South African Department of Health and other stakeholders attempting to achieve tuberculosis control should be directed towards early diagnosis and rapid initiation of effective treatment for all drug-resistant cases, including those with extensively drug-resistant (XDR) tuberculosis. Our objective was not to preferentially emphasise or detract from any particular aspect of tuberculosis control. Clearly, control of drug-resistant tuberculosis requires a multifaceted approach addressing socioeconomic factors, education, preventive strategies, early and rapid diagnosis, initiation of effective treatment, and social and sex-based issues, amongst others. Although all these are important, including the points raised by Helen Cox and colleagues, there is also the issue of appropriate care for patients discharged into the community who are therapeutically destitute (patients for whom there are no further therapeutic options because of very high grade resistance) within the context of the South African National TB Programme. We have previously raised our concerns regarding community-based transmission. In particular, we need a coordinated national strategy in South Africa that combines home-based care with long-term community stay facilities, and appropriate palliative care facilities. The reality is that such facilities are virtually non-existent in South Africa and there is an urgent need to provide such facilities until more effective drug regimens and interventions are available.

Although there are many priorities including protection of health-care workers, we believe an important area of emphasis should be strengthening of the national tuberculosis programme and trialling and introducing an effective regimen for multidrug-resistant tuberculosis. As Cox and colleagues point out, we do not have effective drugs to deal with the problem and thus introduction of newer drug regimens for tuberculosis, including drug-resistant tuberculosis, remain a major priority.

I declare no competing interests.

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**Department of Error**

Chung S-C, Gedede R, Nicholas O, et al. Acute myocardial infarction: a comparison of short-term survival in national outcome registries in Sweden and the UK. Lancet 2014; 383: 1205–12—In this Article (April 12), the copyright licence should have been CC BY. This correction has been made to the online version as of August 15, 2014.

Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990—2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2163–96—In this Article (Dec 15/22/29), Donald Silberberg has been added to the author list and the affiliation details have been updated. These changes have been made to the online version as of August 15, 2014.

Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYS) for 291 diseases and injuries in 21 regions, 1990—2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2163–96—In this Article (Dec 15/22/29), Donald Silberberg has been added to the author list and the affiliation details have been updated. These changes have been made to the online version as of August 15, 2014.