THE PRICE OF A PANDEMIC

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BRIEFING ON THE G20'S BIGGEST INFECTIOUS KILLER

INTRODUCTION

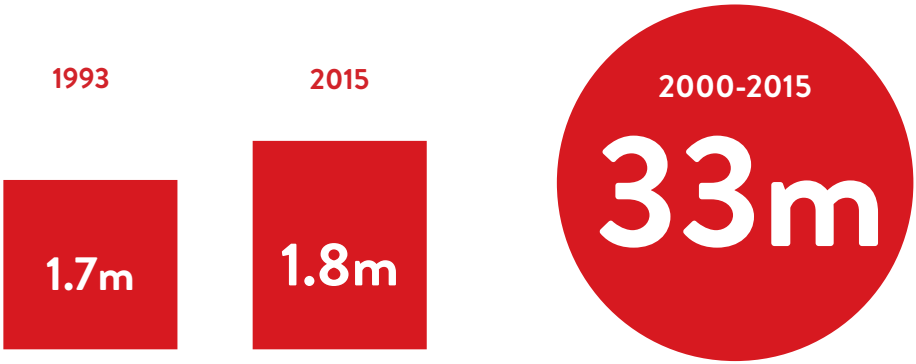
Multi-drug resistant tuberculosis (MDR-TB) is a major component of the global threat posed by antimicrobial resistance (AMR). It is a drug-resistant strain of TB, the world's biggest infectious killer, and as such is the world's only major, airborne, drug-resistant infection. Strains of TB which are resistant to nearly all existing treatments have been found in nearly 100 countries around the world.

This briefing will detail why TB has developed multi-drug resistant strains and the projected impact of the spread of MDR-TB over the next 35 years. In doing so, it will highlight why TB is of particular threat to G20 nations and why overcoming the market failure around the development of TB drugs should be considered a priority during upcoming G20 initiatives on AMR.

KEY FIGURES

TB is the deadliest infectious disease in human history and remains the world's biggest communicable killer.

DEATHS FROM TB



In 1993 the WHO declared TB a global health emergency

More people died from TB in 2015 than from HIV and malaria combined.

The Millennium Development Goal on TB was "achieved" despite 33m deaths from the disease between 2000 and 2015.

FUTURE COSTS

The following figures were generated by the independent Review of Antimicrobial Resistance. They estimate the future impact of drug-resistant TB unless urgent action is taken. [1]

G20 STATES		NON-G20 STATES
33m	ADDITIONAL DEATHS BY 2050	42m
US$10.5 trillion	LOST ECONOMIC OUTPUT	US$6.2 trillion

The impact will be felt most profoundly in sub-Saharan Africa, South Asia, and Eastern Europe where roughly 90% of the non-G20 costs will be felt.

IMPACT ON GDP BY 2050:

SUB-SAHARAN AFRICA

3.21%
LOWER GDP AS A RESULT OF MDR-TB.

LOW-INCOME COUNTRIES

2.45%
LOWER GDP AS A RESULT OF MDR-TB.

1. Extracted from a report prepared by KPMG LLP in the UK, derived from research commissioned by the Wellcome Trust, as part of an independent review into anti-microbial resistance supported by the Department of Health and the Wellcome Trust.

THE BIOLOGY OF DRUG-RESISTANCE

When bacteria reproduce, naturally occurring variations can make some of the second generation bacteria more resistant to drugs than others. When exposed to antimicrobials, the more resistant bacteria survive longer, and thus pass the same traits onto their offspring.

If treated with a combination of drugs that work in different ways, bacteria that have developed resistance to one drug can be killed by the other drugs. However, if effective treatment is not continued long enough to kill all bacteria present then the resistant bacteria will survive and reproduce and eventually produce strains that are completely drug-resistant.

If the infection is communicable, this means that drug-resistant strains may then be transmitted to other people. This is the case with drug-resistant TB.

MARKET FAILURE

Modern drug discovery is hugely challenging. There are high rates of failure during the process and development takes many years of costly research. Accordingly, pharmaceutical companies are rarely prepared to commit the resources needed to bring a product to market unless there is the prospect of a financial return for that product.

When new antibiotics are developed they are often used as 'treatments of last resort.' Accordingly, private sector drug-developers know that the likelihood of seeing a return on the costs of development are relatively low and have, therefore, largely overlooked investing in antimicrobials. This problem is exacerbated by the opportunity cost of investing in the development of an antimicrobial compared to other health conditions with established markets and proven returns.

TB suffers from a different type of market failure. TB must be treated with a combination of drugs due to its unique biology and the current market model is geared towards the development of individual drugs. There is, therefore, insufficient financial incentive to encourage commercial investors to devote the resources needed to develop a new anti-TB drug.

Although caused by different factors, the solution to the market failure that hampers commercial drug development of anti-TB drugs and other antimicrobials is essentially the same: there is not enough of a market incentive to reward commercial developers of new drugs.

