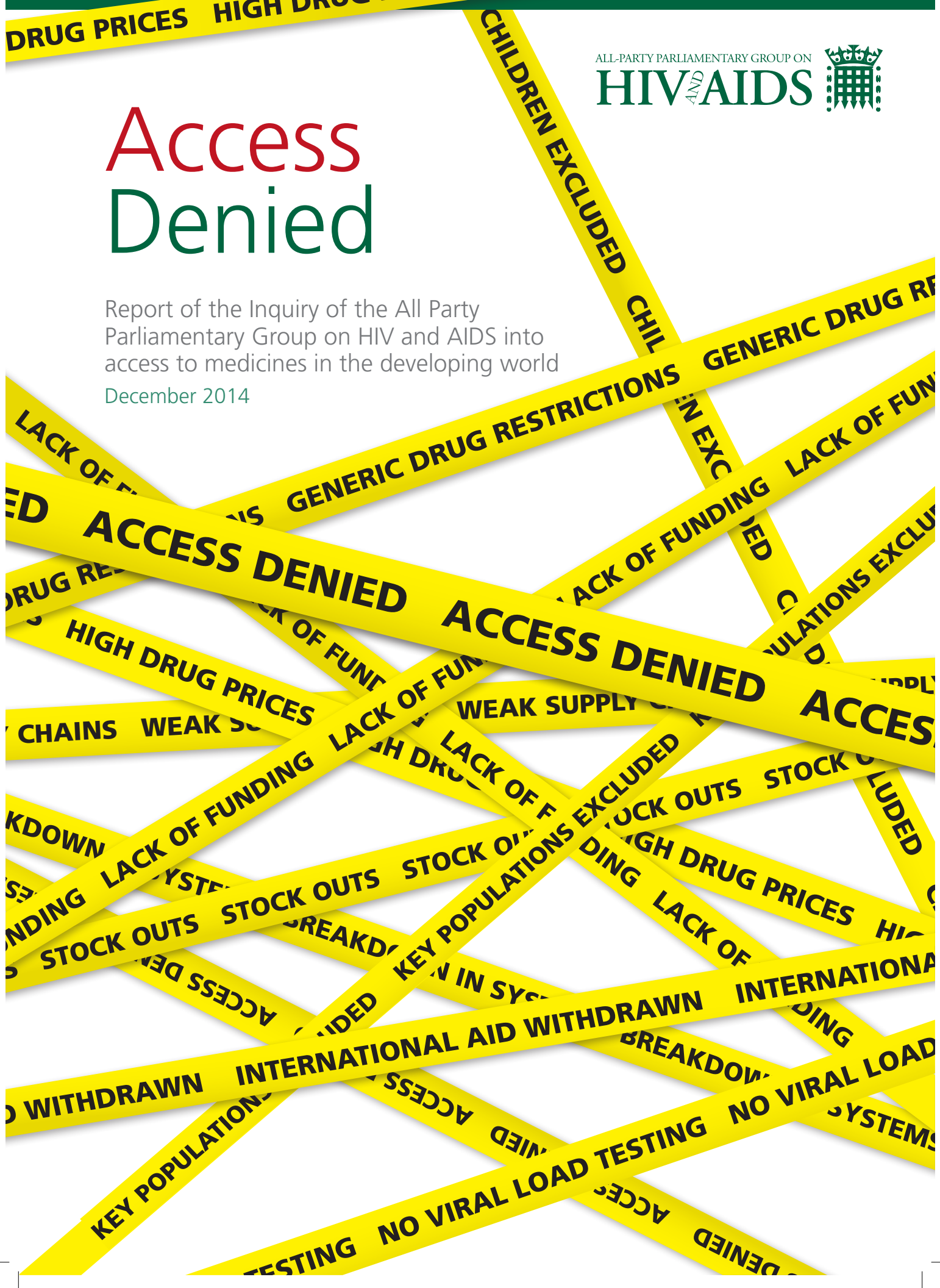


DRUG PRICES HIGH DRUG PRICES HIGH



Access Denied

Report of the Inquiry of the All Party
Parliamentary Group on HIV and AIDS into
access to medicines in the developing world
December 2014



Foreword



Taking shape before us in 2015 is a historic opportunity – I would say a historic imperative – to end AIDS as a public health threat in the coming years. This opportunity has coalesced from years of hard work, heavy engagement and scientific progress against this epidemic. Almost 14 million people are on

lifesaving treatment worldwide, and new HIV infections have fallen by 38% since 2001. We have seen AIDS transform from a death sentence to a chronic, treatable condition, enabling millions of people to live long healthy lives.

But this is far from sufficient to end AIDS by 2030 – or ever. Some 60% of adults living with HIV are still not receiving treatment, and the percentage of children is even higher. We must close the gap between those who have access to treatment and the millions that do not.

Access Denied exposes the inequities and current barriers people face when trying to access life-saving medicine. It gives voice to the millions of men, women and children who have been left behind and shut out of HIV treatment. It highlights the persistent challenges of bringing affordable, high-quality diagnostics and drugs to all people in need across the world.

It also demonstrates that ending AIDS is an investment that can deliver returns both economic and social. Reaching for the 2030 target – which is both realistic and measurable – can contribute significantly to the overarching sustainable development goal of reducing extreme poverty. And it can serve as a catalyst for delivering a “grand convergence” for ending diseases of inequity, delivering social goods and ensuring human rights for health in the post-2015 era.

Ending the AIDS epidemic will deliver empowerment for women and girls. It will deliver social justice and legal equity. It will deliver the financing to provide universal access to quality health services. It will deliver solutions to deep structural development challenges. And it will also deliver the next great ideas in development.

For example, this report explores the benefits of building an R&D agenda driven by the health needs of billions rather than demands of profitability. When we bring millions of people into the market who were previously absent, volume can drive profits instead of high prices. This approach makes sense not just for ending AIDS but for energising development across the board. It opens a path for creating a global R&D fund that could reward all entities who contribute to it.

Further, this report proposes that the UK negotiate with the pharmaceutical industry and civil society to create a R&D Treaty that would provide the framework for such a fund. These are the sorts of out-of-the-box innovations that pushing towards a global goal to end AIDS by 2030 can stimulate.

