Drug-Resistant Tuberculosis: Old Disease – New Threat
(April 2013)
This report was written by the APPG on Global Tuberculosis’s Policy Adviser, Simon Logan, in close consultation with the APPG Chair and other Officers.

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The photograph on the front cover was kindly provided by The Global Fund to Fight AIDS, Tuberculosis and Malaria and the photograph on the back cover was kindly provided by Medicins Sans Frontieres.

Front: St. Peter’s Hospital, Addis Ababa, where two women are being treated for multidrug-resistant tuberculosis. Thanks to support from The Global Fund, the two-year treatment program is provided free of charge, and drug shortages, which once were frequent, are now nonexistent. Since the start of the program, more than 500 patients have been successfully treated at this facility alone. © Global Fund / John Rae

Back: Aphe, caretaker of Abino (pseudonym), 20 years old, MDR-TB patient gives her anti-TB medicines. Abino says, "I live in a big family of 10 members. Yet no one cares for me or talks to me, except my sister in law, Aphe. When I could not get up, she brought me food and water. She gives me the medicines on time every day.”

Since 2010, Medecins Sans Frontieres (MSF) has been comprehensively supporting the Civil Hospital in Mon – a remote area of India’s north easternmost state, Nagaland. Together with the local authorities, MSF started treating patients with drug-susceptible TB and drug-resistant-TB (DR-TB) in April 2012. People in this remote and mountainous region have severely limited access to health care, with very few health workers and almost no medical specialists. They must often travel for hours to reach the nearest hospital. For this reason, MSF has introduced the decentralized model of care in Mon. Medicines are given to these patients and their caretakers on a monthly basis, so that they can avoid the need to travel to clinic more often – an expense they can rarely afford.

copyright Siddharth Singh 8th March, 2013, India
Foreword

Despite being preventable and treatable, tuberculosis (TB) remains a leading cause of death and a major public health concern worldwide. But if that isn’t bad enough, there is now another manmade crisis spreading at an alarming rate across the European continent and the world – multi-drug resistant (MDR) and extensively-drug-resistant (XDR) TB.

MDR-TB is a form of TB that is resistant to the two main first line drugs, much more expensive to treat and requires careful and often prolonged treatment and care. XDR-TB is resistant to both first and second line drugs. Drug-resistant TB (DR-TB) is all too often a death sentence for many given the inadequate access to treatment, including for people living with HIV where TB is responsible for one in four HIV-related deaths, but it does not have to be this way – we have the means to cure it.

There are 440,000 new cases of MDR-TB each year, with almost 80,000 cases occurring in Europe, and only around 15% of people have access to diagnosis and treatment. The cost difference to treat these resistant strains is staggering, not to mention the difficulty in obtaining and administering medicines for up to two years, many of which have extreme and toxic side effects for the patient. For a ‘normal’ case of TB, the cost of a course of drugs can be as low as twenty US Dollars, but a drug-resistant case can be over four hundred and fifty times as expensive in developing countries.

While the number of drug-resistant cases of TB in the UK is relatively low, we cannot be complacent. London has the highest overall TB rate of any capital city in Western Europe. Rates of MDR-TB have doubled in the UK in the last decade, and while the majority of developed countries (notably the US) have achieved sustained reductions in the number of cases, TB rates continue to rise here. Indeed, if current trends continue there will be fewer new cases each year in the US than in the UK despite our considerably smaller population.

TB does not respect borders, and drug-resistant strains pose a major risk to the health of the British people. This is an urgent and pressing issue, and our report identifies the main challenges facing the UK and the world in controlling drug-resistant strains of TB and makes constructive recommendations for how the UK can best focus its efforts.

Progress in reducing rates and deaths from TB is being made globally, and the Department for International Development has played an important part in this, but drug-resistant TB is a serious threat and it is clear that swift action needs to be taken. With a renewed effort, focused on key areas where the biggest impact can be made, the UK can make a significant contribution to controlling this global threat.

Andrew George MP, Chair of the All-Party Parliamentary Group
List of acronyms and abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>BCG</td>
<td>Bacille-Calmette-Guérin</td>
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<tr>
<td>BRICS</td>
<td>Brazil, Russian Federation, India, China, South Africa</td>
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<td>CMO</td>
<td>Chief Medical Officer</td>
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<td>CSOs</td>
<td>Civil society organisations</td>
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<td>DFID</td>
<td>Department for International Development</td>
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<td>DOT</td>
<td>Directly observed treatment</td>
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<td>DOTS</td>
<td>The internationally recommended basic package that underpins the Stop TB Strategy to control TB</td>
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<td>DR-TB</td>
<td>Drug-resistant tuberculosis</td>
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<td>DST</td>
<td>Drug susceptibility testing</td>
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<td>FIND</td>
<td>Foundation for Innovative New Diagnostics</td>
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<td>GDF</td>
<td>Global Drug Facility</td>
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<td>GeneXpert</td>
<td>Xpert MTB/RIF is a WHO approved rapid test for the simultaneous detection of TB and rifampicin directly from sputum in under two hours.</td>
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<td>GFATM</td>
<td>The Global Fund to fight AIDS, Tuberculosis and Malaria</td>
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<td>Global Plan</td>
<td>Global Plan to Stop TB, 2011–2015</td>
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<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>HPA</td>
<td>Health Protection Agency</td>
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<td>JCVI</td>
<td>Joint Committee on Vaccination and Immunisation</td>
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<td>KNKC</td>
<td>Royal Netherlands Tuberculosis Association</td>
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<tr>
<td>MDR-TB</td>
<td>Multidrug-resistant tuberculosis (resistance to, at least, isoniazid and rifampicin)</td>
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<td>MSF</td>
<td>Médecins Sans Frontières</td>
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<td>NGO</td>
<td>Nongovernmental organization</td>
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<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
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<td>NTP</td>
<td>National tuberculosis control programme or equivalent</td>
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<td>PDP</td>
<td>Product Development Partnership</td>
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<td>POC</td>
<td>Point-of-care</td>
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<td>PPM</td>
<td>Public–Private Mix</td>
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<td>PHE</td>
<td>Public Health England</td>
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<td>R&amp;D</td>
<td>Research and Development</td>
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<td>Stop TB</td>
<td>Stop TB Partnership</td>
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<td>STB Dept</td>
<td>Stop TB Department</td>
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<td>TSO</td>
<td>Third sector organisation</td>
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<td>TB</td>
<td>Tuberculosis</td>
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<td>TBAG</td>
<td>TB Action Group</td>
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<td>UNITAID</td>
<td>International facility for the purchase of diagnostics and drugs for diagnosis and treatment of HIV/AIDS, malaria and TB</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>XDR-TB</td>
<td>Extensively drug-resistant TB, defined as MDR-TB plus resistance to a fluoroquinolone and at least one of three injectable second-line drugs</td>
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Aim and methodology of the inquiry

The All-Party Parliamentary Group (APPG) on Global Tuberculosis is an interest group that sits in, and is recognised by, the UK Parliament. The group comprises members from all major political parties in the UK and works to promote innovative and effective ways to tackle the devastating impact of TB within the UK and around the world.

Aim of the inquiry

This paper seeks to give an overview of the current challenges drug-resistant (DR) TB poses in the UK and globally. This report specifically focuses on the current and future response of the UK Government in addressing DR-TB based on the written and oral evidence received during the APPG inquiry.

The Parliamentary Office of Science Technology (POST) – Parliament’s in-house source of independent, balanced and accessible analysis of public policy issues related to science and technology – published a note on drug-resistant TB (DR-TB) in July 2012 which highlighted the scale, scope and challenges DR-TB poses in the UK and around the world. The POST Note has been used throughout this report as well as written and oral evidence received and the most up to date reports e.g. World Health Organisation and Health Protection Agency TB reports.

It is not the role of POST to provide recommendations in reports that it publishes. It is for this reason that the APPG sought views on the current challenges of DR-TB in the UK – specifically in relation to NHS reforms due to come into effect in April 2013 – and in developing countries, as defined in the four page POST Note.

Methodology

The APPG conducted a two-stage inquiry from late 2012 to early 2013. The initial ‘written call for evidence’ phase of the inquiry received over 30 responses from civil society organisations, advocacy groups, multilaterals, academics and key TB experts in the UK and around the world.

The second ‘oral evidence’ phase of the inquiry involved four hearings – two focusing on the UK and two on the global burden of DR-TB – where members of the APPG explored in more detail issues emerging from the written evidence and POST Note.

All evidence received by the APPG can be found on the group’s website www.appg-tb.org.uk. Oral evidence was given at the hearings by TB researchers, representatives from the Health Protection Agency (HPA), the NHS Commissioning Board and international institutions (such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and the World Health Organisation), NGOs working on TB and representatives from the Departments of Health and International Development. In addition, articles, reports, parliamentary questions and debates were consulted to complement the inquiry’s work. This evidence informed the main recommendations outlined in this report. These recommendations are those of the APPG and are based on their evaluation of the evidence received.

See references throughout this report
Conclusion

Tuberculosis in the UK reflects the global reality. TB is one of the most common deadly infectious diseases worldwide. Unfortunately, little progress has been made toward the elimination of TB in the UK, with almost 9,000 new cases each year, and global progress is painfully slow. The disease remains an urgent public health problem which is exacerbated by drug-resistant strains that are significantly more expensive and difficult to treat.

The first line of defence against drug resistance is appropriate management of ‘normal’ TB and the strengthening of DOT to prevent resistant strains from developing. Rates of DR-TB are small in terms of the global burden of the disease, accounting for 440,000 of the 8.7 million new cases each year, but the financial and treatment burden is substantial. For example, in South Africa, which has the third highest burden of TB and the highest burden of HIV in the world, DR-TB consumed about 32% of South Africa’s US$ 218 million national TB budget (2011), despite the fact that it only accounted for about 2% of all TB cases.

Unfortunately, a case like South Africa is the rule and not the exception. The projected funding needed to implement TB care and control in low and middle-income countries from 2013 to 2015 is up to US$ 8 billion per year, a quarter (US$ 2 billion) of which is required for DR-TB despite it only accounting for around 7% of cases.

The WHO estimates that if funding gaps are filled it could enable full treatment for 17 million TB and MDR-TB patients and save six million lives over the next three years. Failure to invest now means we will pay a heavy price, both in terms of lives lost and high costs of future treatment of DR-TB cases.

DR-TB is also on the rise in the WHO European Region, particularly in Eastern Europe (including Russia). Almost 80,000 MDR-TB cases occurred in the region in 2011, accounting for nearly a quarter of all MDR-TB cases worldwide.

The UK is not immune to this problem. London has the highest TB rate of any capital city in Western Europe and MDR-TB in the UK has gradually but significantly increased since 2000. MDR-TB now represents nearly 2% of all cases. The majority of the 81 new cases in 2011 (95%) were born in South Asia, Eastern Europe and sub-Saharan Africa, with an additional six of these being the most extreme form of the disease (XDR).

International travel increases the potential for spreading resistant bacteria from regions where they are frequent – particularly newly prosperous countries where antibiotic use is generally heavy and infection control relatively weak – to the UK.

The concern this threat presents to the UK recently led the CMO for England, Dame Sally Davies, to warn that antimicrobial and infectious disease resistance pose a serious threat. One of her key recommendations was for the UK Government to campaign for it to be given a higher priority internationally.

Financing mechanisms like the Global Fund to Fight AIDS, Tuberculosis and Malaria play a crucial role in funding programmes for diagnosing and treating TB in low and middle-income countries, and it accounts for almost 90% of international TB funding. For many countries there would not be a response to TB or DR-TB without the Global Fund’s support. The threat of DR-TB is not something we can afford to allow to rise unabated or to wait and pick up the fight in five years’ time when the financial climate is better. The spread of resistant strains is increasing and the Global Fund is on the front line of our response.
The Global Fund is asking donor governments for new funding at a replenishment conference in late 2013, and the UK government has a crucial role to play in ensuring this process is successful so that the Global Fund can continue its leadership role in the fight against TB.

A key area and challenge in responding to the rise in DR-TB is increasing access to diagnosis, which remains a major barrier. However, new tools have been brought to market that can diagnose DR-TB in hours, not days or weeks. In the absence of a point of care test, which is at least two years away, the roll-out of these new technologies, through multilateral mechanisms like The Global Fund, UNITAID and TB REACH will be crucial to scale up access to diagnosis and treatment of DR-TB.

In the history of the fight against TB, there have been periods of urgency and there have been periods of innovation. But only rarely have urgency and innovation come together. The rise of DR-TB has given a new sense of urgency to global TB efforts, and after a decade of focused investment in TB innovation we have a promising pipeline of new tools.

It is clear that in order to address rising rates of DR-TB action is needed at national and international levels to address the danger it poses to us all. Below, the APPG has set out a number of recommendations that, if implemented, seek to put the UK onto the front foot in the fight against this serious public health threat.

# Recommendations

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<th>Department of Health</th>
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<td>HO</td>
<td>Home Office</td>
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<td>HWBB</td>
<td>Health and Wellbeing Boards</td>
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<td>NHSE</td>
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<td>PHE</td>
<td>Public Health England</td>
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<td></td>
<td>BTS</td>
<td>British Thoracic Society</td>
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<td>NICE</td>
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<td>WHO</td>
<td>World Health Organisation</td>
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## Recommendations

The strategy should aim to reduce health inequality in communities, reducing the stigma often associated with TB, especially where there are levels of deprivation due to problems accessing healthcare, and should bring together the following recommendations:

- **NICE guidelines**: Guidelines on the management and treatment of drug-resistant TB should be developed by NICE building on WHO guidelines (2011). However, the guideline on its own is not sufficient as UK practitioners that have no expertise in the management of DR-TB should not be treating and managing cases using guidelines only. As a result a centralised service to manage and treat cases of DR-TB should be developed to provide consistent and agreed clinical management of all DR-TB patients in the UK.

- **Patient to nurse ratios**: NICE Guidance (PH37) which recommends one TB nurse per 40 cases of DS-TB and one TB nurse per 20 complex cases of TB should be implemented across England and the role of third sector organisations supporting DOT and treatment completion rates should be explored.

- **TB specialist nurses**: It is important that any new protocols relating to TB prevention, care and control in the UK e.g. LTBI screening and treatment, are appropriately resourced to manage increased case loads. This should include appropriate training of TB specialist nurses – possibly by adding a TB module to the Diploma of Public Health.

- **Latent TB Infection**: Pre-entry active TB screening for those coming into the UK from countries with high TB burden for six months or more is a welcome step forward, but this policy needs to be accompanied by implementation of NICE guidelines on a coordinated programme for LTBI screening and treatment across the UK.

- **Global Target**: Given the global nature of the disease, the UK Government should set a specific target on their contribution internationally to tackling DR-TB.

- **Access to anti-TB drugs**: Dialogue between the Department of Health and NHS experts on how best to mitigate interruptions in TB and DR-TB treatment should continue to achieve the aim of a consistent and reliable supply of anti-TB drugs.

- **GP registrations**: Discussions with NHS experts, affected communities, hard to reach groups and general practitioners on a targeted approach to increasing GP registration rates among new entrants should take place.

- **Role of Third Sector Organisations**: It is important that any strategy is complemented by the role of third sector organisations, particularly support for DOT and treatment completion rates.

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### Organisation

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<td>UK Government, DH, PHE, NHSE, HWBB, DFID, HO, NICE, TSOs, NHS London</td>
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specifically targeting ‘hard to reach groups’ should go hand in hand with a broader TB awareness strategy, in close consultation with affected communities, aimed at limiting the stigmatising aspect of the disease.

• **Find and Treat:** The highly-rated “Find and Treat” service in London should be adequately, and continually, financed and supported by NHS London to improve equipment provision and staff retention and its expansion, into other high burden urban centres, explored.

• **BCG:** JCVI should review their decision on BCG immunisation, especially in London where a pan-London approach is needed.

**Key reason for these recommendations**

A national strategy for TB has never been developed despite the public health risk the disease presents. The UK has seen rising rates of tuberculosis since the 1980s and DR-TB increased by 26% in the last year alone. London remains the ‘TB Capital of Western Europe’ and if rates of the disease continue on an upward trend the UK will have more new cases of TB each year than the United States. The changes in the health service brought about by the Health and Social Care Act (2012) offer an opportunity to reverse rising rates of TB and DR-TB under the new structures, allowing for flexibility at a local level, if it is public health led.

