

capture techniques could have an adverse impact on recruitment, retention, selection bias, and the ability to collect samples. Therefore, the *Strategic Review* recommends that the merits of adopting these less costly approaches should be considered on a case by case basis and adopted where appropriate. UK Biobank collected extensive data at baseline clinics but all follow-up information is via record linkage and online questionnaires. The *Strategic Review* recommends that, where possible, broad and enduring consent should be obtained from the participants of all cohorts to obtain additional information through linkage to routine data.

Trustworthy research use of personal data using robust governance processes in secure environments with safeguards that protect confidentiality is fundamental to understanding the causes of disease and improving public health. In addition to spotlighting individual cohorts, the *Strategic Review* contains a series of recommendations for the MRC and others. Although enhancing awareness of cohorts and sharing of data and samples are already policy for the MRC and other funders, more could be done to enable well-governed use of these resources. Therefore, the *Strategic Review* recommends that cohorts be included in online directories and appropriate meta-data provided. Also, cohorts should use standardised and validated approaches, where possible, to facilitate cross-cohort comparisons. The findings from the cohorts are of great value in informing policy and practice in the UK, as well as further afield, and the *Strategic Review* highlights the need for closer working with policy makers. It is envisaged that the *Strategic Review* will encourage more

extensive use of UK cohort studies in the future; they are an invaluable national resource that few other countries can match.

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World TB Day 2014: finding the missing 3 million

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On April 23, 1993, WHO declared tuberculosis a global health emergency.¹ Tuberculosis is now about to come of age as a global emergency—April, 2014 marks the 21st anniversary of that declaration. Arata Kochi, manager of WHO’s tuberculosis programme in 1993, aptly called the disease “a forgotten epidemic” and “humanity’s greatest killer”. Tuberculosis might no longer be humanity’s deadliest disease in terms of annual deaths but, 21 years after the declaration, it remains a serious and substantial threat to the health of people worldwide, causing 1.3 million unnecessary deaths every year.²

Much progress has been made in the control of tuberculosis in the past 21 years, but we are only halfway to 2035—the target of WHO’s Global Tuberculosis Programme as the year that tuberculosis will no longer be a threat to global public health. At that point, 42 years will have passed from WHO labelling tuberculosis a global health emergency; several more years than the average age of the disease’s victims. So at this halfway point, we stand at a crossroads. Since 1995, 56 million people have been cured of tuberculosis and 22 million lives have been saved,² showing implementation of more effective

tuberculosis programmes than those in place before WHO's declaration. However, more than 30 million people have died from tuberculosis in the past 21 years.² How many more people will die of tuberculosis in the next 21 years is entirely in the hands of governments and donors. Do we let more people die from a disease for which effective treatment has been available for the past 50 years, or is it now time for a resolute change (as envisaged with the more ambitious WHO targets set for 2035) to stop this epidemic from taking its toll?

For rapid progress to be made in tuberculosis control, there are two essential requirements: first, commitment and resolve at the highest political level, and second, the necessary resources. To achieve unity for these aims, on World Tuberculosis Day, March 24, 2014, the UK All Party Parliamentary Group on Global Tuberculosis has joined with parliamentarians from the Group of Eight (G8) countries to call for coordinated global action on tuberculosis. We call for substantial investment in scaling-up existing interventions; in development of new drugs, diagnostics, and vaccines; and in innovative projects and programmes to diagnose and treat all individuals with tuberculosis. These steps will, we hope, see an end to the scourge of tuberculosis, not in 100 years but in the next 20 years.³ This is an ambitious goal, but not an impossible one. Achievement depends on several factors. In particular, to ensure that all people with tuberculosis are diagnosed and given high-quality treatment to cure them effectively and render them non-infectious.

Every year about 3 million people with active tuberculosis are not diagnosed and continue to spread the disease in the community, with many dying.⁴ Other patients are diagnosed but not officially reported, eluding public health systems. The consequences of failing to diagnose and properly treat these 3 million people will impede gains made in tuberculosis control. Quite simply, unless large increases occur in tuberculosis case-finding and provision of high-quality treatment for both drug-sensitive and drug-resistant tuberculosis, we will never truly get a grip on the disease. The global spread and rise in the number of cases of multidrug-resistant and extensively drug-resistant tuberculosis reached 450 000 people in 2013⁵—due, in no small part, to the incomplete or insufficient treatment of patients with tuberculosis. 20% of patients previously treated for tuberculosis who then relapse have multidrug-resistant tuberculosis.² Of concern, Pietersen and colleagues⁵

reported on patients in South Africa with multidrug-resistant tuberculosis or extensively drug-resistant tuberculosis being released into the community to die after failure of treatment in hospital. Drug-resistant forms of tuberculosis are much more expensive and difficult to treat, with treatments having a large burden on patients in terms of adverse events and on health service delivery as a whole.