The UK government is setting a potent example for the world, exceeding its 0.7% target on ODA and closely scrutinising its investments in the context of sustainable development and value for money.

The All Party Parliamentary Group on HIV and AIDS has been a formidable advocate for continued investments in the AIDS response, and for pushing leaders to address injustice in all its forms. I congratulate the Group on this timely and insightful report and I hope that all of us – governments and the private sector, multilateral and bilateral partners, civil society and pharmaceutical companies – will join together to achieve the vision of ending AIDS, which is well within our grasp.

Michel Sidibé
Executive Director, UNAIDS



Access Denied is the result of our All Party Parliamentary Group (APPG) spending much of 2014 conducting an inquiry; gathering written and oral evidence from the expertise of a wide range of organisations and individuals across the world, including in the UK and during our invaluable visits to South Africa and India.

It has been abundantly clear to me in my time as Chair of the APPG just how successful *The Treatment Timebomb* was in influencing international thinking and policymaking on access to medicines. We have seen tremendous success in the fight against HIV in the five years that have passed since then but also new, daunting challenges. I felt it was now time to revisit the crucial issues highlighted in *The Treatment Timebomb* by our predecessors and examine the current obstacles to access to HIV medicine.

This inquiry has been enriched by the vast amount of input from civil society, government, the private sector, academics and more. I would like to give my sincere thanks to all those who contributed their time, knowledge and advice to our inquiry and this resulting report.

I would like to give special thanks to STOPAIDS and the International HIV/AIDS Alliance for their help in arranging the APPG's meetings in South Africa.

Thank you also to all of the organisations, listed at the end of the report, who met with us and facilitated our visits to South Africa and India. I must also pay tribute to the APPG's advisor, Susie Pelly, who has dedicated months of work to this inquiry and I am extremely grateful for her making this report a reality. Final thanks must go to UNAIDS Executive Director Michel Sidibé; I am delighted that he has given his support to *Access Denied* and I appreciate his kind words about our work.

Access Denied may be the culmination of the APPG's research, but it is only the start of what we hope will be a successful campaign to hold governments, multilateral donors and the private sector to account in the quest to improve access to medicines in the developing world.

We are at a crossroads in the epidemic. If we take our foot off the pedal now, we risk allowing HIV to flourish. Whilst we do not yet have a cure or a vaccine for HIV, we do have the knowledge and technology to allow people living with HIV to live long and healthy lives, and to create an AIDS free generation. Each of the barriers detailed in *Access Denied* can be overcome with human determination and coordination. Now is the time for each of us to make renewed and bold calls to give access to medicines for all people living with HIV, and ensure that no one is left behind.

Pamela Nash MP

Chair of the All Party Parliamentary Group on HIV and AIDS

Special thanks also to: Baroness Barker, Lord Norman Fowler, Mike Freer MP, Graham Jones MP, and Russell Brown MP. The final report was compiled by Susie Pelly, Policy Advisor to the APPG. If you would like further copies of the report, please contact susie.pelly@parliament.uk

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Methodology

The All Party Parliamentary Group (APPG) on HIV and AIDS announced in February 2014 that it was going to conduct an inquiry into access to HIV treatment in low and middle income countries (LMICs). The purpose of the inquiry was to investigate barriers to the access of HIV treatment in LMICs and to provide an update of *The Treatment Timebomb* report, which was produced by the APPG on HIV and AIDS in 2009.¹ We issued a call for written evidence to a wide range of stakeholders including civil society organisations, universities, government departments and the private sector.

We received around 40 submissions to the inquiry, undertook visits to India and South Africa and held three oral evidence sessions in Parliament. In both India and South Africa we met with representatives from a cross-section of organisations involved in HIV including local civil society, international NGOs, generic drug companies and government officials.

The initial focus of the inquiry was to assess concerns around the high prices of drugs in developing countries. This was based on the conclusion of *The Treatment Timebomb* report in 2009, that the high prices of second and third line drugs would be the major barrier to access in the future. However, it became clear throughout the inquiry process that several other issues deserved our attention. The report addresses these other barriers, such as lack of access to viral load testing, the neglect of key populations, lack of prioritisation of paediatric care, growing concerns about access in middle income countries (MICs), research and development (R&D) gaps, weak health systems, and inadequate supply chain management.

1. *The Treatment Timebomb*, All Party Parliamentary Group on HIV and AIDS, [Online] <http://www.appg-aids.org.uk/Publications/treatment%20timebomb.htm>, 2009.

Executive summary

Five years have passed since the APPG's *Treatment Timebomb* report was published. Since then the AIDS response has moved on considerably with a decrease of 35% in AIDS-related deaths since 2005² and a vast improvement in access to first line treatment in LMICs.³ However, we should not allow these positive figures to mask the alarming truth that 1.5 million people died from AIDS-related causes in 2013.⁴

That is a vast number, particularly when put into context: those within the developed world living with HIV are more likely to die of old age than of AIDS-related co-infection due to effective treatments, which allow a long and healthy life. Access to treatment is still being denied to too many people. This report attempts to go some way towards breaking down the causes of, and exploring the potential solutions to, this challenge.

We have reached a crossroads in the AIDS response. Great progress has been made over the last five years; however, international aid and public interest in HIV and AIDS is diminishing. The World Health Organization (WHO) has changed its guidelines on antiretroviral (ARV) treatment, thus making the 2011 UN General Assembly declaration to reach 15 million people with ARV treatment by 2015 appear somewhat unambitious.⁵ Under the new guidelines the estimated number of people now eligible for treatment is around 28.6 million.

Underpinning the changes in WHO guidance is increased scientific understanding of HIV. We now know, for example, that starting treatment earlier saves lives and, thanks to ground-breaking research published since the first *Treatment Timebomb* report, we now have proof that treatment is highly effective at preventing transmission of the virus. This new tool, combined with improved targeting of a range of effective prevention interventions, means that we could significantly reduce the number of new cases of HIV by scaling up our response. But, despite our greater understanding of what is needed to finally bring the epidemic under control, political and financial momentum are sadly lacking. According to figures from the United Nations Programme on AIDS and HIV (UNAIDS), international donor funding for the HIV response is stagnating with funds remaining largely the same since 2008.⁶ With the post Millennium Development Goals currently under negotiation, this is a crucial moment to reassess what is needed at a global level to ensure we confine AIDS to the history books.