**Strengthen the Global Fund**

**The Global Fund to Fight AIDS, Tuberculosis and Malaria** is crucial in the response to TB and evolving DR-TB. The UK Government should at least double (from £128m per year to £256m) its contribution to the Global Fund, assuming good progress on reforms and delivery on the ground – with a positive MAR update, to address the threat of TB and DR-TB in low and middle-income countries at a time that leverages more from other donors. The most obvious next available opportunity to do so is the G8 in June 2013.

**Key reason for recommendation**

International donor funding almost entirely comes through the Global Fund (including around 90% of the UK Government’s). In 22 high TB burden countries six are totally reliant on funding from the Global Fund (100% of financing) and for another 15 high burden countries two thirds (60%) of their budget comes from GFATM financing. In order to scale up access and treatment for DR-TB the resources GFATM has at its disposal needs to increase to meet the unmet need and the UK Government has a key role to play in the replenishment in 2013 having been a key driving force behind the reforms it has undertaken. The UK is also in a position to show this leadership due to the increase in DFID’s budget as part of the UK reaching 0.7% of GNI being invested in ODA.
Invest in R&D DFID has a strong record supporting investment in TB R&D, as one of the leading funders into new technologies to tackle TB in the world, and its holistic approach supporting investment in research to find new diagnostic tools, drugs and vaccines, as well as operational research should be at least maintained and ideally scaled up. The Department for Business, Innovation and Skills also has a role to play supporting TB R&D due to the potential return on investment to UK academic institutions and businesses.

Key reason for recommendation

Any new technologies, such as a reduction in the time or number of pills required to cure TB, are likely to have a direct positive impact on reducing rates of the disease in the UK. Due to the recent success of many Product Development Partnership (PDP) initiatives we have some new tools and many more in the pipeline that will need continued assistance to get to market. UK universities and firms are amongst those involved in such partnerships.

Invest in innovation Value for money considerations infuse all national programmes combatting TB, with the most cost-effective interventions being prioritised for the highest impact. TB REACH is targeted at driving innovation and high impact. The UK Government should become a donor to TB REACH, beyond its contribution of core funding to the Stop TB Partnership, to maximise its investments in UNITAID and support the expansion of new diagnostic tools to detect, and ultimately treat, cases of DR-TB. The level of funding allocated should be directed by the evaluation of the Stop TB Partnership due in 2013.

Key reason for recommendation

In order to increase case detection among the estimated three million people that currently go undiagnosed and fail to access treatment each year, we need to be more innovative and strategic about investments to scale up interventions, particularly around diagnosis. TB REACH and UNITAID initiatives are some of the world’s best vehicles for channelling this investment in improving access to diagnosis and treatment for DR-TB to those who need it.

Managing risk in the private sector The private sector is growing in many low and middle-income countries and is already diagnosing and treating large numbers of patients. It will be essential that the public and private sectors are appropriately coordinated, through the public private mix (PPM) model and joined-up to ensure access to reliable diagnosis and quality approved drugs.

| **GLOBAL** |
| **UK Government, DFID and BIS** |
| **GLOBAL** |
| **UK Government, BIS, DFID, and DH** |
| **GLOBAL** |
| **WHO, Private Sector, and national governments** |
Introduction

This introduction gives a brief synopsis of rates of TB and DR-TB in the UK and around the world. Further information can be found in the World Health Organisation’s (WHO) ‘Global Tuberculosis Report (2012)’ and the Health Protection Agency (HPA) ‘Tuberculosis in the UK 2012: report’.

An overview of TB and drug-resistant TB in the UK and around the world

Tuberculosis (TB) is a major cause of death globally, and progress in the control of the disease is threatened by drug-resistant strains.
TB is an airborne infectious disease caused by the bacterium Mycobacterium tuberculosis (Mtb). TB bacteria are very hard to kill. The standard WHO regimen is a combination of four first-line drugs taken for six months. The drugs used are isoniazid and rifampicin supplemented by two further drugs (pyrazinamide and ethambutol) for the first two months.

The bacteria usually attack the lungs but can affect any part of the body. TB is easily spread through the air from one person to another when a person with TB disease of the lungs or throat coughs, sneezes, speaks or sings.

Global rates of TB

One third of the world’s population, around two billion people, is infected with Mtb bacterium but does not have active TB disease. This is often referred to as dormant or ‘latent’ TB. Only a small proportion (around 10%) of these people develop the active form of the disease during their lifetime and become sick and potentially infectious.

In 2011, some 8.7 million people contracted TB causing 1.4 million deaths, including 430,000 deaths among HIV-infected persons. Progress has been made in tackling the epidemic. Globally, the number of new/relapsing cases has fallen each year since 2006, albeit very slowly, and TB death rates have dropped by more than a third since 1990 levels.

Medical risk factors for TB include co-infection with HIV. People living with HIV are up to 34 times more likely to develop TB and accounted for about 13% of all TB cases globally in 2011. HIV increases the likelihood that a person infected with latent tuberculosis will progress to active disease, shortens survival times among co-infected individuals and increases the likelihood of atypical tuberculosis manifestations that can be difficult to diagnose (for example, TB of the kidneys or TB Meningitis).

TB continues to be an important health problem in children and a high proportion of childhood TB cases continue to be caught from a family member with active infection. Diagnosis of TB in children is particularly difficult because of the challenges in obtaining sputum.

The Bacillus Calmette–Guérin (BCG), which is one of the most widely used childhood vaccinations in the world, provides limited immunity to TB and protects against the most severe forms of disease, such as TB meningitis in children, but provides very limited immunity against TB of the lungs - the most common and most infectious form. The impact of BCG vaccination on transmission of Mtb is therefore limited. Today, it is estimated that more than 1 billion people have received BCG making it one of the most widely used of all current vaccines. However, in the UK its use is limited to newborn children in high risk groups with the aim of preventing severe forms of disease.

Box 1: How effective is the BCG?

The Bacillus Calmette–Guérin (BCG) immunisation, first developed in 1921 and the only licensed TB vaccine available today, increases a person’s immunity to TB and protects against the most severe forms of disease, such as TB meningitis in children, but provides very limited immunity against TB of the lungs - the most common and most infectious form. The impact of BCG vaccination on transmission of Mtb is therefore limited. Today, it is estimated that more than 1 billion people have received BCG making it one of the most widely used of all current vaccines. However, in the UK its use is limited to newborn children in high risk groups with the aim of preventing severe forms of disease.

Key facts:

- Globally, 1.4 million people died from tuberculosis (TB) in 2011, even though the disease is curable with drug treatment.
- TB is the leading killer of people living with HIV/AIDS, accounting for one in four AIDS related deaths.
- Drug-resistant strains are now estimated to account for about 10% of all TB deaths.
- Drug resistance is a man-made problem, resulting from misuse of anti-TB drugs and poor management of the disease.
- Treatment for drug-resistant TB is much more expensive, toxic and takes much longer than treatments for ‘normal’ TB.
- Early and rapid diagnosis and treatment completion are essential for controlling TB.
- In the UK, TB is a particular problem among people born abroad and hard to reach groups.
- Funding is required to develop better diagnostics, vaccines and anti-TB drugs.
What is drug-resistant TB?

Drug-resistant strains have developed through inappropriate use of anti-TB drugs (see Box 2) and poor management of the disease (including infection control).

DR-TB can develop if:
• patients do not complete the full course of treatment;
• the correct therapies are not prescribed or available (including if treatment is interrupted due to drug stock-outs);
• the drugs are of sub-substandard quality.

DR-TB is spread the same way that TB is spread. People nearby may breathe in these bacteria and become infected. There are several types of DR-TB recognised by the WHO:
• Multidrug-resistant (MDR) TB is resistant to the two most effective first-line drugs, rifampicin and isoniazid
• Extensively drug-resistant (XDR) TB is MDR-TB which is also resistant to drugs called fluoroquinolones as well as to at least one of the second-line injectable drugs (e.g. amikacin, kanamycin). In recent years, XDR-TB patients infected with strains resistant to many other anti-TB drugs have been reported
• Poly-drug resistant (PDR) TB is the name given to all forms of resistance to more than one of the first-line drugs which are neither MDR-TB nor XDR-TB

There are two DR-TB classifications that are not currently defined or recognised by the WHO - extremely drug-resistant (XXDR) and totally drug-resistant (TDR) TB. These names emerged in 2009 when a cohort of 15 patients in Iran were resistant to all anti-TB drugs tested. The emergence of TDR-TB has been documented in three major publications since the Iran cohort; however this is not accepted WHO terminology and these cases are officially defined as XDR-TB.

How long does it take to treat someone with DR-TB and how much does it cost?

Drug-resistant forms of TB do not respond to the standard six-month treatment with first-line anti-TB drugs. They can take up to two years or more to treat with drugs that are much more powerful, toxic and expensive.

A course of standard TB drugs cost approximately US$ 19, but DR-TB treatment can cost over 450 times as much – up to US$ 9,000 for a standard 18-24 month treatment course in developing countries, if available at all.

These high prices are a reflection of the fact that current market demand is low because most people who have the disease don’t have enough resources to pay for treatment and due to the limited capacity to diagnose and treat DR-TB, which does not provide the market incentive to manufacturers.

By comparison, in the UK – where there is universal access to diagnosis and treatment - a typical TB case is estimated to cost around £5,000 to treat, but a case of MDR-TB costs between £50,000 and £70,000, rising to over £100,000 per patient for the most extreme forms.

What is the scale of the problem?

Drug-resistant TB (DR-TB) threatens global TB control and is a major public health concern in countries. DR-TB is estimated to cause about 10% of all TB deaths. Headline figures for TB rates are shown in Table 1.

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Box 2: How does drug resistance develop?

Resistance to anti-TB drugs can occur when these drugs are misused or mismanaged. Examples include when patients do not complete their full course of treatment; when healthcare providers prescribe the wrong treatment, the wrong dose, or length of time for taking the drugs; when the supply of drugs is not always available; or when the drugs are of poor quality.

Fluoroquinolones are a broad-spectrum antibiotics that have become indispensable in the treatment of DR-TB. They include the following, in order of potency: moxifloxacin, gatifloxacin, levofloxacin, ofloxacin and ciprofloxacin.
Incidence is defined as the number of new and relapse cases occurring during a given time period. Prevalence is defined as the number of individuals in a population found to have TB at any moment in time. The figures on the global burden of TB (Table 1) are estimated. This is due to a lack of good quality surveillance data and non-standardised surveillance method – many countries have never carried out surveys of DR-TB. However, representative surveillance data on levels of MDR-TB is due to be available from all 27 high MDR-TB burden countries in 2013.

Globally, around 4% of new cases and 20% of previously treated cases are estimated to have MDR-TB. Previously treated patients are more at risk of MDR-TB and therefore should be investigated for drug susceptibility. Such patients require that their specimens should be obtained for culture and drug sensitivity testing (DST) at the start of their therapy. Currently, only 6% of those previously treated have access to tests capable of diagnosing MDR-TB.

Levels of MDR-TB remain high in some parts of the world, notably countries in Eastern Europe and Central Asia. In several of these countries (Russia, Belarus and Ukraine), between 9 to 32% of new cases and more than 50% of previously treated cases have MDR-TB.

The WHO estimates there were 440,000 new MDR-TB cases in the world in 2011 (incidence), but there are 650,000 cases of DR-TB in total in the world at any one time (prevalence, see Table 1). Of these cases, around 10% (65,000) have the most extreme form of the disease known as XDR-TB. XDR-TB can be cured, but the likelihood of cure is smaller than in patients with ‘normal’ TB (>85% successfully treated) or even MDR-TB (48% cases successfully treated).

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**Box 3: Active TB diagnosis: how do you test for TB and DR-TB?**

Many countries still rely on a long-used method called “sputum smear microscopy” to diagnose TB. Trained laboratory technicians look at sputum samples under a microscope to see if TB bacteria are present. With such tests, diagnosis can be made within a day, but this test does not detect many cases of less infectious forms of TB ie. TB in other parts of the body other than the lung, as the bacteria may simply not be present in the lungs to be coughed up and seen on the slide.

Diagnosing MDR-TB and HIV-associated TB can be more complex and takes longer to diagnose. TB is also particularly difficult to diagnose in children as often they are not able to produce enough sputum to test for active disease.

A new two-hour test that has proven highly effective in diagnosing TB and the presence of drug resistance is now being rolled-out in many countries (GeneXpert).

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**Table 1: Headline TB Rates**

<table>
<thead>
<tr>
<th></th>
<th>Estimated Global 2010</th>
<th>Notified UK 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB Incidence*</td>
<td>8.7 million</td>
<td>8,963</td>
</tr>
<tr>
<td>TB Prevalence</td>
<td>12 million</td>
<td>Not reported</td>
</tr>
<tr>
<td>MDR-TB cases</td>
<td>650,000 (prevalent* cases)</td>
<td>81 (out of a total of 431 DR-TB cases)</td>
</tr>
</tbody>
</table>

*Incidence is defined as the number of new and relapse cases occurring during a given time period. Prevalence is defined as the number of individuals in a population found to have TB at any moment in time.
Of the new cases of MDR-TB each year, globally only around 60,000 people (less than 15%) were identified and treated. To put this into perspective, the Stop TB Partnership’s Global Plan aims for 75% of MDR-TB patients to be treated successfully by 2015 and estimates that between 2011 and 2015 about one million MDR-TB patients will need to be detected and placed on treatment. To date only 30 out of 107 countries have achieved the 75% treatment success target (MDR cases starting treatment in 2009).

About 60% of cases of DR-TB occur in Brazil, China, India, the Russian Federation and South Africa (“BRICS”, middle-income countries), but the problem is not confined to these five countries. The number of cases of MDR-TB reported by the 27 high MDR-TB burden countries almost doubled between 2009 and 2011.2

It is important to highlight the cost implications of diagnosis and treatment of DR-TB. A recent study found that DR-TB consumed about 32% of South Africa’s total estimated national TB budget (2011) of US$ 218 million, despite the fact that it only accounted for 2% of TB cases.19

**Tuberculosis financing and funding gaps**

The World Health Organization (WHO) and the Global Fund to Fight AIDS, TB and Malaria (GFATM) estimate that there is an annual anticipated demand for at least US$ 1.6 billion in international support to bridge the funding gap over 2014-2016 in 118 low and middle income countries which are eligible for financing from the Global Fund.

It is projected that domestic contributions could cover the bulk (over 65%) of financing required for TB care and control in these 118 countries, equivalent to US$ 3.2 billion. This will require that TB funding

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**Figure 1: Percentage of new tuberculosis cases with MDR-TB**


IV Treatment success is defined as the sum of patients that are cured or have completed treatment (see below). Cure: A patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear – or culture-negative in the last month of treatment and on at least one previous occasion. Completed: A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion.
increases in line with economic growth and that there is increased political commitment, especially in countries that currently underperform in comparison to their ability to pay.\textsuperscript{20}

Of the international donor funding expected by national TB control programmes in 2013, almost 90\% is from the Global Fund to Fight AIDS, Tuberculosis and Malaria. The Global Fund is also DFID’s preferred instrument in the response to TB in low and middle-income countries with over 90\% of its funding to tackle TB and DR-TB channelled through the Global Fund.

In the absence of any other major streams of international donor funding for TB, the Global Fund plays a crucial role in sustaining and ensuring further progress in TB care and control worldwide.\textsuperscript{2}

\textbf{Figure 2: Percentage of previously treated tuberculosis cases with MDR-TB}\textsuperscript{17}

\textbf{TB in the UK}

Tuberculosis is a serious public health problem in the UK. The incidence of TB in the UK has continued on a general upward trajectory since the late 1980s, with 8,963 new cases reported in 2011 (see figure 3).\textsuperscript{3} This trend runs counter to the majority of developed countries where rates of TB are in decline. For example, if the current trend is maintained, in two years’ time the UK will have more new cases of TB each year than the US, despite the UK’s much smaller population.\textsuperscript{21,22}

The majority of UK cases are likely to result from latent TB infection in persons who were born in high incidence areas outside the UK. Hence, despite improvement in treatment completion in the last decade, TB incidence has not yet declined.

