Correspondence


Authors’ reply

We thank O Kaya Koksalan and colleagues for their correspondence about our study, which assessed the performance of Xpert MTB/RIF in the context of community-wide screening for tuberculosis.1 We acknowledge that the concern regarding our approach to estimating sensitivity and specificity is a valid one. However, in the present study, we have not sought to estimate the sensitivity of Xpert.

What we have done, on a large scale, is to directly assess the positive predictive value of the Xpert test in the screening context. Positive predictive value is estimated only in people with positive test results; in this case the 169 people with a positive Xpert result. We have used a range of plausible criteria for establishing which of these people with a positive Xpert result were true positives and which were false positives. One of these criteria is the presence of a positive culture for *Mycobacterium tuberculosis*. An alternative criterion is the presence of an abnormal chest radiograph consistent with a radiological diagnosis of tuberculosis. We have acknowledged that this was not investigated in a blinded way and could overestimate the number of true positives. Nevertheless, we think it is reasonable to assume that the true positive rate lies somewhere between these two estimates (61–84%).

We then made a range of plausible assumptions about the sensitivity of Xpert, using data from a Cochrane review of 22 studies and almost 9000 individuals,2 and the prevalence of tuberculosis in the population, using data from the present study and from a previous prevalence survey.3 With these data, we have reverse-calculated what the specificity must have been to result in the observed positive predictive value. In our original Article, table 3 shows that, under a wide range of plausible assumptions, the specificity must have been at least 99.57% and was probably higher than this.

Although this is a novel approach, we stand by its validity. The reference standards used included a gold standard microbiological reference, and a composite reference that also included chest radiography. A study by Theron and others4 done on 480 individuals suspected of having tuberculosis in South Africa, also suggested that a composite reference standard could be more appropriate to assess the diagnostic accuracy of molecular tests for tuberculosis, especially in settings where mycobacteria culture facilities can be overburdened and under-resourced.

Because of the many Xpert tests used in this study, we were able to estimate the positive predictive value and specificity of this test with more precision than previous studies combined.5 Both the positive predictive value and specificity of Xpert for *M. tuberculosis* detection were substantially greater than previous estimates.5 Taken together with previous data on the sensitivity of the test, our data suggest that the accuracy of Xpert is adequate to support its role as a primary screening tool for detecting patients with tuberculosis in the context of community-wide screening in a moderate to high prevalence setting.

We declare no competing interests.

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Prejudice and reality about infection risk among Syrian refugees

In their Personal View, Mishal Kahn and colleagues1 propose that policy decisions about the risks of infectious diseases among migrants and refugees should be based on evidence for health risks and burdens to health systems, rather than prejudice or unfounded fears. Although the perception and generalisation that migrants and refugees carry a higher load of infectious diseases is questionable, it is undeniable that the Syrian conflict produced suitable conditions leading to the re-emergence of tuberculosis, cutaneous leishmaniasis, poliomyelitis, and measles.2 In this Correspondence we aim to add data about infections in Syrian refugees.

As of July 20, 2016, Turkey hosts 2·7 million of 4·8 million Syrian refugees.3 In Turkey, 10 689 refugees were screened for tuberculosis by the Ministry of Health in 2014–15 and the prevalence was 18·7 per 100 000, which is not higher than that in the Turkish population. Thereafter, Turkey
discontinued screening refugees for tuberculosis. However, most refugees are not in the camps; they are living in even worse conditions in big cities and many are homeless. Rate of tuberculosis might be higher in these groups. Lebanon and Jordan have increased rates of tuberculosis among Syrian refugees compared with resident populations.

There is an ongoing cutaneous leishmaniasis outbreak in Syria, and breakdown in disease control programmes and disruption of the health services has caused a further increase in cases. Recent news reports claimed that corpses thrown into Syrian streets are causing cutaneous leishmaniasis outbreaks. However, cutaneous leishmaniasis is transmitted only by sandfly vector and female sandflies require the blood of living animals to develop their eggs—they do not feed on human remains.

The coverage rate of polio vaccination decreased to 60% in 2012 and even to 50% in some regions and more than half of 2 million children born after the conflict could not be vaccinated. After a polio-free 15 years, Syria reported a poliomyelitis outbreak of 37 cases in 2013. One case was reported in 2014, with no new cases reported since.

Any misinformation reported in the press and on social media about refugees is the source of prejudice among the public and it should be firmly countered by evidence and epidemiological data. We declare no competing interests.

Risk of reproductive complications following chlamydia testing

Bethan Davies and colleagues1 use data from a cohort of chlamydia-tested women and never-chlamydia-tested women constructed from a Danish registry study to estimate the risk of reproductive complications. The analyses show associations between chlamydia testing (positive, negative, and Untested) and reproductive outcomes during the subsequent 15 years. However, their Article and an accompanying Editorial2 overinterpret the data.

Loose language crosses the line between causation and association. For example, statements such as “a positive chlamydia test increased the risk… by at least 30%”, “a single diagnosed chlamydia infection increased the risk…”, or “…a repeat diagnosis… increases the risk…” strongly imply causality. The study design is similar to the earlier Uppsala study.3 An expert group from the US Centers for Disease Control and Prevention4 identified a series of methodological difficulties with studies of this type, among them confounding by sexually transmitted infections risk profile and the already insurmountable problem that women testing positive were given treatment. Meaningful, causal estimates simply cannot be derived from studies of this type, and the Editor’s assertion that the paper “quantifies the serious complications attributable to chlamydia infection” is incorrect.5

Because the study gives no evidence that the single or repeated events of Chlamydia trachomatis diagnosis (positive or negative) cause an increase in the risk of complications, it cannot substantiate claims that preventing these events will be effective. So although the conclusion that “control programmes must be designed to prevent both first and repeat infections” to improve women’s reproductive health could be correct, this study adds no relevant information to support it or to the Editor’s recommendation of “a more intensive approach than test and treat.”

We published estimates of the risks of reproductive damage attributable to C trachomatis in the UK. Central estimates are that every 1000 C trachomatis infections in women on average cause 170 episodes of pelvic inflammatory disease, 70 episodes of salpingitis, two ectopic pregnancies, and five episodes of tubal factor infertility. These estimates, which include undiagnosed chlamydia, pelvic inflammatory disease, and salpingitis, were based on estimates of chlamydia incidence, prevalence, and duration in the UK, an estimate of the risk of pelvic inflammatory disease following C trachomatis infection based on randomised evidence, and many other sources of systematically identified evidence. These estimates were constructed in a way that makes them internally coherent and consistent with data on the incidence of pelvic inflammatory disease, ectopic pregnancies, and tubal factor infertility in the UK.

Finite mixture modelling of serology data might be another route towards estimating the proportion of reproductive damage attributed to chlamydia,6 but this method needs further validation.

PJH reports personal fees from Aquarius Population Health, Crown Prosecution Service, and British Association for Sexual Health and HIV; grants, personal fees, and non-financial support from Cepheid; grants from Mast Group; grants and personal fees from Hologic, outside the submitted work. Additionally, PJH has a patent for a salidase spot test to diagnose bacterial vaginosis, issued to University of Bristol. MJP and AEA declare no competing interests.

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