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2. *The Gap Report*, UNAIDS, [Online] http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2014/UNAIDS_Gap_report_en.pdf, 2014.
 3. *New Country Classifications*, World Bank, [Online] <http://data.worldbank.org/news/new-country-classifications>, 2013.
The report uses the World Bank classifications of development. As of 1 July 2013, the World Bank income classifications by GNI per capita are as follows:
 - low income: \$1,035 or less
 - lower middle income: \$1,036 to \$4,085
 - upper middle income: \$4,086 to \$12,615
 - high income: \$12,616 or more
 4. *Fast Track, Ending the AIDS epidemic by 2030*, UNAIDS, [Online] http://www.unaids.org/en/resources/documents/2014/JC2686_WAD2014report, 2014.
 5. *Resolution adopted by the UN General Assembly*, United Nations, [Online] http://www.unaids.org/en/media/unaids/contentassets/documents/document/2011/06/20110610_UN_A-RES-65-277_en.pdf, 2011.
 6. *UNAIDS World AIDS Day report*, UNAIDS, [Online] http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/JC2434_WorldAIDSday_results_en.pdf, 2012.

In 2009, the APPG warned that we were heading towards a “treatment timebomb” as the number of people needing treatment would rise dramatically beyond 2015. Today, these projections remain relevant with only 34% of the 28.6 million people eligible for treatment currently receiving it in LMICs⁷ and with upwards of 55 million people expected to need ARV therapy by the year 2030.⁸ With access to medicines remaining a major barrier to tackling the HIV and AIDS epidemic, the APPG decided to re-visit this issue to understand why treatment remains elusive to so many, despite the continuing decrease in price of quality first-line ARVS. This treatment is currently available for around US\$140 per person per year (pppy) a significant decrease from 2000 when treatments were still under patent and priced at more than \$10,000 pppy.⁹

This inquiry demonstrates that while the prices of ARVS are coming down for first-line treatment, second and third-line treatment is still largely out of reach for the majority of people living in LMICs. This is not solely due to price, although high prices of second and third-line treatment continue to be major barriers to access. Within this report we explore the other obstacles to treatment access including:

- the lack of political prioritisation of key populations (men who have sex with men, sex workers, drug users and transgender people¹⁰) for treatment
- the damage inflicted by stigma and discrimination
- poor supply chain management
- weak health systems
- lack of access to viral load testing
- lack of streamlining in drug registration processes
- the withdrawal of international funding from MICs coupled with lack of access to generic drugs
- lack of investment in R&D, particularly for paediatric medicines.

Based on these barriers, this report outlines a set of updated recommendations, which we feel must be addressed holistically to end the AIDS epidemic and achieve the Millennium Development Goal “to halt and reverse the spread of HIV and AIDS”. This report calls for:

- the UK government to ensure R&D works for people as well as profits so that paediatric medicines are as effective as adult treatment
- the UK government, the pharmaceutical industry and multilateral organisations to work together to make second and third-line ARV drugs available and affordable to all, including marginalised populations and people living in MICs
- the Global Fund to prioritise viral load testing to become the gold standard of treatment for **everyone**
- the UK government to ensure that health and drug distribution networks are strengthened before withdrawing aid (regardless of a country’s Gross National Income (GNI) status) to enable the long-term sustainability of any aid-assisted development.

7. *AIDS by the numbers*, 2013.

8. *The Treatment Timebomb*, 2009.

9. *Untangling the Web of Antiretroviral Price Reductions*, MSF, 17th edition, [Online] http://www.msfacecess.org/sites/default/files/MSF_UTW_17th_Edition_4_b.pdf, July 2014.

10. *UNAIDS Terminology Guidelines*, UNAIDS, [Online] http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/JC2118_terminology-guidelines_en.pdf, 2011.

REPORT FORMAT

Section 1

Provides an overview of the main barriers to access to medicines in LMICs

Section 2

Looks at the underlying causes for high drug prices and potential solutions

Section 3

Analyses other barriers to access

Section 4

Looks at the current gaps in R&D for HIV and what is needed for the future

Section 1

Overview of barriers to access in low and middle income countries

The number of people receiving antiretroviral treatment (ART) has increased. However, significant population gaps still remain. UNAIDS' data indicates that treatment coverage for children living with HIV in 2012 was less than half that for adults: key populations continue to fall behind the general population in terms of access to medicines.¹¹ According to WHO, the uptake of second-line and third-line treatment regimens in LMICs remains low despite changes in WHO guidance.¹²

The considerable data available highlights clear trends within the LMICs. However, there is a dearth of data on the price of medicines in upper middle income countries (UMICs) such as Brazil, Kazakhstan, Ukraine, Latin American and Asian countries.¹³

This lack of information is exacerbated by the fact that the majority of these countries do not receive funding for HIV medicines Global Fund or other major donors. These countries face a serious challenge: they cannot afford to purchase generic medicines but their international aid is simultaneously being withdrawn. This causes major problems for people living with HIV in these UMICs. They are caught in an impossible situation with their own governments unable or unwilling to pay for their treatment.

This section will summarise APPG's key findings on the continued existence and exacerbation of gaps in access including:

- lack of viral load testing and R&D investment in paediatric medicines,
- high prices for medicines in MICs
- a lack of prioritisation of key populations
- weak and inefficient health systems and supply chains.

We explore the underlying causes and potential solutions to overcome these barriers in greater detail in later sections.

11. *AIDS by the numbers*, 2013.

12. *Access to Antiretroviral drugs in low and middle income countries 2014 update: Technical Report*, WHO, 2014.

13. *Ibid.*

Barrier 1: Poor standards of monitoring = poor standards of treatment

Viral load testing is the gold standard of HIV treatment monitoring and is used routinely in the developed world. Despite being recommended by WHO, it remains out of reach for the majority of people living with HIV in the developing world.¹⁴

Viral load testing allows clinical staff to pick up on issues with treatment adherence or drug resistance rapidly when the amount of virus in the body spikes rather than waiting for that increased viral load to attack the immune system leading to a drop in CD4 count. Viral load testing therefore acts as an early warning system, reducing the likelihood of drug resistance developing. Without viral load testing, some patients do not receive second or third-line treatment until their symptoms are so bad that they risk fatality.