The majority of case notifications came from urban centres amongst young adults (15-44), those from countries with high TB burdens and those with social risk factors for TB. Just over half of the reported new cases (4,603) had TB of the lung.\textsuperscript{3}

According to the Chief Medical Officer’s Report (2011), over 86,000 individuals were diagnosed with TB in the UK between 2000 and 2011. More than 70\% of cases were diagnosed in the most deprived 40\% of the UK population. Not only do deprived groups have higher rates of TB, there is also

\textsuperscript{17} Reproduced from WHO’s global tuberculosis 2012 report, by permission of the World Health Organisation
evidence of a significant association between levels of deprivation and diagnostic delays, often due to problems among these groups in accessing healthcare. Undiagnosed TB of the lungs increases the probability of transmission.

Other risk groups, such as individuals with a history of drug use, homelessness and/or a history of imprisonment, also have a higher risk of TB. Between 2009 and 2011, about 10% of TB cases in the UK had at least one such risk factor. The importance of these risk groups lies in the fact that they have the highest risk of transmission in the UK, the highest risk of acquiring drug resistance strains and are least likely to complete treatment.3

Figure 3: Three-year average tuberculosis case rates by local areas, UK, 2009-2011

Drug-resistant TB in the UK

The number of DR-TB cases in the UK continues to rise with 431 cases (8.4%) resistant to any first line drug reported in 2011, up from 342 in 2010 – an increase of 26%. The number and proportion of isoniazid resistant and MDR cases increased in 2011, almost 8% and 2% respectively. Over the last decade, the proportion of MDR cases has gradually but significantly increased. The proportion of cases resistant to any first line drug was higher in those with a history of TB diagnosis, compared to those without and in non-UK born cases compared to UK born. This pattern is similar for MDR cases.23

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3 Reproduced from the HPA’s Tuberculosis in the UK: Annual report on tuberculosis surveillance in the UK (2012), by permission of the Health Protection Agency.

23 TB that is resistant to any first line drug, including: Isoniazid, Rifampicin, Pyrazinamide, Ethambutol and Streptomycin.
The concern relating to the increase in DR-TB cases led the Chief Medical Officer (CMO) for England, Dame Sally Davies, to warn that antimicrobial and infectious disease resistance pose a serious threat. One of the key recommendations in the CMO’s Annual Report was for the UK Government to campaign for it to be given a higher priority internationally.24

Most UK regions reported below the national and WHO target of 85% treatment completion rates for drug susceptible TB, and globally non-completion of treatment significantly contributes to increases in drug resistance.

The majority of patients in the UK with DR-TB were born in areas of the world where DR-TB is common, such as the Indian subcontinent and Eastern Europe.

There were six cases of XDR-TB (the most extreme form, which is much more difficult and expensive to treat) reported in 2011 and a total of 24 cases between 1995 and 2009. The majority were non-UK born (18, with 9 of these from Eastern Europe) and had pulmonary (TB of the lungs and thus infectious).3

Completing the 18-24 month course of DR-TB treatment is difficult and involves taking 8-11 tablets per day for at least two months, plus additional daily intravenous injections for the first six to eight months. In order to ensure completion of treatment, it is essential that patients have adequate care and support.

It is important for services to tailor treatment and care to the patients’ needs and for there to be good links between the health service and the local community. Treatment can have physical and physiological side effects.

London, which has the highest TB rates of any capital city in Western Europe and accounts for 39% of all UK cases4, and the West Midlands have been the most affected regions in the last decade.5 The worst affected borough in London is Newham with TB incidence rates of 122 per 100,000 people,6 which is over eight times the UK average (14.4 per 100,000 people) and comparable to high-burden developing countries. Brent, Ealing and Hounslow also have rates well above the UK average.3

There have been attempts to reduce rising rates of TB. A TB Action Plan “Stopping Tuberculosis in

VIII Reproduced from the HPA’s Tuberculosis in the UK: Annual report on tuberculosis surveillance in the UK (2012), by permission of the Health Protection Agency.
England: An action plan from the Chief Medical Officer”, was developed in 2004 to curb rising rates of the disease, but it has had little effect on the number of cases, as successive HPA TB reports have shown.

Also in a survey carried out in 2007 by the British Thoracic Society, nine out of ten TB specialists believed the number of TB cases in the UK was set to rise over the next five years, and there has been a failure to implement the Government’s TB Action Plan. This has unfortunately been shown to be the case.26

The need for new TB drugs, vaccines and diagnostics27

After decades of no progress, new or re-purposed TB drugs and novel TB regimens to treat TB or DR-TB are now advancing in clinical trials and regulatory review. Eleven vaccines to prevent TB are moving through development stages and a new diagnostic tool (GeneXpert) is being rolled out, particularly through TB REACH and with support from UNITAID. GeneXpert can diagnose TB and resistance to one of the front-line drugs within 100 minutes, a dramatic improvement over current technologies that can take weeks to provide similar information.

The development of new drugs, diagnostics and vaccines is progressing through the Product Development Partnership (PDP) model, and the outlook is positive. However, challenges still remain, particularly around R&D finance and the issue of access to new technologies for countries where the TB burden is highest.

Results of one study suggest that new and improved TB drugs, vaccines, and diagnostics could reduce the global incidence of TB by 71 % by 2050, a reduction of more than 6.5 million annual cases.

Research and development global funding

Over the last seven years, cumulative investments in TB research and development (R&D) totalled US$ 3.6 billion.28 Yet, each year annual spending toward research for new and improved TB tools falls far from the $2 billion global target defined by the Stop TB Partnership’s Global Plan to Stop TB 2011–2015.

The Treatment Action Group 2012 Report on Tuberculosis Research Funding Trends, 2005–2011, found that while TB R&D funding increased by 3% from 2010’s US$ 630 million to US$ 649 million, investment still falls short of requirements.28 Current levels of funding for R&D into new tools (targets and investments) can be seen in figure 5 below.

Figure 5: Annual Global Plan Research Funding Targets vs. 2011 Investments 29

Tuberculosis in the United Kingdom

Treatment completion targets
The national treatment completion rate target for TB is 85% in the UK, in line with WHO guidelines. The UK is not meeting this target, although rates have improved from 78% in 2001 to 83% in 2010. Death was the most common reason for not completing treatment (5%) and 4% failed to complete treatment because they were lost to follow up, the majority of whom moved abroad. However, three regions in the UK did exceed the treatment completion target for TB, and treatment completion rates for MDR-TB cases were also high (80% in patients notified in 2009). DR-TB occurring by chance is minimal, and inappropriate regimens are strongly associated with resistance developing. Failure to complete treatment stimulates resistant strains of the disease developing and if no improvement is seen DR-TB is likely to arise. Evidence received suggests that it is crucial that TB and DR-TB services are joined up to avoid complacency. Given the cost implications, DR-TB cases are at least ten times more expensive to treat, effective management of TB is one of the cheapest forms of DR-TB control.

Directly Observed Therapy
Directly Observed Therapy (DOT), which is the global strategy to prevent drug-resistance, was only used to treat 40% of patients in 2011 that had at least one risk factor. Cases that report at least one social risk factor were also more likely to have DR-TB disease. While it is not necessary for all patients that have active TB to be put on DOT, it is necessary to carry out a risk assessment for adherence to treatment with a central pillar of a patient centred approach. For example, of patients with a history of homelessness, problems with drug or alcohol use and/or imprisonment only 75% completed treatment, and a higher proportion died or were lost to follow up. It is essential that when DOT is recommended that more flexible interventions centred around the patient are considered e.g. patients receiving DOT from a well-known supermarket chain because that is the only place they are going to access it.

Learning from other countries
Treatment should include the possible provision of DOT in all cases, through an appropriate risk assessment. The United States experienced a similar problem to the UK 20 years ago with rates of TB rising, 26,000 cases per year – they now have rates around 10,000. As mentioned above, if the current upward trend is maintained the UK will very soon overtake the US in terms of TB rates despite having a much smaller population. New York, in particular, had very high rates of the disease and to address this they designed treatment around the patient and ensured that everyone was entitled to be provided DOT. It involved looking innovatively at how patients can receive treatment.

Box 4: What is (DOT)?
DOT means that a trained health care worker or other designated individual (excluding a family member) provides the prescribed TB drugs and watches the patient swallow every dose.

21
Nurse to patient ratios and the role of third sector organisations

One of the reasons that only half of patients are placed on DOT is nurse to patient ratios. NICE Guidance (PH37) recommends: one TB nurse per 40 cases of TB and one TB nurse per 20 complex cases of TB. In many areas, including London which has a ratio of one nurse for every 34 patients,³² this recommendation is not being met. This is having an impact on services’ ability to manage caseloads and carry out contact tracing³³ to prevent the spread of the disease and place patients on DOT that require it.

As stated in the Royal College of Nursing (RCN) cohort review (March 2012), nurses contribute greatly in TB control, providing screening services, expert patient care and supporting non-clinically qualified case managers.

Third sector organisations (TSO’s) are often uniquely placed to assist clinical services, including TB nurses and case managers, to achieve WHO targets on completion rates, especially among hard to reach groups through implementation of DOT, where necessary.

In addition, TSO’s can play a key role in active case finding and contact tracing as well as helping to mitigate the stigmatising effects which targeting specific populations may bring. Adressing stigma may be assisted through ‘The Truth About TB programme’ facilitated by UK charity TB Alert.⁴

Patient support

Social and financial barriers also often affect the way in which people seek TB care and treatment and their ability to complete the full course of treatment. TSO’s like TB Alert provide a ‘Small Grants and Patient Support Fund’ to ensure that people with no recourse to public funds have the money to attend clinic appointments and eat a nutritious diet whilst on treatment.

TB Alert also facilitates the ‘Truth about TB’ programme, which seeks to build capacity and awareness of the disease within the TSO’s and their client groups including: homeless people, refugees, asylum seekers, migrant community and drug and alcohol users that involves those affect by TB, given that awareness of the disease may be low in these groups

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**Recommendation**

NICE Guidance (PH37) which recommends one TB nurse per 40 cases of TB and one TB nurse per 20 complex cases of TB should be implemented across England and the role of third sector organisations supporting DOT and treatment competition rates should be explored.
Active Case Finding

Experts agree health services should focus more effort on actively seeking out cases. This can be done by testing people the patient has come into contact with, screening high risk groups and systematically reviewing the outcomes of all cases in an area.

It requires multidisciplinary teams capable of delivering all elements of TB services from diagnosis to cure. Find and Treat is an example of one such UK NHS service.

Box 5: Find and Treat

Find and Treat is a London-based NHS initiative that uses a mobile x-ray unit to screen almost 10,000 homeless people and drug users a year for active TB. It provides early diagnosis and supports patients to take a full course of treatment and get cured. In recognition that TB is not just a medical problem but a socially complex disease, Find and Treat is a multidisciplinary team of TB nurse specialists, social and outreach workers, radiographers and technicians. The service has been shown to be extremely cost-effective in an independent review carried out by the HPA, because it limits onward transmission - patients detected by F&T are more likely that those who are detected passively to receive treatment before they become infectious - and the high treatment cost of late diagnosis.

This is supported by the International Union against TB and Lung Disease (The Union) which highlights that active case finding, in patients with risk factors for TB, should be a priority in a TB programme. Therefore, the role of the active case finding in these groups of patients is essential to try and reduce the incidence of DR-TB.

Contact tracing

Anecdotally, TB patients and members of the TB Action Group (TBAG) have reported varying degrees of contact tracing, including lack of follow-up for people who have not attended for screening and contact being given images of negative, positive and strongly positive skin test reaction from which to judge their own body’s responses.

Active case finding among the homeless

TB incidence among the homeless in London is 50 times higher than the national average. The homeless are also very likely to present late for treatment and much less likely to complete treatment, creating the perfect conditions for development and transmission of DR-TB.

“It is a time bomb in our hostels and TB is on the verge of being a health emergency”, Charles Fraser from St Mungo’s, a leading homeless charity stated when talking about DR-TB. Mr Fraser echoed the F&T observation that this population is easier to find than it is to treat, highlighting that it is not people that are hard to reach but services.

Services should be designed around people and a needs assessment ought to be carried out for all patients starting TB treatment in line with NICE guidelines (PH37) on TB in hard to reach groups. Increased capacity of the F&T service, which has been peer reviewed by the HPA and shown to be cost effective and potentially cost saving, has an opportunity to not only actively find and treat cases of TB in the early stages of infection but also other diseases including Hepatitis C, HIV and influenza.

The NHS in London, which has funded the Find and Treat service since 1 April 2011, will continue to fund this service in 2013-14, but the services are operating at full capacity with aging, and increasing unreliable equipment.
The Chief Medical Officers 2nd Annual Report (2013) highlights that the successful control of tuberculosis in major cities in the UK depends on our ability to target interventions at deprived groups. The report highlights that the Find and Treat Service in London needs to be continued alongside national implementation of NICE guidelines.

Variations in Screening and Care

A 2011 report highlighted that current TB screening and control guidelines are not applied consistently across London and that standardisation of TB services is urgently required. There is significant variation in the configuration and governance of the five London TB networks and no performance management role. Notably, staffing profiles and provision of Directly Observed Treatment vary but not in relation to need.

Patients view of screening and care

TBAG have highlighted that their personal experience screening and care varies greatly. For example, for most patients their TB nurse is their greatest source of support, but some patients are never allocated a named TB nurse and have no support from services outside the clinical setting.

One TB patient was discharged from hospital with a bag of TB medication with no follow-up instructions. Eventually she re-entered the health system and was put in touch with ‘Find and Treat’ where she became a peer educator.

It is vital that all TB patients, regardless of existing risks or lifestyle choices, are fully assessed to identify support needs to help mitigate social and financial hardship. It is also equally important to ensure that consideration is given to specific linguistic and cultural requirements, especially for migrant populations, in the treatment of TB.

Drug availability

A UK study of anti-TB drugs between 2007 and 2009 found that almost two thirds of treatment centres had experienced difficulties obtaining anti-TB drugs, which resulted in NHS trusts interrupting or altering treatment regimens for both drug-sensitive and drug-resistant TB. The study concluded that difficulties obtaining drugs to treat both TB and drug-resistant disease are common in the UK.
There are currently only two licensed second line drugs for DR-TB in the UK and of the WHO essential list, seven drugs aren’t available in the UK, four of which can be imported from abroad and three of which are difficult to find quality assured versions of from overseas.

Very few liquid formulations for children are available to treat TB. Often hospitals will prepare a liquid by crushing up tablets and mixing them with a suitable diluting agent. Patients have to crush a tablet for every dose, mix it with water (10ml) and then take just a small proportion which does not give an accurate dose. Speaking about variation in doses of anti-TB drugs for children, one pharmacist commented that because there is no consistent approach in the UK for DR-TB everybody’s doing something different.44

The Department of Health and the pharmaceutical industry published joint best practice guidelines, “Notification and Management of Medicines Shortages” to avoid drug shortages or interruptions in treatment for TB occurring. These recommend that companies communicate with the Department as soon as possible about impending shortages that are likely to have an impact on patient care, so that the options for mitigating and managing the shortage can be explored.

Marketing Authorisation Holders also have a statutory duty to inform the Medicines and Healthcare products Regulatory Agency if a product is not going to be available either temporarily or permanently. The Department expects companies to communicate directly with pharmacists and physicians where there is an interruption to the supply of a medicine.

The Department is also working with a group of National Health Service experts to investigate what can be done to improve security of supply of TB medicines for children and others.45

Guidelines for the management and treatment of MDR-TB

In the absence of guidance of the management of DR-TB, experts and organisations in the UK have called for guidelines to be produced by NICE to standardise treatment.46 However, this does raise concerns that UK practitioners who are not experienced in dealing with DR-TB cases may try to treat patients using the guideline alone.31

Generally UK practitioners use 2011 WHO guidelines.47 The guidelines are intended for health professionals in EU member states to develop a comprehensive framework for the management and care of MDR and XDR-TB.

In the UK the only advice beyond the WHO guidelines available to practitioners is from a voluntary online dialogue between experts and service users on aspects of the management of patients with MDR-TB (British Thoracic Society (BTS) MDR-TB Clinical Advice Service).

It is argued that the presence of agreed UK guidelines, possibly building on the WHO guidance, developed by NICE and coupled with the a centralised service to manage and treat cases of DR-TB would help in providing consistent and agreed clinical management of all DR-TB patients in the UK.