Given the significant public health threat posed by antimicrobial resistance, and the failure of the market to offer a solution, it falls to public and philanthropic funders to build models that create the right incentives to unlock new drug development.

TB DRUG-RESISTANCE IN DETAIL

TB is the biggest killer in human history and remains present in nearly every country in the world. In 2015, 1.8 million people died from the disease, more than from HIV and malaria combined.

TB is particularly susceptible to developing drug-resistant strains because of the length of the current standard treatment:

- The TB bacteria has a unique waxy shell that makes it naturally more resistant to drugs than other bacteria. This means that TB treatment is long and requires a combination of four, often toxic, drugs. Because treatment is long and arduous, patients are sometimes forced to break off treatment before the infection is completely cleared. This creates the perfect conditions for the development and spread of drug-resistance.

- Due to the minimum six-month duration of TB treatment, patients are at particular risk of experiencing interruptions to treatment and this can facilitate the development of resistance.

A new, shorter, treatment regimen would have a major impact on the current burden of TB as well as preventing the further spread of drug-resistance with the associated human and economic impact on page 3.

TB – THE G20'S AMR CHALLENGE

Of all prospective drug-resistant infections, TB is the one which currently kills the greatest number of people. It is also the biggest infectious killer among the G20 nations.

	G20	NON-G20
DEATHS	800,000 (45%)	1,000,000 (55%)
CASES	5,500,000 (54%)	4,900,000 (46%)
MDR-TB CASES	322,580 (59%)	227,420 (41%)

Addressing the market failure which has blocked commercial TB R&D for decades will require a comprehensive mechanism with backing across the G20 states but the rewards would be significant across the world, particularly in G20 states.

A novel anti-TB regimen, which works quickly and with few side-effects, could be immediately deployed against drug-resistant TB and standard strains of the disease. New drugs, therefore, would have an immediate and significant global health impact. Further, quickly and effectively treating standard TB is also the best way of preventing the development of drug-resistant TB given the lack of an effective vaccine. A new anti-TB regimen would save trillions in future MDR-TB costs – as outlined in the tables below.

A mechanism that developed a new anti-TB regimen would have the added advantage of acting as a path-finder for mechanisms that address the need to develop single antibiotics to combat other forms of AMR. Unfortunately, however, any mechanism that only incentivises the development of individual antimicrobials will have limited impact for TB.

TB has killed more people than any other infectious disease, but the standard treatments we use today are close to 50 years old. New drugs are urgently needed to reduce the enormous human and economic impact of the disease, and to overcome the major threat to the future health and wealth of nations posed by MDR-TB. **The G20 has an opportunity to unlock the development of those new drugs to safeguard the health and wealth of current and future generations. It should take it.**

> **"The burden of TB is too great, and the need for new treatments too urgent, for it not to be a central consideration in the role and objectives of a global intervention to support antibiotic development."**
>
> ***The independent Review of Antimicrobial Resistance***

CUMULATIVE ECONOMIC IMPACT

COUNTRY	CUMULATIVE GDP LOSSES, 2014 bn US$	GLOBAL RANK
INDIA	3,668.26	1
CHINA	2,303.84	2
SOUTH AFRICA	1,715.64	3
INDONESIA	869.40	5
RUSSIA	499.98	8
BRAZIL	305.70	10
KOREA, SOUTH	288.10	11
EU (EXC FR, DE, IT, AND GB)	278.56	12
JAPAN	129.97	18
MEXICO	103.30	21
UNITED STATES	85.80	26
FRANCE	66.41	33
TURKEY	63.71	34
GERMANY	38.52	45
ITALY	32.75	49
ARGENTINA	29.85	52
AUSTRALIA	22.79	60
CANADA	16.00	68
UNITED KINGDOM	12.70	75
SAUDI ARABIA	9.44	88
TOTAL	**$10,540.72bn**	

CUMULATIVE MORTALITY

COUNTRY	MORTALITY	GLOBAL RANK
INDIA	18,176,100	1
CHINA	4,915,400	3
INDONESIA	4,001,400	4
SOUTH AFRICA	3,886,300	5
RUSSIA	960,500	15
BRAZIL	478,000	23
EU (EXC FR, DE, IT, AND GB)	385,600	25
KOREA, SOUTH	244,900	34
TURKEY	139,500	47
MEXICO	136,100	50
JAPAN	104,800	56
UNITED STATES	58,400	70
ARGENTINA	52,600	73
FRANCE	48,700	76
GERMANY	36,000	81
SAUDI ARABIA	29,800	84
ITALY	28,200	86
CANADA	9,700	105
UNITED KINGDOM	9,400	107
AUSTRALIA	8,500	108
TOTAL	**33,710,510** additional deaths from MDR-TB by 2018	