On the APPG's recent visit to India we heard how the lack of viral load testing is proving a major barrier to treatment. We spoke with NGOs and the government in India who had differing views about the availability of second-line treatment for people living with HIV. The National AIDS Control Organisation (NACO) assured us that India is planning to scale up viral load testing in the next year but Médecins Sans Frontières (MSF) India highlighted a number of major concerns. Primarily, that there are only nine viral load centres in India with capacity for 10,000 people. This capacity falls far short of covering the 2.1 million people currently living with HIV in India.



CD4 COUNTS

CD4 is a glycoprotein found on the surface of immune cells.

800+ is a healthy CD4 count.

350 – at this count patients start treatment in the UK. WHO now recommends that patients start treatment when their CD4 count falls to 500.

100 – the average count of people starting treatment in developing countries is just above this number. This is dangerously low and people will already be very ill.

Members of the All Party Parliamentary Group on HIV and AIDS and the leadership of the National Coalition of PLHIV in India (NCPI+) with the staff of the Vihaan Care & Support Centre, implemented by the Network of People Living with HIV in Mumbai.

14. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: Recommendations for a public health approach, WHO, 2013.

In addition, for those living in rural areas it is a lengthy process to get tested and can take up to a year to get treatment. In order to get the viral load test HIV patients must present themselves to, and get the approval of, a panel of experts. MSF argue this is a bureaucratic process which serves no purpose other than to suppress demand because the government does not have the capacity to get everyone tested. MSF report that in one particularly tragic case, a person died giving evidence to the panel. Given that a viral load test is an early indicator of the need for second-line treatment, it is clear that many people simply are not receiving the life-saving treatment they should.

It became apparent from these discussions and numerous submissions that, despite the need for viral load testing, it is not being rolled out in all countries to the extent required. This is partly due to the current complexity of the test, which requires specialised laboratory facilities. The majority of people living with HIV in India live in remote settings, and district level laboratories often do not have the power supplies, technology, staff and transport to effectively carry out the tests.¹⁵ This situation is common to other LMICs. MSF do point out that newer, cheaper, and simpler technologies have been developed, but need to be prioritised by the international donor community as the next phase in the AIDS response.

In a recent study of six countries MSF also highlighted the issue of lack of transparency regarding the cost of testing as a barrier to access. The cost of a comprehensive viral load test ranges from US\$24.90 to \$44.07. However, MSF's data also suggests that if countries responding to their survey had access to the lowest available price, the range of comprehensive costs, including implementation, would drop to US\$16.78–\$29.14. MSF states that prices are coming down for viral load testing, given the relatively low cost of manufacture and opportunities to achieve economies of scale. However, there is still considerable room for price decreases through negotiations with large volumes (based on reliable forecasting), and by optimising throughput (efficiency) of each instrument, to reduce per test costs.¹⁶

Considerable efforts are being made to address market barriers to diagnostics by market shaping organisations such as UNITAID and the Clinton Access to Health Initiative (CHAI) and supported by the Department for International Development (DFID). For example, between 2012 and 2014, \$20mn has been committed by UNITAID to CHAI and its partner UNICEF to lower barriers and accelerate access to point-of-care HIV diagnostics (viral load, early infant diagnostics and CD4) in seven high-volume, early adopter countries: Ethiopia, Kenya, Malawi, Mozambique, Tanzania, Uganda and Zimbabwe. UNITAID purchasing power will be leveraged to drive demand and lower costs to ensure that testing sites outside the target countries also have access to high quality, affordable point-of-care HIV diagnostics. In addition, UNITAID and CHAI are working with new suppliers to help them with the regulatory and policy approval process to scale-up support.

Another important recent development was the announcement by healthcare company Roche on 25th September 2014 regarding a major Global Access Programme to sharply reduce the price of HIV viral load tests in LMICs. This new initiative creates a ceiling price of US\$9.40 per test, and will reduce Roche's average price by more than 40% in LMICs. When fully implemented, the Global Access

15. *Undetectable load: How viral monitoring can improve HIV treatment in developing countries*, MSF, [Online] http://www.msfaaccess.org/sites/default/files/MSF_assets/HIV_AIDS/Docs/MSF_ViralLoad_Report_FINAL_Sept2012_webres.pdf, September 2012.

16. *How low can we go? Pricing for HIV Viral Load Testing in Low- and Middle-Income Countries*, MSF, Access Campaign, December 2013.

Programme is projected to save more than US\$150 million in costs over the next five years. The agreement was designed and driven by the CHAI as part of DFID's "market shaping for access to safe, effective and affordable health commodities" programme. The price reduction is possible due to bulk procurement agreements negotiated by CHAI. This is an excellent example of public-private partnerships achieving tangible successes. Although this does not address other barriers to accessing viral load testing, such as the need for affordable point of care tests, it is certainly a significant step in the right direction.

Barrier 2: Some middle income countries cannot afford treatment

The Global Fund, UNITAID and other global funders have played a central role in facilitating greater access to medicines in LMICs. We must analyse the role that the global players need to play to ensure access to medicines is sustained and increased in future.

International funding for the AIDS response has stalled. On the other hand, according to DFID's latest position paper on HIV *Towards Zero Infections – Two Years On*, "domestic spending on HIV has increased, accounting for 53% of global HIV resources in 2012."¹⁷ This increase in domestic funding should be applauded, but the stagnation and withdrawal of international funding is causing problems in many MICs, particularly MICs outside of Sub-Saharan Africa.

Many MICs are trapped in an impossible position due to the combined effect of international aid withdrawal and barriers to accessing cheaper generic medicines. The procurement of cheaper drugs involves complex negotiations between national governments and the pharmaceutical industry. Countries receiving international aid have so far relied on the Global Fund and other donors to enable access to cheaper drugs. This has been achieved through international cooperation between the pharmaceutical industry, international donors and generic drug companies. Without these interventions MICs will, in many cases, find it much harder to purchase cheaper drugs.

International donors and the multilateral health agencies must take into consideration the fact that as more countries graduate from low income to middle income status, the problem above will be exacerbated.