Bacillus Calmette–Guérin

The Bacillus Calmette–Guérin (BCG) vaccine increases a person’s immune response to TB and protects against the most severe forms of disease, such as TB meningitis, but provides limited immunity to TB of the lungs and its effects wear off after adolescence.48

The BCG is no longer routinely given to children in the UK. Vaccination policy, based on the expert advice of the independent Joint Committee on Vaccination and Immunisation (JCVI), changed in 2005 from vaccinating all children to only those children at high risk of contracting the disease or where rates of TB are 40 per 100,000 or above.49

Current uptake of BCG vaccination, based on the JCVI’s advice, varies. For example, London Health...
Programmes highlighted that both uptake of neonatal BCG in London and how it is administered varies considerably. They noted that if the London TB rate were taken as a whole, all new born children in the city would be given access to the BCG vaccine. The advantage to a uniform BCG policy across London is that it is both pragmatic and easier for the public and healthcare staff to understand than a policy which varies across different boroughs. The downside of this approach is that BCG would be administered in some boroughs with a lower TB rate, which would not be consistent with JCVI guidance and may be an ineffective use of resources.\(^\text{13}\)

The JCVI has advised that the current approach is the most effective way to protect those most at risk of contracting tuberculosis. The Committee most recently reviewed the policy in 2010.\(^\text{50}\)

### Recommendation

**Guidelines on the management and treatment of drug-resistant TB should be developed by NICE building on WHO guidelines (2011). However, the guideline on its own is not sufficient as UK practitioners that have no expertise in the management of DR-TB should not be treating and managing cases using guidelines only. As a result a centralised service to manage and treat cases of DR-TB should be developed to provide consistent and agreed clinical management of all DR-TB patients in the UK.**

### Recommendation

**Dialogue between the Department of Health and NHS experts on how best to mitigate interruptions in TB and DR-TB treatment should continue to achieve the aim of a consistent and reliable supply of anti-TB drugs.**

### Recommendation

**JCVI should review their decision on BCG immunisation, especially in London where a pan-London approach is needed.**
Commissioning of TB services

The management of tuberculosis is highly complex and includes many clinical, public health and social factors. Public health groups are concerned that the health service reforms in the Health and Social Care Act 2012, due to come into effect in April 2013, could potentially result in a fragmented approach to TB care and control.  

Challenge and opportunities

While the changes represent a challenge, the new responsibilities of local authorities and Public Health England (PHE) provide an excellent opportunity to improve TB prevention, care and control, if appropriately implemented.

Moving public health responsibility into local authorities has real opportunities for tuberculosis because it is a very socially complex disease and local authorities understand their communities and how to work to improve health of their local populations.

NHS Commissioning Board (NHS England, April 2013)

The NHS Commissioning Board (NHSCB) has acknowledged the complexity of TB and DR-TB and highlighted that all options, with regard to how TB should be commissioned under the new legislation, are being considered.

Options include: recommending a select number of Clinical Commissioning Groups (CCG’s) collaborate on TB services with a lead CCG; or that some TB services are appropriately commissioned locally and that other TB services for DR-TB or more complex cases are centrally commissioned; alternatively that all TB services should be centrally commissioned.  

It was highlighted that there were pros and cons to each option. For example having everything centrally commissioned has the obvious appeal of being standardised and consistent, but there may be advantages to doing things differently as local decision making can improve TB services.

The NHSCB has set up a subgroup of the respiratory and infectious disease clinical reference groups, which have a responsibility for writing commissioning guidance and service specifications i.e. what should be in the contract that would be delivered nationally for the services, to look at how TB could be commissioned.

The commissioning and the management of TB services vary considerably around the country for a number of reasons. For example the epidemiology of TB varies from place to place, or areas where populations at higher risk of active TB spread over a very large geographical area without many major population centres, compared to London or Bradford and other cities with a very large migrant population.

However, the HPA highlighted - in Oral Evidence Session 2 - that ultimately it should not matter where you are geographically located as treatment for TB services should be to a very high standard across the country.

Public Health England

The formation and role of Public Health England is crucial. While the control of TB is highly complex and includes many clinical, public health and social aspects, evidence from developed countries demonstrates that a sustained reduction in TB incidence results primarily from improved public health measures.

Public Health England is ideally placed to provide leadership, ensuring that fragmentation of services are avoided, by making certain of a whole system view of the planning pathway, allowing for local
variations, and ensuring appropriate footprints for commission among CCG’s are appropriate according to need.

Large geographical commissioning footprints, integrated services and local TB plans are being recommended in key NHS and Department of Health documents: ‘A framework for collaborative commissioning between clinical commissioning groups’ (August 2012) and ‘Health protection and local government’ (September 2012). This should be supported and implemented.

**National strategy for tuberculosis**

Experts and leading TB organisations in the UK have called for a national strategy for tuberculosis. There are a number of reasons for this, including: 1) rates of TB, and now DR-TB, have been rising since the 1980’s 2) there has never been a national strategy to tackle rising rates of the disease beyond the CMO’s action plan developed almost a decade ago which has been ineffective 3) the changes in the health service, coming into effect in April 2013, offer the perfect opportunity for public health leadership and local engagement to reduce rates of the disease.

The Public Health Minister, Anna Soubry MP, acknowledged that TB is a growing problem and that the Department of Health is “exploring the effectiveness of an approach across health sectors for a national strategy on TB, while ensuring that we recognise the local variances. We need to improve in that area”. 51

**Recommendation**

- A comprehensive TB strategy, led by Public Health England, should be developed to seize the opportunity the changes under the Health and Social Care Act (2012) present to reduce rates and deaths from TB.

**Migration and travel**

The ease, availability and duration of travel, with large numbers of people travelling internationally, increases the likelihood of exposure to people with infectious TB and other airborne and droplet-borne diseases.

With an estimated 2.5 billion air passengers each year by 2015 52 and the fact that around one third of the world’s population have latent (dormant) TB infection, it is easy to see why the term ‘TB anywhere is TB everywhere’ is repeatedly used. Ultimately TB in the UK reflects the global reality. TB is one of the most common infectious diseases worldwide. 53

**Pre-entry screening policy**

The UK Border Agency announced in May 2012 that it is rolling out pre-entry screening for Active TB using a chest x-ray following a pilot scheme started in 2005, covering 15 countries, in line with countries like Australia, Canada, New Zealand and the US. 54

Migrants, from 82 countries with high incidence of TB, staying in the UK for six months or more, will be required to use the x-ray to obtain a certificate confirming that they are free from active tuberculosis before applying for a visa. The only exceptions are children under 11 years old, diplomats
and their families, returning residents, and holders of certificates of entitlement.

However, as noted by the Immigration Minister Damien Green MP when he announced the new policy, a third of the world is carrying [latent] tuberculosis and a chest x-ray will not detect latent TB. The majority of UK cases are likely as a result from the reactivation of latent TB infection in people who were born in high incidence areas outside the UK.

### Latent TB infection

Some experts have argued that the new pre-entry screening system will only be fully effective if combined with screening for latent TB infection (LTBI) in high risk new arrivals given that 74% of people with TB in 2011 were born outside the UK.

It is not currently known in the UK why some progress to the active form and others do not (up to 15% of adults with latent TB go on to develop active TB at some point in their lives and the risk in children may be much higher), although in people who have a weakened immune system (for example, if they are HIV positive), the chance of developing active TB within 5 years of infection is up to 50%. Detection of latent TB is therefore important in controlling the disease.

NICE guidelines highlight that healthcare professionals, including primary care staff, responsible for screening new entrants should maintain a coordinated programme to: detect latent TB and start treatment.

Dr Fergus Macbeth, Director of the Centre for Clinical Practice at NICE, also emphasized that it is important that strategies that are used to detect the disease before it has the opportunity to develop into active TB are as robust as possible and based on the best available evidence.

Studies have shown that screening for latent infection can be implemented cost-effectively at a level of incidence that identifies most immigrants with latent tuberculosis, thereby preventing substantial numbers of future cases of active tuberculosis. However, parts of the UK with the highest burden of TB are those doing the least screening for latent TB, the opposite of what should be the case, despite the guidelines from NICE on a national programme for LTBI.

To make a significant impact on TB rates in the UK it is clear the NICE guideline on nationally quality assured screening for LTBI should be implemented fully across the UK. In many ways this is essentially the bottom of the iceberg from which the majority of new cases arise.

### General Practitioners role and new entrants registration

When considering the challenges presented by infectious disease to the adult population, it is clear that there remains a vital role for medical practitioners in the early identification of infectious diseases like TB. This will require GPs to accurately identify those individuals at higher risk and act appropriately.

Medical practitioners need to give consideration to patients’ country of birth when evaluating their risk exposure; this will aid differential diagnosis of presenting symptoms such as tuberculosis, as well as blood-borne viruses including HCV, HBV and HIV.

Offering LTBI testing when a new entrant from a high burden TB country registers with a general practitioner (GP) is already carried out in the UK as part of the standard health check during registration. However, registration rates with GPs in new entrants to the UK are extremely low.

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**Box 6: Latent TB infection**

LTBI is where a patient is infected with Mycobacterium tuberculosis, but does not have active tuberculosis disease. Patients with latent tuberculosis are not infectious and it is estimated that one third of the world population has LTBI. The main risk is that approximately 10% of these people will go on to develop active TB at a later stage of their life.
Only a third of recent entrants to the UK registered with GPs in 2011, leading the HPA to call for targeted action to improve registration rates. The HPA team also highlighted that they could not identify why some groups were less likely to register, but did stress that solutions to the problem were needed.

**Stigma**

Any policy that targets specific communities has the potential to be interpreted as stigmatising. It has been argued that if a policy were to be developed, targeting LTBI screening and treatment amongst people at higher risk of the illness, it is vital that relevant TSO’s and affected communities are engaged in development and implementation to mitigate stigma where possible.

It is also essential, as highlighted in NICE guidelines, that treatment and care, and the information patients are given about LTBI, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

Many experts highlight that LTBI infection screening and treatment is just one element of many aspects of the TB care and control package, as it was in areas that achieved significant reductions in rates such as New York, and is not seen as the answer to rising rates of TB in the UK by itself.

It is important that LTBI screening is part of a broader TB awareness strategy to ensure all affected communities are able to engage and respond to tackling TB, increasing adherence of TB treatment and thus preventing spread of TB and drug-resistant strains.

The HPA and PHE are currently looking at ways to improve the process of screening patients and offer treatment for LTBI.

**Recommendation**

**Pre-entry active TB screening for those coming into the UK from countries with high TB burden for six months or more is a welcome step forward, but this policy needs to be accompanied by implementation of NICE guidelines on a coordinated programme for LTBI screening and treatment across the UK.**

**Recommendation**

**Discussions with NHS experts, affected communities, hard to reach groups and general practitioners on a targeted approach to increasing GP registration rates among new entrants should take place.**
Global tuberculosis

Access to diagnosis and treatment for DR-TB

Access to diagnosis and treatment for DR-TB is extremely poor. Globally only 60,000 of the estimated 440,000 new annual cases of DR-TB were reported to the WHO in 2011 – around 15%.

Some of these cases may be treated in the private sector,65 but given the high cost and limited availability of drugs, treatment is out of reach of many. Also, for those patients who do access treatment in the private sector they may not receive the correct drugs which can create an even more extreme form of the disease (XDR) which many have called ‘virtually untreatable’.66

Patients with MDR-TB must take a daily cocktail of drugs, as many as 20 pills a day, and in the early stages of treatment a daily painful injection. The side effects of such treatment range from persistent nausea to psychosis and total deafness. Some patients find the side effects too arduous to bear and interrupt or stop treatment altogether, which again can lead to XDR-TB developing.67

A patient centred treatment approach for TB and DR-TB is essential to ensure access for the most vulnerable and neglected of patients, such as: HIV co-infected (see box 7); prisoners; homeless etc. who often lack strong representation or advocacy to ensure that they can get access to the services required.68

A key component of case management which helps to ensure patients adhere to treatment, and avoids resistant strains emerging, is directly observed therapy (DOT). DOT is the most effective strategy for making sure patients take their medicines around the world, and means that a health care worker or other designated individual watches the patient swallow every dose of the prescribed drugs.69

There is no denying the scale of the challenge of access to diagnosis and treatment of DR-TB, but it is important to draw comparisons with other similar access problems that have faced TB control. For example, in 2004 only 3% of TB patients in Africa were tested for HIV. In 2011 that figure had jumped to 69%,70 which demonstrates that if appropriate action is taken dramatic results can be achieved.

Diagnosis

Controlling TB transmission and improving patient outcomes depends on rapid diagnosis and treatment completion. For TB diagnosis, the simplest and most common method is analysing sputum samples using a microscope.

Microscopy detects the most infectious cases, but is not a sensitive test and cannot discriminate between TB and DR-TB.1 Availability and affordability of Drug Sensitivity Testing (DST) is extremely
low, with only around 4% of new cases and just 6% of previously treated cases had access to DST,\textsuperscript{71} which is the primary reason why the number of people diagnosed with MDR-TB remains low.\textsuperscript{2}

**Rapid Diagnostics**

Newer rapid diagnostics, like GeneXpert, have been developed to diagnose TB. GeneXpert is a rapid molecular test that can diagnose TB and rifampicin resistance within 100 minutes instead of weeks, and the rapid roll-out of GeneXpert has been impressive.

Between its endorsement by the WHO in December 2010 and the end of June 2012, 1.1 million tests had been purchased by 67 low- and middle-income countries; South Africa (37% of purchased tests) is the leading adopter. Studies from SA have shown a potential increase of 69%-71% in the number of MDR-TB cases diagnosed\textsuperscript{72} as a result, and a 41% price reduction of cartridges (to less than US$10 per test) in 2012 may accelerate uptake.

However, concerns have been raised about affordability of the cartridges and also the machine (US$17,000 per unit\textsuperscript{73}) in high burden developing countries,\textsuperscript{74} despite the recent price reduction. There have been calls for increased efforts to continue the development of a point of care (POC) test, that run in parallel to rolling out rapid diagnostics. It is argued that increasing detection rates now with new rapid diagnostics will trigger an initial scale-up in treatment. This in turn will ensure that treatment systems are not overwhelmed with the introduction of an even more effective POC TB test.\textsuperscript{75}

New diagnostics will not completely replace existing ones in the near term, as these rapid tests still

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**Box 8: Case Study: Timor Leste** (provided by Target Tuberculosis)

Isabelle Pires is 31 years old and lives in Dili, Timor-Leste. She is married with 2 young children. She lives with her husband, children and 3 other family members.

Isabelle became ill with TB in 2006. Two failed courses of treatment left Isabelle extremely weak and continuing to cough up blood. At this point the health centre suspected drug-resistance and sent a sample of her sputum to Australia to undergo drug sensitivity testing. The results indicated that she had MDR-TB.

Isabelle was fortunate that MDR-TB treatment is available in Timor-Leste and was referred to Target TB’s local partner organisation, Klibur Domín, to start her treatment, which she did in June 2010.

At Klibur Domín Isabelle had to take 16 tablets a day as well as a daily injection. She responded well to the treatment and was able to return home to her family and continued treatment with the support of her local health clinic. Isabelle was also able to return to her small business, selling clothes at the market. To reduce any risk of infection, Isabelle wore a mask when in close contact with her children and other family members.

Today Isabelle has been on treatment for 1 year 2 months, and only has 10 months to go to finish. She is feeling well and although struggles to put weight on, is eating well. After 8 months of the intensive phase of the treatment Isabelle’s test results indicated that she had become non-infectious which has reduced the pill burden slightly. Each day she travels to her local health centre by mini-bus to take the tablets in front of health staff there.

Isabelle feels very positive about her future. If she completes the treatment in full, she will be the first MDR-TB patient from Timor-Leste to be cured. At least 10 MDR-TB cases have been identified in the country over the past 2-3 years, but many have died or defaulted from treatment.
require a quality-assured microscopy network to perform sputum smears at two months and at the end of treatment in order to determine cure and failure rates.\textsuperscript{76}

In the absence of a point of care diagnostic test, which according to the Stop TB Partnership is at least two years away from development, rapid diagnostic testing - including GeneXpert – should be scaled up.\textsuperscript{77}

\textbf{Access to treatment}

DR-TB treatment is available to an appallingly low proportion of patients due to a number of factors. Treating DR-TB is complicated from a programmatic perspective: treatment is individualised, tailored according to which drugs a patient is resistant to. It is long and taxing, requiring people to take a course of antibiotics for up to two years and endure often intolerable side effects. Partly as a result of the complexities of treatment, programmes must devote considerable resources to adherence counselling, the management of side effects and psychosocial care, all of which place large demands on human resources. In some countries, the lack of political will to appropriately address these additional aspects of treating DR-TB is a major barrier.