Although the current situation is not optimum, optimism for achievement of WHO's tuberculosis targets comes from renewed donor commitments. At the 2013 Replenishment Conference of the Global Fund to Fight HIV/AIDS, Tuberculosis, and Malaria, the UK Government pledged £1 billion to fight the three diseases, including for delivery of treatment to more than 1 million people with tuberculosis. Other donor countries rose to the challenge and pledged a cumulative US\$12 billion to the Fund. Although the full amount needed by the Global Fund and its partners has not yet been pledged, these numbers show a remarkable commitment to tackling tuberculosis, malaria, and HIV/AIDS. The Global Fund and its partners will be able to use the money to take advantage of developments in new tuberculosis diagnostics and antituberculosis drugs, to find, test, and treat all patients with tuberculosis. Hopes remain high that new tuberculosis vaccines in early stages of development could tip the balance to favour eradication.

Progress is also being made to strengthen health systems and implement new rapid diagnostics for increased tuberculosis detection through Stop TB Partnership's TB REACH tuberculosis case-finding initiative, and research projects funded by major grant awarding bodies such as the European and Developing Countries Clinical Trials Partnership's TB-NEAT,⁶ EuropeAID's Active Detection of Active Tuberculosis,^{7,8} DETECTB,⁹ and ZAMSTAR.¹⁰ Although increased use of existing methods brings down the global tuberculosis rate by 2% every year, further development of new instruments and interventions¹¹⁻¹³ is needed to complete tuberculosis eradication.

In the past 21 years, tuberculosis has claimed many millions of lives, orphaned at least 10 million children, ruined the lives of hundreds of millions of people, and trapped individuals, families, and entire communities in poverty. World Tuberculosis Day provides a unique forum for everyone, from parliamentarians to patients, from drug developers to health personnel and academic researchers, to come together and call for action with one



Sven Torfmann/Paris

For more on the 2013 Replenishment Conference for the Global Fund see <http://www.theglobalfund.org/en/replenishment/fourth>

For more on TB REACH see <http://www.stoptb.org/global/awards/tbreach/>

united voice. We must not miss this unique opportunity to make the strongest possible case for tuberculosis, push it up the political agenda, and secure global commitment and leadership that will steer a new path to end tuberculosis forever.

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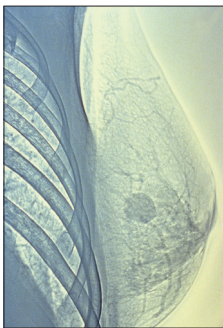
We declare that we have no competing interests. AIZ and AO have an expert advisory role to the UK All Party Parliamentary group on global tuberculosis.

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Breast cancer chemoprevention: little progress in practice?



Visuals Unlimited/Corbis

In *The Lancet*, Jack Cuzick and colleagues report the first results from IBIS-II (International Breast cancer Intervention Study II),¹ in which 3864 postmenopausal women at high risk of breast cancer were randomly assigned to receive the potent, non-steroidal aromatase inhibitor anastrozole or placebo every day for 5 years. After a median follow-up of 5 years, 40 (2%) of 1920 women in the anastrozole group and 85 (4%) of 1944 in the placebo group had developed breast cancer (hazard ratio 0.47, 95% CI 0.32–0.68). This finding is in keeping with those of other similar studies.^{2–4} So far, unsurprisingly, the investigators have not recorded evidence for a difference in breast cancer or all-cause mortality: 18 deaths had been reported in the anastrozole group and 17 in the placebo group.¹

The design of IBIS-II was essentially pragmatic: women enrolled were at increased risk of breast cancer, whether because of family history or previous diagnosis of non-invasive lesions (eg, ductal carcinoma in situ, lobular

carcinoma in situ, and atypical ductal hyperplasia).¹ The predicted cumulative incidence of all breast cancers after 7 years in the control group (5.6%) reflects an increased risk in the participants, and is in line with other similar studies of breast cancer prevention.^{2,3} All the women in IBIS-II had a mammogram and physical breast examination at baseline, unless these procedures had been done within 12 months of enrolment, and then at least every 2 years during the treatment period. 78 (62%) of 125 cancers were detected through screening. At the end of the 5 years, follow-up was as per local practice (including imaging), with no central review of imaging from either before or during the study, or of the lesions (invasive or otherwise) diagnosed before or during the trial.

The issue with studies of pharmacological breast cancer prevention is whether there is true prevention of clinically significant, life-threatening breast cancers, early treatment of tumours overdiagnosed by intrinsic

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