While India leads the way in supplying generic drugs to LICs in the developing world, sales to MICs are limited due to patent restrictions. It is the same scenario for other generic manufacturers in countries such as South Africa and China. Most countries with manufacturing capabilities are subject to World Trade Organization (WTO) rules, which can sometimes stand in the way of public health needs. The reasons for, and consequences of, this will be explored in the second section of the report.

Until MICs are ready to assume the costs and management of HIV treatment and care (including the ability to purchase drugs at higher prices), a strategy needs to be developed to ensure that we do not reverse the progress already made in these countries.

17. *Towards Zero Infections – Two Years On: A Review of the UK's Position Paper on HIV in the developing world*, Department for International Development, November 2013, 8.

The Global Fund sought to address this issue with the Equitable Access Initiative, plans which are still under discussion. Originally described as a “tiered pricing” initiative, it has come under scrutiny and criticism from civil society who are concerned about a narrow focus on limited and controversial solutions, lack of involvement from MICs, the over-involvement of the pharmaceutical industry, and WHO’s role which is restricted to observer status. The purpose of the initiative has shifted since its initial inception. According to Global Fund Executive Director Mark Dybul’s evidence to the inquiry, the current stated purpose is to gather evidence of factors other than GNI in MICs that impact development. This will provide an understanding of how best to achieve access to treatment in these countries. Donors are pulling out of MICs based on an outdated “measure” of development, which has been in place since 1978 (instituted by the World Bank). Therefore, the Global Fund is proposing that donors who invest in health could potentially use coefficients around different classifications (e.g. numbers of people living in poverty) to measure development rather than the current system of GNI.

Civil society concerns are valid to some extent but the project is still at its very early stages. It remains to be seen whether it can address all the obstacles to MICs accessing medicines through global funding or by supporting the implementation of policies that deliver more affordable medicines. The APPG supports the shift in focus away from the original concept towards developing more equitable ways to set thresholds for donor funding.

Barrier 3: Key populations are being left behind

As the *UNAIDS report on the global AIDS epidemic 2013* demonstrates, key populations are being left behind in terms of access to HIV treatment across the globe.¹⁸ Although this problem is not confined to UMICs, it is particularly acute in some of these countries due to the rapidly growing HIV epidemics amongst key populations (e.g. those states of the former Soviet Union and Central Asia). As pointed out by MSF in their submission to the APPG, the problem of pricing in UMICs is compounded by the fact that the epidemics in these countries are not generalised but rather concentrated in marginalised populations (e.g. injecting drug users, sex workers, men who have sex with men, transgender people). As discussed, many global funders are actively restricting funding to these countries. This inevitably creates barriers to access for the most vulnerable groups.

UNAIDS also highlight the barriers to treatment created by punitive and discriminatory legislation which exists in many countries:

“As of 2013, 63 countries have in at least one jurisdiction specific provisions that allow for the persecution of HIV non-disclosure, exposure and/or transmission. Criminalisation of key populations also remains widespread, and 60% of countries report having laws, regulations or policies which present obstacles to effective HIV prevention, treatment, care and support for key populations and vulnerable groups.”

UNAIDS 2013

18. *Global Report: UNAIDS report on the global AIDS epidemic 2013*, UNAIDS, [Online] http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf, 2013.



APPG delegation with the Sex Workers Education and Advocacy Taskforce.

Barrier 4: Paediatric medicines continue to fall behind while treatment is poorly managed

Vital medicines for the survival of children are simply not a profitable market for big pharmaceutical companies as it is mainly in the developing world that children are still being infected with HIV. Global funders have tried to address this issue by focusing largely on prevention of mother-to-child transmission (PMTCT). This has shown considerable results but, it is not sufficient. Children who are already infected must also be able to access treatment, and despite best efforts at PMTCT, it is still estimated by WHO and UNICEF that by 2020, 1.9 million children will require HIV treatment.

UNITAID reports that only 0.6 million or 18% of 3.3 million children living with HIV in LMICs are currently receiving treatment.¹⁹ The figures from UNAIDS show that “without treatment, about one third of children living with HIV die by their first birthday and half die by their second birthday. Initiating ART before the twelfth week of life reduces HIV-related mortality in children living with HIV by 75%”.²⁰ Early infant diagnosis (EID) is a key bottleneck in diagnosing children for a number of reasons, including:

- the difficulty of keeping track of mothers and babies after birth
- poor implementation of early infant testing policies
- lack of routine early infant testing by health workers
- the fact that currently testing is recommended at 6 weeks which may be too late for many babies.