In response to a growing need for DR-TB treatment - and to prevent further drug resistance from developing through improper use of DR-TB drugs - the WHO, together with MSF and other partners, created the ‘Green Light Committee’ Initiative (GLC) in 2000. The core function of the GLC has been to provide technical review of proposed DR-TB treatment projects, and ‘green-light’ them if they meet certain criteria. Approved projects then get access to quality-assured drugs at reduced prices - since 2002, these have been procured through the Global Drug Facility (GDF).\textsuperscript{78}

The GDF, hosted by the Stop TB Partnership, works to expand access to and availability of high-quality anti-TB drugs and has been able to make significant impact on global TB control. Several main areas of impact include: 1) greatly improving availability of quality medicines; 2) providing free medicine grants to needy countries; 3) procuring medicines for countries that still lack capacity to do their own procurements; and 4) providing technical assistance in drug management.\textsuperscript{79}

According to UNITAID (impact 2011 key performance indicators) 17 suppliers are now available in the market for existing medicines which has improved sustainability of anti-TB drug supply. This is critical since the lack of availability of one or more anti-TB drugs can affect a patient’s regimen and stockouts, as explained earlier, can lead to further drug resistance or in the worst case, patient death.

The GDF has reduced the price of several second-line drugs it supplies for the treatment of DR-TB by up to 26% compared to 2011 prices, resulting in a decrease in overall cost of treatment. This led the GDF manager, Joel Keravec, to state that “the availability of drugs is not the limiting factor for scaling up MDR-TB programmes”, but there needs to be more coordination among partners in the fight against MDR-TB to strengthen both the supply and demand sides of the market, which is still quite fragile.\textsuperscript{72}

\textbf{What is the cost of second line drugs for DR-TB?}

The price of DR-TB treatment varies considerably, as treatment must be individualised according to a patient’s drug resistance profile. Drugs procured through the GLC/GDF cost between US$ 4,400 and almost US$ 9,000 per patient for a standard 18-24 month treatment course.\textsuperscript{78} For drugs purchased outside of the GLC/GDF, prices may be even higher. In contrast, first-line TB treatment costs US$ 19 per patient for a six-month treatment course.\textsuperscript{80} Securing greater demand (i.e. diagnosing more patients) is therefore critical to bringing down prices of second-line drugs.
Are fake drugs contributing to the growing rates of DR-TB?
Fake and poorly made antibiotics are being widely used to treat TB. A study published in the International Journal of Tuberculosis and Lung Disease in March 2013 tested samples (713) of anti-TB drugs, in 19 pharmacies and 19 cities in high burden countries. It found that around 10% failed basic quality testing. The failure rate was 16.6% in Africa, 10.1% in India, and 3.9% in other middle-income countries.

The authors of the report have called for large-scale studies of drug quality in all markets as substandard and falsified drugs are readily available in the private marketplace and highly likely to be contributing to drug resistance in low- and middle-income countries.

What is the size of the market for second line drugs?
According to MSFs report: DR-TB Drugs Under the Microscope (2012) for most DR-TB drugs the medicines were developed so long ago that patents, which typically act to prevent competition and thereby keep prices higher for longer, have long run out, and do not act as a barrier.

Current high prices for DR-TB drugs are rather a reflection of the fact that current market demand is low, due to limited capacity to diagnose and treat DR-TB, which does not provide a sufficient incentive to manufacturers.

The global DR-TB market was estimated to be worth US$ 300 million in 2010, with only US$ 125 million procured through the public sector. Of this, only US$ 40 million was channelled through the Global Drug Facility. The market has been growing by approximately 5% per year, with India and China taking the largest share, at 63% and 17%, respectively.

It is important to again highlight that only around 10% of the estimated 650,000 prevalent cases of MDR-TB are diagnosed and treated every year, indicating that the true market size is actually significantly larger.

Is it ethically acceptable to offer drug susceptibility testing when treatments for drug-resistant strains are not available?
Governments have an ethical responsibility to provide free and universal access to TB diagnostic and treatment services. This obligation is grounded in their duty to fulfil the human right to health. Not only does TB treatment significantly improve the health condition of individuals, it also benefits the broader community by stopping the spread of a highly infectious disease.

This duty extends to the provision of DR-TB services. While countries are in the process of scaling up treatment, providing testing is a legitimate interim measure to estimate the magnitude of the problem and guide decisions about how best to treat DR-TB patients.

This is echoed by the WHO publication Guidance on ethics of tuberculosis prevention, care and control which highlights that while countries are in the process of scaling up treatment, the use of drug susceptibility testing can be appropriate as an interim measure even when no second- or third-line drug treatment is available, or when the only available treatment is substandard. Among other benefits, a diagnosis even in the absence of treatment can:

- Provide evidence of a high prevalence of DR-TB in a particular country or region, which can be used to promote advocacy to improve management capacity;
- Ensure that individuals with DR-TB are not inappropriately treated with regular TB drugs, which can harm both the patient and public health by increasing drug resistance;
- Guide decisions about segregating TB patients being cared for in a closed environment;
- Help individuals make life plans, diminish the impact of the disease on family members, and inform important behaviour regarding infection control.
However, countries that implement diagnostic testing in the absence of treatment should do so only as a temporary measure, and should establish a timetable for when treatment for DR-TB will be made available.

Ultimately, both an increased focus on improving the diagnostic and treatment capacities of the most affected health systems, and continued efforts to monitor and forecast the number of patients diagnosed through existing and new technologies and enrolled in the public and private sectors, is required. Communication of this data and trends to manufacturers will certainly help to further consolidate the supply of quality-assured TB drugs for populations in need\textsuperscript{[84]} and facilitate cost reductions second line anti-TB drugs.

**The role of the private sector**

The private sector is playing an increasing role in the diagnosis and treatment of TB and DR-TB, particularly in Asia - where more than 50\% of TB patients might seek care only in the private sector because many believe they will receive poor medical care in the public-run sector\textsuperscript{[85]} - and also in large urban centres in Africa.

A recent market size assessment conducted in India, which has the largest number of TB patients (2.2 million of the world’s 8.7 million) showed that about US$ 222 million is spent on TB diagnosis in India every year, with the private sector accounting for over 60\% of this expenditure – see figure 5.

**Figure 5: Diagnosis and treatment in the Indian private and public sectors**

![Figure 5: Diagnosis and treatment in the Indian private and public sectors](image)

India’s own strategic plan for TB calls for improving medical care in the private sector, in addition to scaling up testing and treatment of drug resistance nationwide, as demonstrated by a recent Wall Street Journal article highlighting the Indian Government’s success in achieving a cost reduction in new rapid diagnostic test for MDR-TB in the private sector.\textsuperscript{[86]}

Traditionally MDR-TB programmes have focussed on donor and government structures, but there are increasing opportunities to strengthen linkages between the public and private sectors, often referred to as the public private mix (PPM), especially in Asia and Africa.\textsuperscript{[77]}

A demonstration of this approach was highlighted in oral evidence when the PPM approach utilized in Karachi (funded by TB REACH) was shown to have doubled TB case notification in a population of 2 million people.\textsuperscript{[77]}

This was achieved by having community laypersons screening those visiting private GP clinics for cough symptoms and then having those people with symptoms x-rayed or tested. By simply engaging the private sector for screening the project provided the patients identified with free drugs through the public programme.

In addition, a written submission to the APPG inquiry from Kenya Medical Research Institute points
out that only a handful of non-state providers in TB endemic countries are engaged with the national TB programme. They argue that using PPM methods and innovative approaches including the use of internet and mobile phone technologies, the proportion of non-state providers engaged by the NTP should be able to expand to become large enough to play their part in reducing rising rates of DR-TB.86

However, they do caution that in many parts of the world DR-TB is generated by poorly knowledgeable private health care providers who are not engaged with the TB control programmes of Ministries of Health.

The importance of linking with private sector approaches was stressed in both written and oral evidence received - given that in many countries the government stops functioning at 1:00 pm while the private sector opens at 2:00 pm and keeps working until 11pm or midnight.77

Importance of strong health systems

In addition, health services must be strengthened in order to deliver a more holistic approach to delivering TB care and treatment. In high burden countries with high levels of TB and HIV clinicians and program managers are increasingly confronted by drug-resistant tuberculosis in people living with HIV and recent studies provide evidence of the difficulty of MDR-TB treatment in high HIV-prevalence settings.

In Lesotho, an innovative community-based treatment model that involved social and nutritional support, twice-daily directly observed treatment and early use of second-line TB drugs was successful in reducing mortality of MDR-TB patients.87 Further research is urgently needed to improve MDR-TB treatment outcomes in high HIV-prevalence settings.88

Recommendation

There is capacity to mobilize increased funding from domestic sources in low and middle-income countries, especially in Brazil, the Russian Federation, India, China and South Africa (BRICS) that already rely entirely or mostly on national contributions. Increased domestic funding in BRICS will be especially critical for scaling up the diagnosis and treatment of MDR-TB.

Key reason for recommendation

About 60% of cases of DR-TB occur in Brazil, China, India, the Russian Federation and South Africa (“BRICS”, middle income countries) and it is crucial that increased resources from these countries are focused on improving access to diagnosis and treatment of DR-TB, as is already being implemented in countries like South Africa.

Recommendation

The private sector is growing in many low and middle-income countries and is already diagnosing and treating large numbers of patients. It will be essential, moving forward, that the public and private sectors are appropriately coordinated, though the PPM model and joined up ensuring access to reliable diagnosis and quality approved drugs.

Key reason for recommendation

In some countries, for example in India and Pakistan, the government (supported by the WHO) runs a national program to test and treat TB free of charge. But about half of TB patients don’t use the government program because many believe they will receive poor medical care in the public-run sector. As a result many TB patients instead seek care from private medical providers, who often offer cheap inaccurate tests and inadequate treatments where patients fail to complete a course of first-line drugs, fuelling the spread of drug-resistant forms of the disease.
R&D into new tools

Importance of new knowledge and technology

The introduction of more effective tools to prevent, treat and diagnose TB could bring a step change in efforts to control the disease around the world. There is no way to eradicate TB without new tools, for example without an effective vaccine able to treat latent TB. Developing new diagnostic tools and operational research are of particular importance because of the low rates of diagnosis, and the need to develop better ways to deliver care in the field.83

The UK Government highlight that developing new drugs, diagnostic tests and vaccines is inherently high risk and every product can fail at any point along a lengthy development and stringent approval process. While public health professionals will always indicate that prevention is better than cure, those patients who do become infected cannot be simply left to their fate – therefore there is a need to keep pushing on several fronts to develop new/better treatment drugs, along with vaccines and diagnostic tests. This is why most development agencies, including DFID, support the development of a portfolio of prevention and treatment products, working closely with other funders and product developers.90

An estimated US$ 2bn is needed each year to advance the development of new drugs, diagnostics and vaccines for TB and conduct other essential research to improve treatment and care. However, financing slowed in 2010, reaching only one-third of this estimated target.1

The fact that TB impacts most heavily on the poorest is perhaps one of the reasons that commercial funding is often difficult to secure, and yet UK pharmaceutical companies and universities are vital stakeholders who are involved in these research efforts and could benefit from the search and eventual development of new tools in the fight against TB.

There is therefore a role for UK Government departments other than DFID, for example the Department for Business, Innovation and Skills, to play a role in supporting TB research due the potential return on investment to UK academic institutions and businesses.

Diagnostics

Diagnosis rates for TB are a major concern. While all areas of R&D into new technologies to diagnose, treat and prevent TB are not reaching the levels of funding required, TB diagnostics suffers the largest relative funding gap: US$ 48 million represents only 14% of the Global Plan’s target of US$ 340 million per year, compared with 31% of the funding target met for new anti-TB drugs and 20% for new TB vaccines.

Despite this gap and after decades of stagnation, accelerated development of new TB diagnostics in the past decade presents real hope that rapid diagnosis of TB and MDR-TB can become a reality, thus removing longstanding barriers to TB care and control.2

In 2011, case detection was estimated at 66% globally and only 19% of the estimated MDR-TB cases are notified each year.2 Delayed diagnosis of TB has detrimental consequences for the prognosis of the patient and for onward transmission of both drug-sensitive and drug-resistant TB.

There have been advances in diagnostics in recent years, most notably the WHO endorsed GeneXpert system,91 but they have often not been designed to help those most in need in resource poor settings. GeneXpert, for example, needs uninterrupted electrical power for the duration of the test (100 minutes) or the test is ruined - new samples must be obtained for the test to be carried out again.

83The MVA85A single dose booster vaccine candidate was originally developed at the University of Oxford
The lack of a cheap, effective test which can be easily administered at the point of care is a major obstacle to improving diagnosis. This exacerbates social and financial barriers to people seeking diagnosis, such as costs associated with travelling to a clinic. It has been estimated that a 100% accurate single visit diagnostic test could save almost half (700,000) of the 1.4 million lives lost to TB each year.92

However, the Stop TB Partnership and WHO highlight that a point of care diagnostic test will not be available in the next two years at the very earliest, and efforts should be made to scale up new technologies including GeneXpert and DST capacities.93 94

Drugs
The current TB drug regimen, developed more than 40 years ago, is inadequate to address the ongoing challenges of treatment. Shorter, simpler treatments would reduce the burden on individuals and the health system, and should result in more people successfully completing their treatment. In turn, less resistant strains of the disease should arise.

On average the latest figures (2009) on treatment success rates (cure or completed treatment) for MDR-TB globally were only 48%.95 Development of new drugs would ideally improve treatment regimens in terms of duration, tolerability (fewer and less terrible side effects) and effectiveness, as well as increase the options available for those in whom current standard treatment regimens are ineffective or inappropriate.

The TB drug pipeline has seen encouraging progress in recent years. There are currently ten new or re-purposed compounds in the clinical development stage, (four repurposed, six new drugs and three new classes of drugs). However, MSF highlight that progress is painfully slow and improved access to shorter regimens, especially where the burden is greatest, should be a major priority.96

Vaccines
There is an urgent need for a modern, safe and effective vaccine that would prevent all forms of TB, including the drug-resistant strains, in all age groups and among people with HIV. The Bacille Calmette-Guérin (BCG) vaccine, created in 1921, is the only existing vaccine against TB.

Unfortunately, it is only partially effective. It provides some protection against severe forms of paediatric TB, but is unreliable against adult TB of the lungs, which accounts for most of the disease burden worldwide.7

No disease can be eradicated without a vaccine, and vaccines are the only long-term, cost-effective solution for addressing TB. The single most cost-effective tool against drug-resistant strains of tuberculosis would be a new vaccine that prevents TB of the lungs in adolescents and adults, who are at highest risk.

There has been significant progress in the field of TB vaccine R&D over the past decade and new effective vaccines to control TB are within reach. However, an intensified and expanded cross-sectoral effort and funding support is needed to ensure that researchers can build on the current momentum and accelerate the conduct of clinical trials required for the licensure of new TB vaccines. With sufficient resources and positive results from clinical trials, a viable TB vaccine could be available as early as 2020 (only 99 years after the development of BCG).

The latest trial results for one of the most advanced vaccines, known as MVA85A, failed to increase protection in babies who had already received the BCG. While it was considered a setback, many highlighted the achievement and opportunities to learn from the results for other vaccine candidates, particularly given that it was the first large-scale study in infants since the BCG vaccine over 90 years ago. It was also highlighted that it was not a terminal prognosis for MVA85A, or for any of the other tuberculosis vaccines in development, and it was stressed that now is a key moment to invest in TB vaccine research.97
The UK Government is a leader and a key partner in the development of new TB vaccines. Continued UK Government support is essential to stimulate R&D and the UK Government can also use its leadership and influence to bring other funders and supporters to the table.98

UK Research

UK-based researchers at an extensive range of universities across the country are leaders in the field of TB research. Supporting their efforts will not only contribute to global efforts to control TB, but will also build on the UK’s science base in an area where researchers have world class expertise but receive comparatively little funding. As noted elsewhere in this report, support for TB R&D need not only come from DFID due to benefits generated in the UK by this R&D.

What support has DFID provided, and will provide in the future, to help develop new tools?

According to written evidence submitted to the APPG, DFID is supporting a range of research programmes to promote the development of new diagnostics, drugs and vaccines for tuberculosis (TB): These include: the Foundation for Innovative New Diagnostics (FIND), the Global Alliance for TB Drugs, and the Aeras Global TB Vaccine Foundation: Funding amounts for the last five years are provided in table 2 below (all figures are in £).

