Drug-Resistant Tuberculosis:
Old Disease – New Threat
Summary Version (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 Medecins 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
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
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

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.¹ 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 2012.

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.

This paper seeks to give an overview of the current challenges drug-resistant (DR) TB poses in the UK.

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, multilateral, 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, and the report in full, 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.¹ 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.

¹ See references throughout this report
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’s (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 (Mtbt). 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 Mtbt 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 (see Box 1), hence it is important to find and trace contacts of adult cases of TB to address childhood TB.

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 standard 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.
Ensuring TB patients adhere to treatment is vital to achieve cure, interrupt further transmission of infection and prevent the emergence of drug-resistance. Directly Observed Therapy (DOT), which is part of the global strategy to prevent DR-TB and means that a designated individual watches the patient swallow every dose, has resulted in major achievements in TB care and control.

**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:
- Drug-resistant (DR) TB refers to strains of tuberculosis bacteria that are resistant to at least one anti-tuberculosis drug. This term is used in this report to include all of the possibilities listed below:
- 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 and 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 (XDR) 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.

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**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.

**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 health-care 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 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.

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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.

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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.

Table 1: Headline TB rates

<table>
<thead>
<tr>
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<th>Estimated Global 2010</th>
<th>Notified UK 2011</th>
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<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>
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<tr>
<td>MDR-TB cases</td>
<td>650,000 (prevalent cases)</td>
<td>81 (out of a total of 431 DR-TB cases)</td>
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*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 that 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 standard TB (>85% successfully treated) or even MDR-TB (48% cases successfully treated).

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).


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.
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 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.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.2

**Figure 2: Percentage of previously treated tuberculosis cases with MDR-TB**

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1 Reproduced from WHO’s global tuberculosis 2012 report, by permission of the World Health Organisation
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). 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 United States of America, despite the UK’s much smaller population.

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

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

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 drug4 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

Figure 4: Proportion of tuberculosis cases with first-line drug resistance, UK, 2000-2011VIII

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4 TB that is resistant to any first line drug, including: Isoniazid, Rifampicin, Pyrazinamide, Ethambutol and Streptomycin

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.
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 or perhaps physiological side effects.

London, which has the highest TB rates of any capital city in Western Europe and accounts for 39% of all UK cases, 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 people25 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 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 diagnostics**27

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 US$ 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

Conclusion and recommendations

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 resistance 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**

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

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.

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• **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 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.

Key reason for recommendation

In some countries, for example in India and Pakistan, the government (supported by the WHO) runs a national programme to test and treat TB free of charge. However, about half of TB patients don’t use the government...
programme 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 use cheap but unreliable diagnostic tests and who provide inadequate treatment where patients fail to complete a course of first line drugs, fuelling the spread of drug-resistant forms of the disease.

| GLOBAL BRICS | BRICS countries response: There is capacity to mobilise 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. South Africa is a leader in this regard, showing it can be done.. |