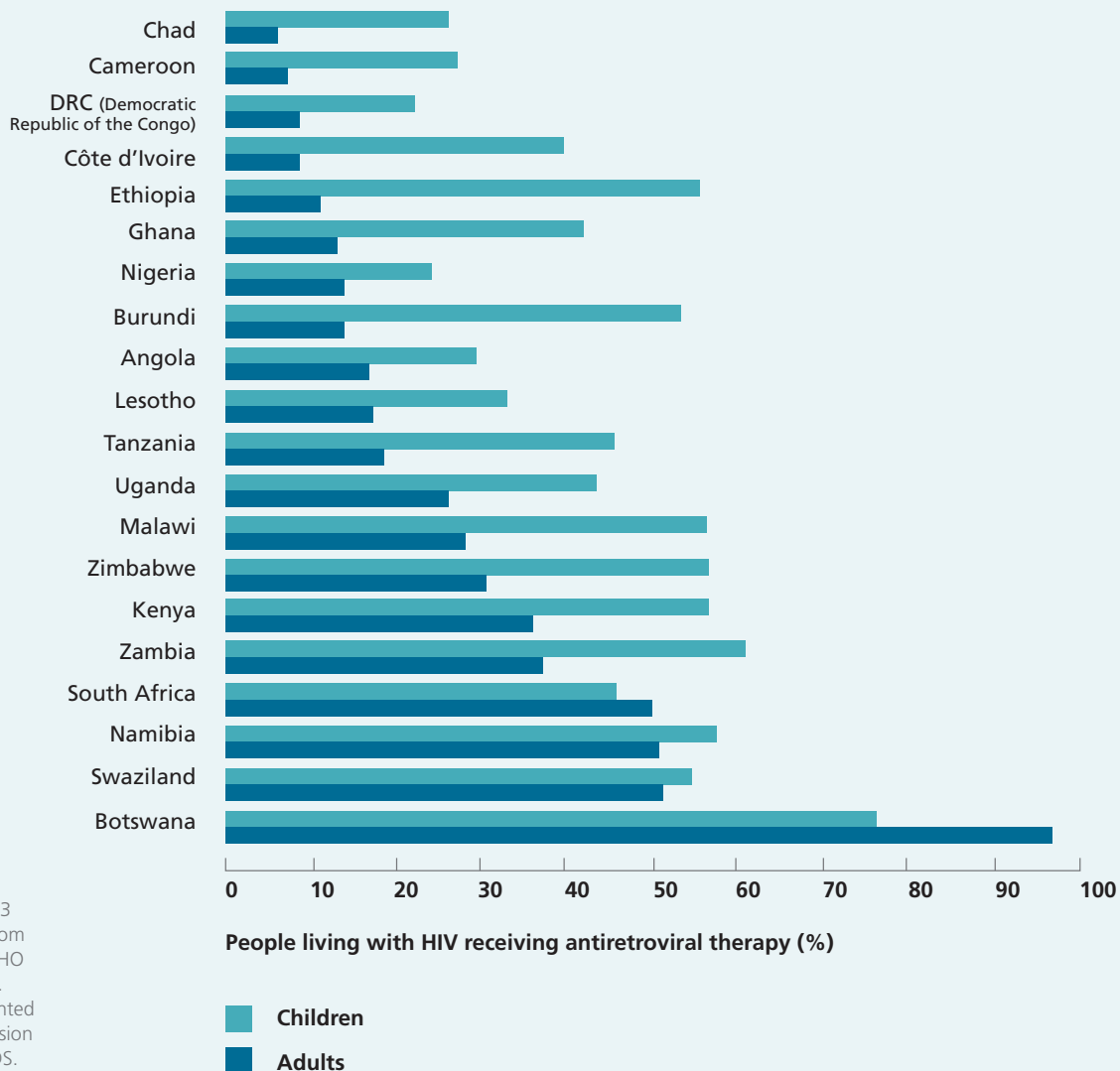
Figure 1 illustrates the disparities in adult and paediatric treatment in HIV.

19. Annex 1: Strategic Review of the Medicines Patent Pool, UNITAID, 2011.

20. The Gap Report, 2014, 238.

FIGURE 1

Percentage of adults (aged 15+) and children (aged 0–14) living with HIV who were receiving antiretroviral therapy in 2013, in 21 priority countries



Source: 2013 estimates from UNAIDS, WHO and UNICEF. Graph reprinted with permission from UNAIDS.

WHO recommended treatment for children under the age of three is a regimen containing lopinavir/ritonavir (LPV/r). As reported by WHO “in 2013, for the first time, a regimen containing LPV/r with 3TC (lamivudine, *Epivir*) and AZT (zidovudine, *Retrovir*) or ABC (abacavir) became available for less than US\$200 ppy”.²¹ The report further points out that this price is still considerably more than that of the secondary option recommended by WHO, which is a nevirapine (NVP) based regimen.

NVP-based regimens are sub-optimal because they have lower efficacy and worse side effects. At half the price, US\$97 ppy, this sub-optimal option remains the most frequently used regimen in paediatric treatment. In addition to the reduced cost, NVP-based regimens tend to be favoured for infants because the current

21. *Access to Antiretroviral Drugs*, 2014.

LPV/r regimen for children under three is a syrup with a very unpleasant taste, which needs to be refrigerated and contains a significant amount of alcohol. These limitations in the treatment are especially important with children.

The treatment available to children is not at the same standard as the regimen in place for adults. Strategies to address lack of R&D in paediatric medicines are discussed in greater detail in Section 5 of the report.

Country Director for Children's HIV Association (CHIVA) South Africa, Juliet Houghton, raised a number of other issues, which affect access to paediatric and adolescent treatment aside from the price and quality of drugs. She argues that children are at risk of negative lifelong consequences including stunting and neurocognitive consequences due to the late starting of treatment and lack of EID, which is often down to mismanagement of treatment in the child's early years and the difficulties of testing for HIV in babies and children. Houghton believes that children and adolescents should be seen as a key population and warns:

“Children are at high risk of developing multi-drug resistance because of their reliance on adult caregivers to enable access to treatment and care, coupled with challenges with capacity of healthcare workers to provide comprehensive management and treatment.”

JULIET HOUGHTON, COUNTRY DIRECTOR OF CHIVA, SOUTH AFRICA

Another major challenge is management of clinical data. Children need to be measured every three months to ensure they have the correct dosage of medicine and there is no centralised system to maintain this data. Furthermore, unless healthcare facilities know how many patients they have, follow-up is almost impossible. This is complicated by stockouts, which are discussed in greater detail later in the report. Specialist HIV healthcare company, ViiV Healthcare, are working with partners in South Africa (including the Department for Health) to develop the Paediatric ART Clinic Software Development Project (PASDP). This appears to be addressing the issue to some degree but, more is needed at a global level to encourage greater cooperation between the private and public sectors to meaningfully tackle the problem on a larger scale.

Barrier 5: Weak health systems, supply chain management, and insecure funding

Other barriers highlighted during the course of this inquiry include:

- huge delays and lack of streamlining in drug registration
- corruption
- poor supply chain management leading to stockouts
- lack of patient data
- inaccurate forecasting from the global funding agencies.

Another key concern highlighted by generic companies is that while WHO recommendations have increased the number of people eligible for treatment up to 28.6 million, there is no commitment from the major donors to finance these increased numbers. The generic companies argued that without this commitment it would be too risky for them to expand their ARV business. This has led to bottlenecks in the supply of active pharmaceutical ingredients (APIs).

DFID in their latest policy paper, state that “due to structural barriers such as stigma and discrimination, and poorly functioning health systems, at least 16 million people in need of treatment are still not accessing services under the new WHO 2013 treatment guidelines.”²² The APPG’s research has found that these issues do pose considerable barriers to access. However, DFID should use its leverage as a donor to ensure multilateral institutions such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, WTO, WHO, World Intellectual Property Organization (WIPO) and UNITAID are doing enough to bring prices and down. It must use its voice to demonstrate leadership on this issue.