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DFID also supports other programmes that include TB research within their portfolio, for instance the WHO Special Research Programme in Tropical Disease Research (TDR), Research Programme Consortia on Delivering Effective Health Services, and the UK Medical Research Council. However, it is not possible to separate out the funding amounts for TB-specific research in these programmes.

DFID issued an open call for bids for PDPs in 2012: 17 partnerships were invited to submit full proposals, for up to five years of funding, after passing an initial rigorous sift. All 17 full proposals are now undergoing an external peer review process and Ministers will then consider Business Cases for funding. Some TB products are included among the 17 proposals under consideration. At this time, it is not possible to say whether any TB products will be funded, or how much new funding (if any) will be made available for TB products.99

Recommendation

DFID has a strong record supporting investment in TB R&D, as one of the leading funders into new technologies to tackle TB in the world, and its holistic approach supporting investment in research to find new diagnostic tools, drugs and vaccines, as well as operational research should be at least maintained and ideally scaled up. The Department for Business, Innovation and Skills, also has a role to play supporting TB R&D due the potential return on investment to UK academic institutions and businesses.

Key reason for recommendation

Any new technologies, such as a reduction in the drug regimen required to cure TB, are likely to have a direct positive impact on reducing rates of the disease in the UK, but due to persistent market failure and the recent success of many PDP initiatives in addressing this failure we have some new tools and many more in the pipeline.
What countries have been successful in reversing rates of DR-TB?

Unfortunately there are few examples, if any, of high burden settings that have managed to reverse rising DR-TB incidence. In countries where there are low numbers of cases of MDR-TB (100 annually at most) universal access to treatment, focused interventions and rapid expenditure of large amounts of resources has led to a lower number of cases. This has been demonstrated in the USA and special administrative region Hong-Kong (China). Other countries like Estonia, Latvia and Israel have shown progress reversing the incidence of DR-TB.

MSF have highlighted that to impact the DR-TB epidemic there must be a movement away from specialised programmes that treat hundreds of cases to those capable of treating thousands. Given the estimated 650,000 prevalent cases of DR-TB globally, better models of care are required to scale up treatment appropriately, in a manner analogous to the scale up of antiretroviral treatment for HIV.

One example of scale up is in Kenya, which has had rising DR-TB cases and has seen a seven fold increase in the number of patients put on treatment from 2007, thanks mainly to a greater allocation to TB control from the GFATM, UNTAID and the development of improved diagnostic tools. A major contributory factor was also increased political commitment in TB control within the Government of Kenya.

What are the key components to the successful reduction of DR-TB?

One of the key components emphasised in all evidence received during the APPG inquiry was political commitment.

Clear and sustained political commitment by national governments is crucial if basic DOTS (see box 7) and the Stop TB Strategy are to be effectively implemented.

Political commitment is needed to foster national and international partnerships, which should be linked to long-term strategic action plans prepared by national tuberculosis control programmes (NTPs). Strategic action plans should address technical and financial requirements and promote accountability for results at all levels of the health system; they should include TB-related and other relevant indicators, and – where appropriate – political commitment should be backed up by national legislation. Local partnerships with many potential contributors will help improve TB care in terms of access, equity and quality.

While making recommendations for civil society actors and others in high-burden countries is outside of the scope of this report, the APPG recognises the role of local civil society groups both in creating political will to tackle TB in-country and for their practical role in the response. In this we echo MSF in their report An evaluation of drug-resistant TB treatment scale-up (2011), which states:

DOTS is the internationally-recommended tuberculosis control strategy which remains at the heart of the Stop TB Strategy.

The five pillars of programmatic management of drug-resistant tuberculosis, built on those of the DOTS Strategy, are:

• Political commitment with increased and sustained financing
• Case detection through quality-assured bacteriology
• Standardized treatment, with supervision and patient support
• An effective drug supply and management system
• Monitoring and evaluation system, and impact measurement

DOTS impact
Since 1995, over 51 million people have been successfully treated and an estimated 20 million lives saved through use of DOTS and the Stop TB Strategy recommended by WHO and described below.
“Civil society groups have an important role to play in the monitoring of global efforts to scale up DR-TB diagnosis and treatment. These groups are particularly well-suited to monitor both access to and quality of treatment at the country level, but should also be involved in the evaluation of international support mechanisms and donor commitments. Some groups are directly involved in providing and supporting treatment and are thus important part of the response to the epidemic.”

Financing TB care and control

Projections of potential funding from domestic sources and funding requirements specified in the Global Plan

The Global Plan to Stop TB 2011–2015 was published by the Stop TB Partnership in 2010 and sets out what needs to be done to achieve the global targets for TB control set for 2015 in 149 low- and middle-income countries, with the associated funding requirements.

From 2013 to 2015, up to US$ 8 billion per year is required for full implementation of TB care and control in low- and middle-income countries. In 2015, about US$ 5 billion is needed for the diagnosis and treatment of TB, US$ 2 billion for diagnosis and treatment of MDR-TB and almost US$ 1 billion for TB/HIV interventions.

There is capacity to mobilize increased funding from domestic sources in low and middle-income countries, especially in Brazil, the Russian Federation, India, China and South Africa (BRICS) that already rely entirely or mostly on national contributions. Increased domestic funding in BRICS will be especially critical for scaling up the diagnosis and treatment of MDR-TB.

International donor funding of up to US$ 1 billion per year is needed for low and middle-income countries 2013–2015 to close funding gaps. This is double the amount of US$ 0.5 billion expected in 2013 but still much less than the amounts being mobilized for malaria (US$ 2.0 billion in 2010) and HIV (US$ 6.9 billion in 2010).

International donor funding is especially critical to safeguard recent gains in TB care and control and enable further progress in low-income countries and in the group of 17 high burden counties outside BRICS. In these country groups, it provides >60% and about one third of total funding, respectively.

Of the international donor funding expected by national TB control programmes in 2013, almost 90% is from the Global Fund. In the absence of any other major streams of international donor funding for TB, the Global Fund has a crucial role in sustaining and ensuring further progress in TB care and control worldwide.

TB and DR-TB funding gaps in 118 countries eligible for Global Fund support

The WHO and the Global Fund to Fight AIDS, TB and Malaria estimate that there is an annual anticipated demand for at least US$ 1.6 billion in international support to bridge the funding gap over 2014-2016, in 118 low and middle income countries which are eligible for financing from the Global Fund.

The total resource requirements to combat TB and MDR-TB for these countries equals US$ 4.8 billion each year and the WHO estimates that if the funding gap is filled it could enable full treatment for 17 million TB and MDR-TB patients and save six million lives over the next three years.

Based on current spending patterns the biggest funding gaps are projected for MDR-TB treatment. If fully funded, by 2016 over 90% of TB patients estimated to have MDR-TB will be detected and provided treatment in seven high-MDR-TB burden countries: India, Indonesia, Kazakhstan, Pakistan, Philippines, Ukraine and South Africa.”
Role of the World Health Organisation
Stop TB Department

The WHO Stop TB Department (STB Dept) has the unique role of providing assured global leadership in the areas of policy making, introduction of innovations such as new rapid diagnostics, standard settings, global monitoring and evaluation, and technical assistance coordination linked to needs by countries being funded through mechanisms like the GFATM.

In the last year the STB Dept has embarked on an ambitious plan to advocate strongly for research for elimination of TB, defining the needs and the strategies, as well as on an initiative targeting rational introduction of new drugs and future vaccines into policy and practice in countries.

This is work that the STB Dept has undertaken successfully for years, as documented by the progressive introduction of DOTS and, later, the WHO’s Stop TB Strategy into virtually all countries worldwide. The outcome of this work has been estimated to have saved 20 million lives and cured 51 million people during the period 1995-2011.103

Moving forward the STB Dept will be working to further strengthen agenda setting for research; the introduction of system innovations and new diagnostics & drugs into affected countries; the increased use of mHealth technology to improve surveillance and care; the measurement of impact of TB control interventions in order to define progress towards MDGs and other international targets; and the promotion of community and non-state sector engagement into TB care and control work.

In view of the fundamental role WHO plays in making policies for TB control, introducing innovations that are evidence-based, monitoring the evolution of the epidemic and the impact of control efforts in collaboration with the Global Fund, and coordinating technical support to countries through collaboration continued support from the UK Government, and governments across the world, is essential to strengthen these key functions making it possible to effectively transform policies into practices in countries.

The UK Government’s response to global tuberculosis

According to the DFID website the UK Government remain committed to helping to achieve the goal of the Global Plan to Stop TB 2011-2015 to halve deaths and illness of TB by 2015, compared to 1990 levels and will also contribute to the UNAIDS and Stop TB Partnership’s goal of reducing TB deaths among people living with HIV by half by 2015.

The most recent DFID policy paper produced on tuberculosis was eight years ago in 2005, entitled ‘The challenge of TB and malaria control: a DFID practice paper’. The paper highlighted that DR-TB and HIV-TB co-infection are increasing problems, particularly in Eastern Europe and countries of the former Soviet Union for DR-TB, and that a core intervention remains support to strengthen health systems.


Written submissions to the APPG highlight that whilst it is acknowledged that DFID gives support through multilateral funding and a combined HIV/TB strategy, there is no stand-alone strategy for
tuberculosis and MSF have stated that there is “no specific evidence of commitment to this disease”. They stress that this is of particular concern at a time when the full extent of the MDR-TB epidemic is just starting to be realized.

While DFID do point to their support to achieve the Global Plan to Stop TB goals, it is unclear what specific targets have been set by the UK Government to address the growing threat of DR-TB in low- and middle-income countries.

DFID bilateral and multilateral support for TB control

Bilateral

DFID supports TB control through a variety of bilateral channels including projects and programmes at the country level and strengthening health systems in partner countries to deliver tuberculosis outcomes. DFID cannot precisely disaggregate DFID expenditure for tuberculosis control from bilateral channels other than direct projects and programmes. Figures for direct spend on tuberculosis are reproduced as follows.104

Table 3: DFID direct spend on TB

<table>
<thead>
<tr>
<th></th>
<th>2008-9</th>
<th>2009-10</th>
<th>2010-11</th>
<th>2011-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burma</td>
<td>700</td>
<td>1,536</td>
<td>2,000</td>
<td>243</td>
</tr>
<tr>
<td>China</td>
<td>2,888</td>
<td>4,414</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>India</td>
<td>4,178</td>
<td>8,188</td>
<td>750</td>
<td>-</td>
</tr>
<tr>
<td>Indonesia</td>
<td>400</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>25</td>
<td>175</td>
<td>98</td>
<td>200</td>
</tr>
<tr>
<td>Pakistan</td>
<td>1,805</td>
<td>37</td>
<td>92</td>
<td>33</td>
</tr>
<tr>
<td>Non specific</td>
<td>11,003</td>
<td>18,696</td>
<td>42,720</td>
<td>8,989</td>
</tr>
<tr>
<td>Total bilateral</td>
<td>21,020</td>
<td>33,048</td>
<td>45,661</td>
<td>9,465</td>
</tr>
</tbody>
</table>

There are concerns that DFID direct support to disease specific programmes is reducing, but DFID argue that their support is more than offset by giving more comprehensive support through health system strengthening.90 The importance of strong health systems was cited repeatedly in both written and oral evidence received in the response to TB, particularly to ensure appropriate management of TB cases to avoid resistance. However, the threat that DR-TB poses requires some specific interventions to provide diagnosis and management of cases.71

Multilateral

Much of DFID’s funding in relation to TB is directed through the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), which is the largest single provider of international funds to fight TB. Aside from the Global Fund, DFID also provide finance towards a number of organisations and projects relating to TB, including:

- UNITAID – to scale up access to treatment for HIV/Aids, Malaria and Tuberculosis for poor people by funding programmes that (often through bulk international procurement and other market shaping activities) lower the price of quality drugs and diagnostics and accelerating the pace at which they are made available.
- Improving the impact of the UK’s TB-related investments (through the Stop TB Partnership) – to help foster greater collaboration, cohesion and integration within the global tuberculosis control movement and as a result improve prioritisation and the efficiency and effectiveness of the global response.
The UK Government is also a major supporter of research into TB and HIV, providing long-term predictable financing for technologies and will continue to support research to develop more effective treatment to tackle TB and HIV/ TB.105

**DFID Multilateral funding: Global Fund to Fight AIDS, Tuberculosis and Malaria**

GFATM was created, in 2002, to dramatically increase resources to fight three of the world’s most devastating diseases, and to direct those resources to areas of greatest need. Soon after its founding, the Global Fund became the main multilateral funder for all three diseases, alongside PEPFAR (for HIV/AIDS).

**The Global Fund Impact**

Since 2002 The Global Fund has invested US$ 2.9 billion to support TB programs in 117 countries, detecting and treating 9.7 million cases of tuberculosis,106 and saving over 8.7 million lives through interventions to address all three diseases.107 Through the support of the UK and other donor governments to the GFATM, its’ programmes are achieving real and measurable impact.

Of the US$ 0.5 billion international donor funding for TB control programmes in 2013 the overwhelming majority (almost 90%) comes from the Global Fund. In the absence of any other major streams of international donor funding for TB, the Global Fund has a crucial role in sustaining and ensuring further progress in TB care and control worldwide.2

Of the 27 high MD R-TB countries in the world, 20 have received Global Fund support and a cumulative of 64,000 MD R-TB cases were treated in these countries since 2002. Among these 22,785 were from Eastern Europe and Central Asia. The Global Fund accounts for majority of international financing on MD R-TB in low and middle-income countries.

According to the Global Fund, TB grants - especially in high DR-TB countries - are being reprogrammed to prioritize investments to scale-up MD R-TB responses. However, the funding gap in the response is significant and additional funding for the Global Fund will be critical to scale up diagnosis and treatment of TB and DR-TB.46

This was demonstrated during Oral Evidence session 4 when Dr Amar Kahn, Chair Stop TB Working Group on MDR-TB, stated:

“Funding globally is inadequate relative to the global threat, and certainly for drug-resistant TB. The Global Fund is a life line for our patients, for my patients, the ones that we treat every day in Pakistan, Tajikistan, and several countries we’re working in. We need those drugs, we need the global fund to exist to provide support to governments, and to provide us the drugs and everything else to get these programmes out to our patients.”

This was reiterated in numerous submissions to the inquiry. For example, the one from the Kenya AIDS NGOs Consortium (KANCO) highlighted that the successes in TB control in Kenya can largely be attributed to support from GFATM. Out of the 284 MDR-TB cases in Kenya, 185 patients have been supported through the Global Fund entirely.

Kenya is simply unable to support the treatment of MDR-TB without the assistance of the Global Fund. It is true to say that the situation of MDR-TB in Kenya would be grave without the presence of the Fund.101

In addition to the role the Global Fund plays in low-income countries it is also playing a critical role in many middle-income Eastern European countries in financing DR-TB programmes.88 However, with many of these grants due to finish in 2014 and given significant changes within the GFATM financing criteria to deal with the recent shortage of available resources, this means that many high burden MDR-TB countries in Eastern Europe will no longer qualify for the levels of funding previously available. This dramatically increases the risk of development and spread of drug resistance in the region unless national governments can fill the gap.
What percentage of Global Fund resources go to TB?

Historically tuberculosis has received the smallest percentage of funding (16%) allocated by the Global Fund to the three diseases, with both HIV (52%) and Malaria (32%) receiving considerably higher allocations. Countries previously submitted proposals to the GFATM and all ‘good’ proposals (as decided by the Global Funds rigorous Technical Review Panel) were funded.

However, due to an overall lack of funding, the new funding model has been forced to limit funds available. The Stop TB Partnership has been saying for some time that even the historical 16% share for TB did not provide enough resources to properly fight the disease. This view was supported by written evidence provided by MSF which highlighted that “donor support currently does not reflect the extent of the problem”.

Table 4: Disease split – Projected funding for 2013–2014

<table>
<thead>
<tr>
<th>Disease</th>
<th>Existing communities ($10.3 billion)</th>
<th>Uncommitted funds for transition ($1.9 billion)</th>
<th>Total ($12.2 billion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>55%</td>
<td>54%</td>
<td>55%</td>
</tr>
<tr>
<td>TB</td>
<td>19%</td>
<td>11%</td>
<td>18%</td>
</tr>
<tr>
<td>Malaria</td>
<td>26%</td>
<td>34%</td>
<td>27%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

The GFATM Executive Director, Dr Mark Dybul, acknowledged that the split for all projected funding for 2013–2014 does not fully align with the historic split, but said the Secretariat’s hands were tied by the rules set out by the Board.