Conclusions

The current state of access to second and third-line drugs is low in all LMICs due to lack of financing, low availability of viral load testing and high drugs prices, with progressively higher drug prices for MICs and UMICs. Paediatric treatment also remains considerably behind adult treatment due in part to the very low number of at-risk children with access to diagnosis, a lack of R&D into new, improved medicines, and inadequate management of treatment.

Access to first, second and third-line treatment is restricted in UMICs, particularly for marginalised populations, due to a combination of withdrawal of aid, inability to access generic medicines and punitive legislation. The Global Fund is working towards addressing the access to treatment issues in MICs but it is too early to say whether this will have a significant impact. It has, however, abandoned any focus on tiered pricing, which is a step in the right direction.

Baroness Liz Barker talks to doctors at an HIV clinic in Delhi.



22. *Towards Zero Infections – Two Years On: A Review of the UK’s Position Paper on HIV in the Developing World*, 2013.

Recommendations

- 1.** The pace of the roll-out of affordable viral load monitoring tools needs to be drastically increased and prioritised by international donors. Prices of viral load testing should be transparent and measures taken to decrease prices.
- 2.** Lack of access to funding and treatment for key populations must be urgently addressed by international donors such as DFID and the Global Fund:
 - i.** DFID should significantly increase its funding for key population groups' advocacy for better access to treatment and services, including an increase in its investment in the Robert Carr Networks Fund
 - ii.** The Global Fund should reassess its decision to withdraw funding from key population groups in MICs unless there is clear evidence of how funding for services and treatment will be provided.
- 3.** A comprehensive strategy needs to be found by international donors and multilateral health organisations to address the gap in funding to MICs as international donors pull out, while countries are being forced to pay higher prices for ARVs and to introduce strict Intellectual Property (IP) rules.
- 4.** The Global Fund's Equitable Access Initiative should be closely monitored by DFID and WHO to ensure it focuses on issues of graduation of MICs from development assistance, and not on trying to introduce tiered prices for MICs. If the initiative successfully delivers on providing new global development indicators, DFID should use the Global Fund's findings to influence future funding decisions.
- 5.** DFID should place greater emphasis on the treatment of children and adolescents living with HIV in its policy and programming. Children and adolescents should be given the same priority as key populations, given the added complexities involved in EID and management of therapy, as well as the neurological damage that can be caused by the late starting of treatment in these vulnerable populations.
- 6.** DFID should lead the way in harnessing donor support for the Global Fund to cover the cost burden of the increased numbers of people (28.6 million) now eligible for ARV treatment under WHO guidelines.

PART 1

Section 2

Underlying causes and potential solutions for high drug prices

The last APPG report concluded that generic competition was the most effective method of reducing the price of antiretroviral drugs. This was based on the role it played in bringing down the price of ARVS from US\$10,000 pppy to approximately US\$100 pppy in under a decade. This was reiterated by a number of academics in the *Bulletin of the World Health Organization* in 2009.²³ It was also recommended that countries use flexibilities granted under the Trade Related Aspects of Intellectual Property Agreement (TRIPS) and update their IP laws to enable generic competition. This section will examine whether generic competition continues to enable greater access to treatment and the extent to which countries have utilised TRIPS flexibilities and reformed IP legislation to encourage drug price reductions.

Second and third-line treatments are still too expensive and inaccessible

Since *The Treatment Timebomb* was written, the landscape for ARVs has changed considerably. At the time, more toxic stavudine (d4T)-based regimens were predominant in LMICs. Today, as recommended in the report, preferred tenofovir (TDF)-based regimens of first-line treatment have become more affordable in almost all countries.²⁴ This has been largely thanks to generic competition and continued pressure from civil society to ensure the best and most effective medicines are available to people in the developing world. According to WHO, the Medicines Patent Pool licence with Gilead on TDF has also helped open up the market for TDF-based combinations.²⁵

The story is not quite the same for second and third-line treatment. Second-line drugs remain twice the price of first-line for LMICs at US\$243 pppy for the most affordable combination, which is not available in all LMICs. However, this does represent a 75% decrease from 2006 when MSF reported that the cost of second-line drugs was US\$1,198 pppy.²⁶ This price decrease has been largely due to a successful opposition to a patent in India on lopinavir/ritonavir (LPV/r) and later

23. Waning B, Kaplan W, King AC, Lawrence DA, Leufkens HG, Fox MP, Global Strategies to reduce the price of antiretroviral medicines: evidence from transactional databases, *Bulletin of the World Health Organization*, July 2009, 87(7):520-8.