However, Dr Dybul did provide assurances that 11% was an aberration due to unique factors that are rooted in the overall lack of resources available to the GFATM at this time. He highlighted the need for a full, successful replenishment to allow the disease split to move back to more stable levels.

Global Fund reforms

In response to over-sensationalised reporting of minor corruption amongst a small number of Global Fund grants that surfaced in early 2011, the Global Fund commissioned the ‘Report of the High Level Independent Review Panel on Fiduciary Controls and Oversight Mechanisms’. The report recognised the overall good and essential work of the Fund but found some weaknesses across its systems and procedures. In response, the Fund’s Executive Board embarked upon a transformation process to improve risk management and strengthen its controls still further, as well as reform the Funds overall management and business model.

The International Development Select Committee (IDC) carried out an inquiry into the GFATM in 2012 and was impressed by the good progress in reforming its management structures and monitoring of financial risk, under the guidance of Simon Bland (Chair of the Board and Senior DFID Civil Servant).

Reflecting on the progress of reforms Mr Bland stated, in November 2012:

The Global Fund is now in robust health after enacting major changes in the way it does business. Simply put, 2011 was the year that the Fund came to realize it had to make serious changes and 2012 has been the year to make those changes. The Fund is a learning organization. The recommendations from the High Level Panel that looked at our oversight and control functions, our own internal work on reform and our new strategy have all guided the changes over the past year. The Fund did not rest on its laurels, when challenges emerged in 2011 it responded.

Current and future contribution to the Global Fund from the UK Government

The UK will be providing a total of £128 million in each of 2012, 2013 and 2014 to the Fund, which
constitutes around 8% of contributions received (with a potential for significant further increases in 2013 and 2014 subject to reforms underway). Donors do not earmark their contributions to any particular disease, country or activity. The cumulative proportion of actual grant expenditure between the three diseases, as of March 2013, is 52% HIV, 32% malaria and 16% TB.

The Global Fund has launched its call for replenishment in April 2013, with the actual replenishment conference in September/October 2013. There, world leaders will make new commitments to the Global Fund that will fuel its work on all three diseases in 2014-2016 inclusive.

Speaking about the importance of a successful replenishment, the Executive Secretary of the Stop TB Partnership, Dr Lucica Ditiu, highlighted that of the 22 high TB burden countries six are totally reliant on funding from the Global Fund (100% of financing) and for another 15 high burden countries two thirds (60%) of their budget comes from Global Fund financing. Thus any failure in the replenishment of the Global Fund in 2013 will trigger a dramatic impact on these countries ability diagnose and treat TB.

Furthermore the WHO and the Global Fund anticipate a gap of US$ 1.6 billion in annual international support for the fight against TB in 118 low and middle-income countries that are eligible for financing from the Global Fund. If this gap were filled, it could mean 17 million patients with TB and multi drug-resistant TB could be fully treated, saving about six million lives between 2014 and 2016.

The Global Fund’s Executive Director Dr Dybul also highlighted that if donors did not act now, costs of dealing with drug-resistant TB could rocket, stating: “It is invest now or pay forever”.

The UK Government have indicated that they are willing to “up to double” their contribution to the Global Fund, subject to continued good progress on its reforms.

The IDC found that DFID is a key donor and reliable partner to the Global Fund whose commitment and leadership could unlock funds from other donors. While the committee strongly support the Secretary of State’s commitment to increase the UK’s contribution to the Global Fund significantly, subject to reform, they were concerned at the continuing delay in providing these funds.

The committee has strongly urged the Department to do all possible to commit funds early by prioritising its assessment of the Global Fund ahead of, and separately from, its broader update of the Multilateral Aid Review (MAR – see below) and to announce it additional funding at a time which raises the most amount of money from other donors.

**Update of the Multilateral Aid Review**

The UK’s MAR, published in March 2011, provided a comprehensive overview of the strengths and weaknesses of the multilateral organisations that DFID works with, including GFATM. The review confirmed that the multilateral system is a critical complement to what the UK government can do alone.

The GFATM received the highest possible rating, “very good value for money”, in the review and it was highlighted that the Fund offers an exciting opportunity for the UK to use aid funding to make a real difference to poor people’s lives and stands ready to boost funding significantly. However, in 2011 the Fund was going through a period of significant transformation and the UK Government emphasised that any increased contribution was dependent on progress of reforms and impact on the ground.

DFID is updating the MAR assessments in 2013 focusing on the extent to which the UK’s reform priorities have been taken forward since the MAR was carried out. The full report on all multilaterals is due to be published in November, after the GFATM replenishment conference, but it is expected that the individual report on GFATM will be available in the summer (2013).

However, it is anticipated that the findings of the MAR update will play out in dialogue and negotiations leading up to the replenishment of the Global Fund later in 2013 and that the Fund is
now set up to go through a successful replenishment, partly because of the efforts of the UK—driving through reforms.\textsuperscript{20}

\begin{center}
\textbf{Recommendation}
\end{center}

\textbf{Recommendation}

The Global Fund to Fight AIDS, Tuberculosis and Malaria is crucial in the response to TB and evolving DR-TB. The UK Government should at least double (from £128m per year to £256m) its contribution to the Global Fund, assuming good progress on reforms and delivery on the ground— with a positive MAR update, to address the threat of TB and DR-TB in low and middle-income countries at a time that leverages more from other donors. The most obvious next available opportunity to do so is the G8 in June 2013.

Key reason for recommendation

International donor funding almost entirely comes through the Global Fund (including around 90% of the UK Government’s). In 22 high TB burden countries six are totally reliant on funding from the Global Fund (100% of financing) and for another 15 high burden countries two thirds (60%) of their budget comes from GFATM financing. In order to scale up access and treatment for DR-TB the resources GFATM has at its disposal needs to increase to meet the unmet need and the UK Government has a key role to play in the replenishment in 2013 having been a key driving force behind the reforms it has undertaken. The UK is also in a position to show this leadership due to the increase in DFID’s budget as part of the UK reaching 0.7% of GNI being invested in ODA.

\begin{center}
\textbf{Recommendation}
\end{center}

\textbf{Recommendation}

Given the global nature of the disease, the UK Government should set a specific target on their contribution internationally to tackling DR-TB.

Key reason for recommendation

While DFID do point to their support to achieve the Global Plan to Stop TB goals it is unclear what specific targets have been set by the UK Government to address the growing threat of DR-TB in low and middle-income countries, which do not relate to HIV-TB co-infection, within the plan. In the absence of a recent policy paper on tuberculosis by DFID a specific target on tackling DR-TB should be set, in consultation with DH, to ensure the UK is responding to the threat that DR-TB poses.

UNITAID was established in 2006 by the governments, including the UK, as the “International Drug Purchasing Facility.” UNITAID uses innovative financing to increase funding for greater access to treatments and diagnostics for HIV/AIDS, malaria and tuberculosis in low-income countries.

\textit{TB portfolio}

UNITAID’s portfolio of TB market interventions address the numerous markets shortcomings for TB treatments and diagnostics – deficiencies that contribute to such unacceptably high mortality rates.

Through its implementers, UNITAID is intervening in four key areas:

- Promoting the scale-up of MDR-TB diagnosis using new rapid diagnostic tests, including the ground-breaking GeneXpert diagnostic assay
- Expanding access to quality-assured MDR-TB treatment by stabilizing the supply chain and
increasing the number of manufacturers

- Ensuring the availability of quality assured medicines – the first line of defence against resistant strains
- Supporting access to paediatric TB medicines.

UNITAID impact

According to UNITAID’s impact report (2011) their work has: scaled-up access to MDR-TB testing and treatment; used a “Strategic Rotating Stockpile” of 5,800 MDR-TB treatments to avoid stock outs; provided first-line treatments needed to prevent spread of MDR-TB. Additional UNITAID results include:

- Over 10,000 MDR-TB treatments provided to 14 high burden countries.
- Thirteen low-income, high-burden TB countries now have fully functioning laboratories using state-of-the-art Line Probe Assay tests to detect drug-resistance and start appropriate treatment. Over 4,000 MDR-TB cases have been detected using these facilities.
- 785,080 first-line treatments delivered to 19 countries to prevent treatment interruptions to countries facing stock-outs.
- One of the key areas that UNITAID has focused on is access to new diagnostic test for DR-TB. In June 2012 the executive board of UNITAID approved funding of US$ 30 million to rollout the GeneXpert machine to scale up TB diagnosis in 20 countries. In addition, the Stop TB Partnership initiative TB REACH (see below) announced that it would co-fund up to US$ 10 million to support implementation of the TB tests in countries, bringing the total amount committed to US$ 40 million.116

UK contribution to UNITAID

The UK is a leader in innovative finance and a committed supporter of multilateral organisations like UNITAID, which scored very highly in the MAR in 2011. The MAR highlighted that UNITAID achieved significant price reductions of key medicines, good focus on fragile states and was highly focused on cost-effectiveness. Following the MAR the UK announced a multi-year pledge of £53 million per year for the period 2011-2013, totalling £159 million, and when speaking about the influence of UNITAID DFID Minister Stephen O’Brien stated:

“Together we are supporting ground breaking initiatives designed to help countries get better access to the right drugs at the right prices and at the right time. And it is working. Not only is UNITAID making a difference to people’s lives, other organisation are following our lead and working closely with us, recognising the importance of using and shaping markets.”117

Evidence received during the APPG inquiry highlighted that UNITAID has played a crucial role in driving down market prices of TB drugs, enabling countries to purchase these in bulk, as well as increasing access to modern tools to diagnose TB and DR-TB.

UNITAID has committed to funding these tests until 2013, with the aim of facilitating the response to 15% of the global MDR-TB burden, representing a three-fold increase over the current 5% of MDR-TB cases being diagnosed.88

For example, in Kenya UNITAID is supporting the procurement of essential paediatric treatments and of a further 7 GeneXpert machines. Kenya would not be able to afford these key commodities without assistance from UNITAID, which has proven itself to be an excellent market shaper for TB drugs and diagnostic tools.101

WHO, the Stop TB Partnership (Stop TB), UNITAID and other partners are working in a coordinated manner to improved understanding of how the market forces operate in the case of second-line TB

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The Line Probe Assay (first line drugs) is a DNA strip test that allows simultaneous molecular identification of tuberculosis and the most common genetic mutations causing resistance to rifampicin and isoniazid.
drugs, and to identify the interventions that can fix the current barriers that are limiting access to the drugs.\textsuperscript{118}

**DFID Multilateral funding: Stop TB Partnership**

The Stop TB Partnership, founded in 2001, seeks to serve every person who is vulnerable to TB and ensure that high-quality treatment is available to all who need it. It is recognized as a unique international body. Stop TB has the power to align actors, including: international and technical organizations; government programmes; research and funding agencies; foundations; NGOs; civil society and community groups; and the private sector through its 1000 partners across the world.

Stop TB operate through a secretariat hosted by the WHO in Geneva, Switzerland and seven working groups whose role is to accelerate progress on access to TB diagnosis and treatment; research and development for new TB diagnostics, drugs and vaccines; and tackling drug resistant- and HIV-associated TB. The secretariat is governed by a coordinating board that sets strategic direction for the global fight against TB.\textsuperscript{119}

**Stop TB Partnerships impact**

Evidence received by the APPG focused on two elements of Stop TBs work: Global Drug Facility and TB REACH, both of which are evaluated below.

**Global Drug Facility**

The Global Drug Facility has changed the landscape of TB care since its creation in 2001 by providing high-quality anti-TB drugs to countries that could otherwise not afford them, either in the form of grants or by directly procuring drugs in bulk to get the lowest possible price. At the end of 2011, GDF had delivered more than 20 million treatment courses to 101 countries.

GDF’s business volume, including both grant and direct procurement activities, increased steadily in 2011, from US$ 132 million in 2010 to US$ 155 million. These figures include all costs: the value of goods procured, freight insurance, procurement agent fees, quality control and pre-shipment inspection.

The increase in volume can be primarily attributed to the high demand for second-line drugs from countries that had received grants from the Global Fund and UNITAID to combat DR-TB.\textsuperscript{120} Written and oral evidence received indicates that while the GDF has been ‘instrumental’ in increasing access to second line drugs to treat DR-TB, the cost of some second line drugs has actually increased over the last decade.\textsuperscript{120}

However, work to reduce prices is on-going and the GDF has also increased the number of MDR-TB drug combinations delivered - more than 30,000 patients in 2012, compared to 19,000 in 2011.\textsuperscript{121}

Evidence received also indicates that the availability of drugs in the world at this moment is not the limiting factor for getting patients on treatment. The limiting factor is the availability of diagnosis and having the appropriate systems in place for treatment.\textsuperscript{65}

**TB REACH**

Each year some three million people affected by TB are not diagnosed and treated according to international recommendations. This gap remains one of the most daunting challenges to eliminating TB.

Stop TB Partnership’s TB REACH initiative, launched in 2010, is finding new ways to bring TB care to these unreached millions. The initiative is funded by a multi-year grant from the Canadian International Development Agency (currently the sole funder). It finances innovative and ground-breaking projects targeting poor and vulnerable communities that result in early and increased detection of TB cases and ensure their timely and successful treatment.

Through a wave based funding, TB REACH awards grants up to US $1 million for a one year period to selected institutions or organizations that have put forward successful proposals in a timely fashion.
in order to detect additional TB cases.

In short, TB REACH:  
- Offers one year grants to TB programmes and partners for technically sound, innovative and cost-effective TB case detection interventions.
- Provides fast track funding and results.
- Focuses on poor, vulnerable and marginalized groups, and populations with limited or no access to TB control services.
- Encourages local innovation and bold solutions that may not be funded elsewhere.
- Requires detailed reporting on technical and financial progress and case finding data.
- Ensures external monitoring and evaluation of all projects.
- Delivers results quickly, for improved TB care.

TB REACH has so far funded 75 projects in 36 countries. The first wave of 30 projects (approved in 2010) began activities in 2011, and the results were impressive. In a target population of more than 65 million people, TB REACH projects increased case finding by 33% in a single year, reaching 80,000 people with active TB and preventing almost 200,000 new infections. The average cost per person covered per year was less than US$ 0.20.

As part of the support for TB case finding activities TB REACH has procured over 150 GeneXpert machines and more than 250,000 GeneXpert cartridges making it the largest single procurement mechanisms for the new technology for multicounty initiatives.

Box 10: Case Study: TB REACH Pakistan

APPG Oral Evidence - Dr Aamir Khan, Executive Director, Indus Hospital Research Center, Pakistan: Public Private Mix

The first demonstration of this [PPM] approach that our group has engaged in was in Karachi with TB REACH funding where we doubled case notification in a large part of Karachi with a population of about 2,000,000 people. We doubled case notification by simply having community laypersons screen outside private GP clinics for cough symptoms and have those people x-rayed, or tested by sputum smear or GeneXpert. By simply engaging the private sector for screening we then provided those patients that were identified free drugs through the public programme. We notified each patient in the private sector back to the public programme. So as a facilitator and intermediary we were able to link the public sector and the private sector I don’t think any approach that excludes one or the other is going to be successful, and I do think that we need to go beyond what we call public-private mix which is too a government-led effort to engage the private sector, because in most of our countries the government stops functioning at 1:00 pm and the private sector opens at 2:00 pm and keeps working until 11pm or midnight. And so they live in different time zones in the same country; and you need intermediaries that can bring those two groups together. So that’s what I mean by saying that we should not be exclusive, it’s just that we need more innovative methods of linking the two.

Results
- Nearly 300% increase in case detection in first 9 months of project implementation and 500% increase in paediatric notifications.
- Indus is now the second largest reporting centre in Pakistan.
The demand from prospective applicants to the TB REACH project continues to increase with more than 300 applications submitted by organizations to undertake innovative case detection interventions amongst remote and vulnerable populations under ‘wave 2’ (2011) and 320 in ‘wave 3’ (2012). However, given the limited funding available it is unlikely that all projects can be financially supported.

Evidence received as part of the APPG inquiry highlighted that TB REACH has been extremely successful to date in promoting early and increased TB case detection through new technologies in innovative ways in key populations that would not have access to diagnosis or treatment.

However, there were concerns raised about the sustainability of the projects as funding was only provided for one year, and while second year funding was available it was not guaranteed. Stop TB highlighted that the projects are designed to try and detect as many as possible in innovative ways, use a rapid deployment of funds over a year to demonstrate that it works, and then scale up using other funds e.g national government budgets, GFATM etc.

Advocates for TB REACH highlight that by demonstrating proof of concept in the first year, it is expected that a number of innovative methods for case detection in difficult settings will be documented. This data can then be used in other similar settings and potentially scaled up.

One example of this is a TB REACH project using LED fluorescent microscopes (LED FM) in over 200 medical colleges in India. LED FM is more sensitive than ordinary microscopy and allows lab technicians to examine more sputum slides per day. Introduction of the technology increased the number of smear positive TB cases by between 10 to 15 % and in absolute numbers thousands of additional TB cases were detected. The Government of India, as part of its Revised National TB Control Programme (RNTCP), is now planning to procure and deploy over 2000 such LED FMs to cover the remaining medical colleges and all other busy hospitals at district level and in cities.

During APPG Oral Evidence Session 4, when commenting on the importance of and opportunities TB REACH present Dr Aamir Khan, Executive Director, Indus Hospital Research Center, Pakistan stated:

“We need TB REACH like funding because what’s been lacking in TB in terms of practice is new approaches. Many things have been done the way they were being done 100 years ago, and it’s remarkable when you know other disease areas other than TB, when you compare what’s going on inside TB, what’s remarkable is how current TB approaches seem to be just stuck. So the TB REACH initiative has been in my opinion one of the most successful programmes of the Stop TB Partnership, and I would like to request on behalf of many of us that receive support from TB REACH that this programme should not end, it should in fact be expanded, and if the British government can do anything to support its expansion that would be welcome not by just myself and many of my colleagues, but 75 other programmes like ours that have used that funding to figure out new ways of finding these patients and putting them on treatment.”

When asked about TB REACH the UK Government responded by stating:

“The Department for International Development recognises the importance of the World Health Organisation’s ‘TB REACH’ initiative and appreciates strong Canadian support for this initiative.”

DFID official, Dr Jason Lane, also highlighted during APPG TB Oral Evidence Session 4 that they believed it had been successful to date and if the UK were to announce an increase in funding to TB then TB REACH would be a clear candidate.

UK contribution to Stop TB

The UK Government currently provides £4.9 million of core funding (i.e. unrestricted), over the period 2011 to 2015, to the WHO-hosted Stop TB Partnership to help foster greater collaboration, cohesion, and integration within the global tuberculosis control movement and as a result improve prioritisation and the efficiency and effectiveness of the global response.
Full achievement of the Global Plan to Stop TB 2011–2015 will cost an estimated US$ 47 billion for the five years (approximately £30 billion). The UK investment would pay for itself as long as it leads to an improvement in efficiency in the use of global resources of 0.02% (£5m/£30bn).

An independent external evaluation of Stop TB and its structures will take place in 2013 to review the impact, effectiveness and efficiency of the organisations work and make recommendations to Stop TB going

**Recommendation**

Value for money considerations infuse all national programmes combatting TB, with the most cost-effective interventions being prioritised for the highest impact. TB REACH is targeted at driving innovation and high impact. The UK Government should become a donor to TB REACH, beyond its contribution of core funding to the Stop TB Partnership, to maximise its investments in UNITAID and support the expansion of new diagnostic tools to detect, and ultimately treat, cases of DR-TB. The level of funding allocated should be directed by the evaluation of the Stop TB Partnership due in 2013.

Key reason for recommendation

The GDF, TB REACH and UNITAID initiatives have important roles to play in improving access to diagnosis and treatment for DR-TB, which remains woefully inadequate, to those who need it. In order to increase the number of cases detected in the three million people that fail to access diagnosis and treatment each year we need to be more innovative and strategic about investments to scale up interventions, particularly around diagnosis.
Annex 1: Copy of the ‘Call for written evidence’

Invitation to submit written evidence on:

Britain’s response to the growing threat of drug-resistant tuberculosis
(Deadline for responses 15th October 2012)

About the report and call for written evidence

The APPG on Global Tuberculosis (APPG TB) is producing a short report building on the Parliamentary Office of Science Technology Note (POST Note) on drug-resistant TB (DR-TB) published in July 2012. POST is the Houses of Parliament’s in-house source of independent, balanced and accessible analysis of public policy issues related to science and technology.

The note examines the extent of, and risks posed by, drug resistant TB as well as an overview of UK and international TB surveillance, research into treatments and policy options to limit infections. It is not the role of POST to provide recommendations in reports that it publishes. It is for this reason that the APPG is seeking views on the current challenges of DR-TB in the UK and in developing countries - as defined in the note - with specific attention paid to the current and future response of the UK Government in addressing DR-TB.

This initial evidence will be fed into the report and will also inform subsequent oral evidence sessions. The final report will be submitted to the Departments for International Development (DfID) and Health (DH) and used to inform the All-Party Groups work going forward.

Guidance to responding to the call for evidence

The call for evidence is broken down into 2 sections – “UK and Global”. Please note that you do not need to answer every question or every section. Feel free to only answer the questions relevant to your area of expertise. If you need more space to answer any question, please feel free to add additional pages.

It assists the Group if each written evidence submission:

• be in Word format
• state clearly who the submission is from, ie whether from yourself in a personal capacity (Submission from, eg Mr John Smith) or sent on behalf of an organisation (eg Submission from Insert Name Ltd)
• comprise a single document attachment to the email;
• begin with a short summary in bullet point form;
• have numbered paragraphs

Written evidence may be referenced in the final report. If you wish for your evidence to be anonymous please make this clear.
Submissions should be emailed to the APPG’s Policy Adviser, Simon Logan, at Logans@parliament.uk. If you have any queries about the report or require further information please contact Simon by email, or by calling 020 7499 8238.

The APPG would be grateful for your input into the inquiry and ask you to consider and respond to the written call for evidence questions outlined below. The deadline for submissions is Monday 15th October.

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<td>Contact details</td>
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**Section 1: Improving efforts to tackle DR-TB (United Kingdom)**

**Detection and Treatment targets**
- Treatment completion rates for TB and DR-TB are not meeting the World Health Organisation (WHO) target of 85%. What barriers are there to meeting and/or exceeding this target and how can we improve completion rates in the UK?
- Drug resistance is a man-made problem, resulting from misuse of anti-TB drugs and poor management of the disease. How important is it to manage drug susceptible cases effectively to avoid resistance developing?

**Active Case finding**
- What more could be done to strengthen the control of DR-TB through improved detection and diagnosis and what role does active case finding have in reducing incidences of DR-TB?

**Variations in Screening and Care**
- What guidance exists on the drug treatment and clinical management of MDR and XDR-TB and what can be done to ensure that the clinical management of all MDR and XDR-TB patients is optimal?
- What are the main issues re accessing, prescribing and monitoring second line drugs?
- Are current recommendations and resources for the treatment supervision and case management of DR-TB effective? Please give examples.

**Commissioning of TB services**
- What impact will the Health and Social Care Act 2012 have on the commissioning of TB services in the future?
- “If Clinical Commission Groups (CCG’S) commission TB services collectively and at scale and if services for complex cases of TB such as MDR and XDR were commissioned by the NHS Commissioning Board in the new structure”, as outlined in the POST Note would this improve coordination of TB services under the new structures? Please explain your reasoning for agreeing or disagreeing.
- How do you think the DR-TB prevention, care and control could be improved under NHS Reforms?
TB and Immigration

• The UK Borders Agency is now rolling out pre-entry screening for Active form of TB. What impact – if any – will this have on rates of TB in the UK?

• “Experts argue that new pre-entry screening system will only be fully effective if combined with screening for latent TB in high-risk new arrivals”. Do you agree with this statement? Please explain why you do or do not agree.

Section 2: Improving efforts to tackle DR-TB (Globally)

Work to support diagnosis and treatment

• What policies, actions and resources are needed to reverse the rise in DR-TB globally?

• Should there be a focus on increasing completion rates of drug susceptible TB instead of shifting focus to tackle the transmission and the growing treat of DR-TB in high burden settings, or is it possible to focus on both given the resources available?

• Should and (if so) in what ways could the UK Government increase its support for reversing the increase in DR-TB?

• What is the current availability/affordability of test for DR-TB? How could the availability of these tests be improved?

Best practice in reversing DR-TB

• What examples are there of rising cases of DR-TB being reversed?

Working with multilateral agencies

• How effective/important is the Global Fund to Fight AIDS, Tuberculosis and Malaria in addressing DR-TB and what makes this agency particularly effective/ineffective?

• What other multilateral organisations – if any - are important in the response to combating DR-TB globally?

• Should the UK Government focus more on bilateral/ project specific support to tackle TB, or work via multilateral organisations?

Access to second-line drugs

• How wide-spread is access to second-line TB drugs?

• What work is being done to increase access to these drugs?

• What are the resource implications of scaling-up access to these drugs? Is there sufficient commitment and capacity from both donor and recipient countries for this?

Research and development

• What impact would advances in the development of drugs, diagnostics and vaccines have and what role – if any - does the UK Government have in encouraging the development of new tools to tackle TB?

Please feel free to also submit any other comments you feel are relevant to the inquiry.
Annex 2: Written and Oral evidence

The APPG would like to thank the following individuals and organisations for contributing to the APPG’s written evidence sessions.

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
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<th>Country</th>
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<tr>
<td>Gini Williams</td>
<td>TB Project Director</td>
<td>International Council of Nurses</td>
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<tr>
<td>Prof Jane Anderson</td>
<td>Chair</td>
<td>British HIV Association</td>
<td>UK</td>
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<tr>
<td>Dr Ruth McNerney</td>
<td></td>
<td>London School of Hygiene and Tropical Medicine</td>
<td>UK</td>
<td>Individual – academic</td>
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<tr>
<td>David Moore</td>
<td>Director</td>
<td>LSHTM TB Centre</td>
<td>UK</td>
<td>Individual – academic</td>
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<tr>
<td>Prof H Simon Schaaf</td>
<td>Professor</td>
<td>Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University</td>
<td>South Africa</td>
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<tr>
<td>Muhwa Jeremiah Chakaya</td>
<td>Chief Research Officer</td>
<td>Centre for Respiratory Diseases Research, Kenya Medical Research Institute</td>
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<td>Individual – academic</td>
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<tr>
<td>Prof C Fordham Von Reyn, MD</td>
<td>Professor of Medicine</td>
<td>Director, Dar Dar International Programs Geisel School of Medicine at Dartmouth</td>
<td>UK</td>
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<td>Dr Jelle Thole</td>
<td>Director</td>
<td>Tuberculosis Vaccine Initiative (TBVI)</td>
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<td>Professor Peter Davies</td>
<td>Consultant Physician</td>
<td>Liverpool Heart and Chest Hospital</td>
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<td>Professor Martin Peter Grobusch</td>
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<td>Professor GB Migliori</td>
<td>Director</td>
<td>WHO Collaborating Centre for TB and Lung Diseases, Findazione S. Maugeri, Care and Research Insitute, Tradate, Italy, European Respiratory Society (ERS)</td>
<td>Italy</td>
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<td>Lisa Cunningham</td>
<td>External Affairs</td>
<td>Royal College of Physicians</td>
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<td>Policy and Engagement Officer</td>
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<td>Ernesto Jaramillo/Dennis Falzon</td>
<td>World Health Organisation (WHO), Stop TB Department</td>
<td>Switzerland (global)</td>
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<td>Wing Wai Yew</td>
<td>Honorary Clinical Professor</td>
<td>Department of Microbiology, the Chinese University of Hong Kong</td>
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<td>Individual – academic</td>
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<tr>
<td>Amina Jindani</td>
<td>Honorary Senior Lecturer</td>
<td>St George’s, University of London</td>
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<td>Individual – academic</td>
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<td>Ben J Marais</td>
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<td>Australia</td>
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<tr>
<td>Jose A Caminero and Paula I Fujiwara</td>
<td>International Union against TB and Lung Disease (The Union)</td>
<td>France</td>
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<tr>
<td>Dr Nahid Payam</td>
<td>Associate Professor of Medicine</td>
<td>Division of Pulmonary and Critical Care, University of San Francisco and Director, Chest and High Risk Asthma Clinic, San Francisco General Hospital</td>
<td>USA</td>
<td>Individual – academic</td>
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<td>The Global Fund to Fight AIDS, Tuberculosis and Malaria</td>
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<td>Agnes C Gebhard</td>
<td>Senior Consultant</td>
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<td>Netherlands</td>
<td>CSO</td>
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<tr>
<td>Nicolette Dawson</td>
<td>Communications Officer</td>
<td>LEPRA Health in Action</td>
<td>UK</td>
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<td>Dr Helen Cox and Dr Jennifer Hughes</td>
<td></td>
<td>MSF (Doctors Without Borders), Khayelitsha, DR-TB Program, Cape Town, South Africa</td>
<td>South Africa</td>
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</table>
The APPG would like to thank the following individuals and organisations for contributing to the APPG’s oral evidence sessions:

Oral evidence session 1 (UK)
Thursday 29th November, 10 – 11:30 am, Thatcher Room, Portcullis House
Witnesses: Charles Fraser CBE FRSA - Chief Executive, St Mungo’s, Gini Williams, International Council of Nurses (ICN), Toby Capstick is the Lead Respiratory Pharmacist at Leeds Teaching Hospitals NHS Trust, Amy Mcconville, TB action group (TBAG)

Oral evidence session 2 - UK
Thursday 12th December 2012, Committee Room 21, Houses of Parliament
Witnesses: John Watson (Health Protection Agency), Mike Mandelbaum (TB Alert), Professor Keith Willett, (National Clinical Director for Trauma Care -for future commissioning NHSCE) and Professor Peter Moss (specialised commissioning CRG Chair for infectious diseases)

Oral evidence session 3 - Global
Thursday 24th January, 10 – 11:30 am, Committee Room 17, Houses of Parliament
Witnesses: Svend Robinson, Senior Specialist, Parliamentary Affairs, The Global Fund to Fight AIDS, Tuberculosis and Malaria; Beverly Collin, Health Policy and Practice Advisor, MSF-UK (Doctors Without Borders); Agnes C. Gebhard MD, Public Health and TB specialist, KNCV Tuberculosis Foundation.

Verbatim report 4 - Global
Wednesday, 13th February, 10:30 – 12 noon, Committee Room 20, Houses of Parliament
Witnesses: Dr Lucica Ditiu, Executive Secretary, Stop TB Partnership, World Health Organisation; Dr Aamir Khan, Executive Director, Indus Hospital Research Center, Pakistan; Dr Jason Lane, Senior Health Adviser (TB), Department for International Development (DFID);

For full details of all written evidence (35 written responses) and oral evidence (4 verbatim reports of sessions held in the House of Commons) received visit www.appg-tb.org.uk.
References


21 APPG Oral Evidence(2012), Mike Mandelbaum, Chief Executive, TB Alert.


24 BBC (2013) Antibiotics resistance ‘as big a risk as terrorism’ – medical chief. Available at


31 APPG Oral Evidence (2012), Professor Peter Moss, Clinical Reference Group Chair for specialised commissioning - infectious diseases.


33 APPG Oral Evidence (2012), Mike Mandelbaum, Chief Executive, TB Alert.


35 APPG Written Evidence (2012), International Union Against Tuberculosis and Lung Disease.


37 APPG Oral Evidence (2012), Charles Fraser CBE FRSA, Chief Executive, St Mungo’s.


40 APPG Written Evidence (2012), St Mungos.


46 APPG written and oral evidence (2012)


76 APPG Written Evidence (2012), The International Union Against Tuberculosis and Lung Disease.
77 APPG Oral Evidence (2013), Dr Aamir Khan, Executive Director, Indus Hospital Research Center, Pakistan and Chair Stop TB Working Group on MDR-TB (hosted by the Stop TB Partnership).
86 APPG Written Evidence (2012), Centre for Respiratory Diseases Research, Kenya Medical Research Institute.
88 APPG written Evidence (2012), UK Coalition to Stop TB.
89 APPG on Global TB (2011) The UK’s response to global tuberculosis.
90 APPG Oral Evidence (2012), Dr Jason Lane, Senior Health Adviser, DFID.
93 APPG Written Evidence (2012), Stop TB Partnership.
96 APPG Written Evidence (2012), MSF
98 APPG Written Evidence (2012), Aeras TB Vaccine Foundation.
99 APPG Written Evidence (2013), DFID additional written evidence.
100 APPG Written evidence (2012), MSF Cape Town.
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108 Dybul Explains transition disease split
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