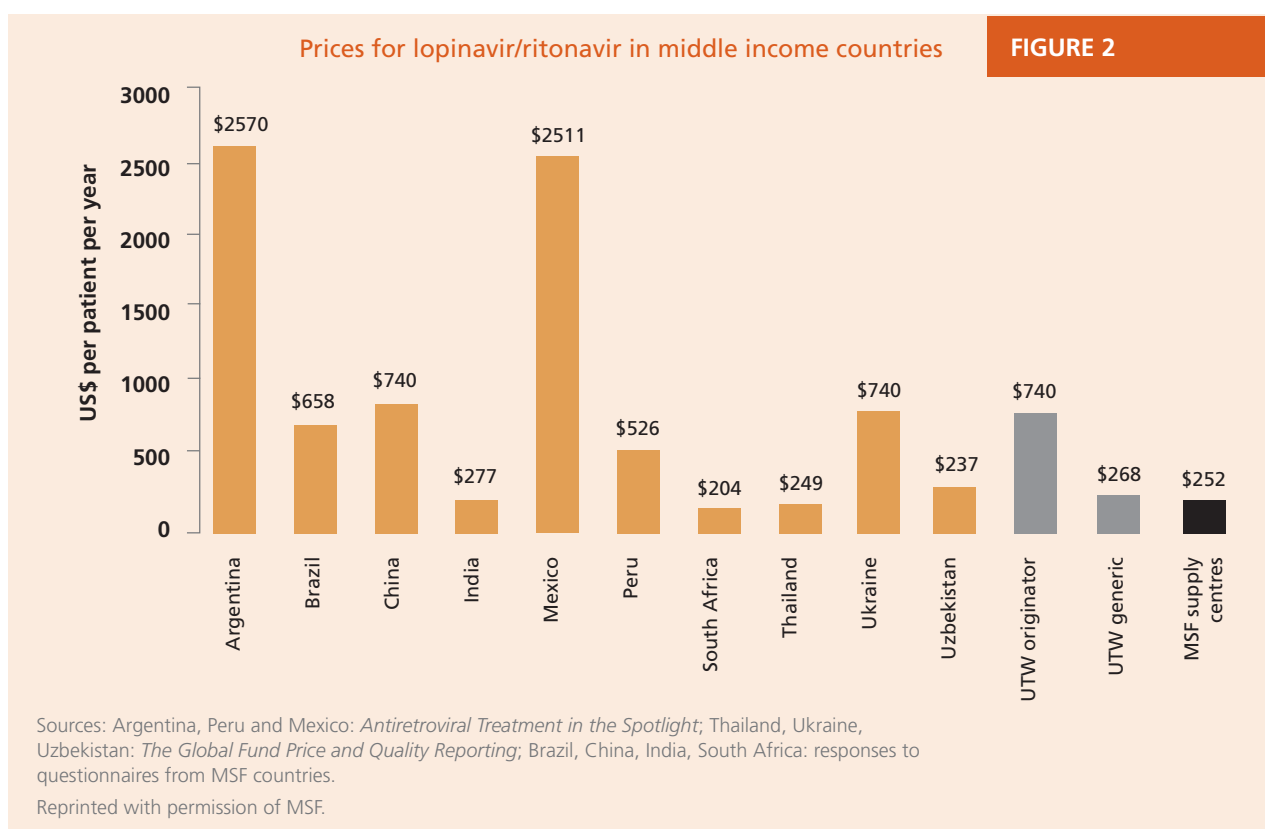
24. Partnership for Supply Chain Management submission: "The concerns about the costs of Tenofovir (TDF)-based fixed dose combinations (FDCs) have been largely overcome by market forces as volume demand for TDF-based FDCs has ramped up. Prices of generic TDF FDCs are now at around \$11 per bottle, excluding freight and delivery costs, which is not dissimilar to Stavudine (d4T) products. The FDC lamivudine, Zidovudine, Nevirapine is now around \$8 per bottle. Cost is therefore not a significant barrier to the phase out of d4T."

25. *Increasing access to HIV treatment in middle income countries: Key data on prices, regulatory status, tariffs and the intellectual property situation*, WHO, 2014.

26. *Untangling the Web*, 2014.

atazanavir/ritonavir (ATV/r), both WHO recommended regimens for second-line therapy. Given that the Indian generic industry accounts for over 90% of ARVs sold in developing countries, a successful patent opposition there can provide benefits to the rest of the developing world. The recent MPP licence on atazanavir (ATV) should also help to make the ATV/r combination more affordable in more countries in the near future. Clearly, second-line treatment is available and reasonably affordable in most LMICS. However, as stated earlier in the report, access is still seriously restricted by lack of viral load testing and in some MICs, high prices.

According to MSF's latest *Untangling the Web* report, MICs, especially those in Latin America, continue to pay exorbitant prices for LPV/r for use in second-line regimens. Argentina (US\$2,570 ppy) and Mexico (US\$2,511 ppy) paying over 12 times more for LPV/r than South Africa (US\$204 ppy). *Figure 2* demonstrates the prices paid across a range of middle income countries.²⁷



At present there are still no WHO pre-qualified generic versions of the three new drugs raltegravir (RAL), etravirine (ETR) or darunavir (DRV), which are used for third-line treatment. The prices of these drugs remain extremely high with the best possible price for a regimen at US\$2,006 ppy in the poorest countries. It is also worth remembering that the prices discussed here are the best case scenarios in the poorest countries that benefit from global procurement and does not include UMICs, many of which are paying astronomical prices for medicines.

27. *Untangling the Web*, 2014.

New drugs for co-infections TB and hepatitis C are out of reach to people who need them most

The high prices of new drugs to treat TB and hepatitis C (HCV) have also been raised as major concerns/potential opportunities throughout the APPG inquiry. More people living with HIV die from TB than any other co-infection.

December 2012 was a landmark moment for people who suffer from multi drug-resistant TB (MDR-TB) with the FDA approval of bedaquiline, the first new drug available for TB in 50 years. A second new drug, delamanid, has recently been approved by the European Medicines Agency. However, bedaquiline is still not reaching the 1 million people who may need the drug. This is due to the high price at US\$3000 in MICs, US\$30,000 in upper income countries and \$US 900 in LICs coupled with a lack of access to diagnostic services.²⁸

According to MSF current access schemes for bedaquiline are not sufficient to enable LMICs to purchase the medicines. Action must be taken to ensure this new drug is not a missed opportunity to treat MDR-TB in the world's most affected places.²⁹

WHO estimates that there are as many as 130–150 million people, or 3% of the world's population, currently living with HCV.³⁰ Although HCV is a global epidemic, it disproportionately affects marginalised groups, such as people living with HIV and people who inject drugs. It results in more than 350,000 liver-related deaths per year. According to the Open Society, while the disease is curable, the vast majority of people affected by HCV live in LMICs where treatment is virtually inaccessible.³¹ The International HIV/AIDS Alliance also pointed out in their submission to the inquiry that HCV affects 20% of people living with HIV worldwide and 1 in 10 cases are due to injecting drug use.

The scale of the problem of HCV is vast. However, Gilead has recently developed a drug, sofosbuvir, that has the potential to cure HCV completely when combined with other direct acting antivirals. Here, we will address what more can be done to ensure access to treatment.

Currently, Gilead proposes to sell the drug to limited populations of patients in the public or voluntary sector in low income countries (LICs) and a few select MICs for at least US\$900 for a 12 week course of treatment. The branded drug would be sold at substantially higher prices in MICs and UMICs.³²

Gilead has also recently issued bilateral voluntary licences to a number of Indian generic drug companies for sofosbuvir and ledipasvir drugs to treat HCV. This will enable cheaper production and sales of the drugs to the developing world market. These agreements go some way to addressing access issues in approximately 90 countries. However, it should be noted that the majority of countries that will benefit from these agreements are low income. Given that 73% of HCV patients live

28. Erica Lessem, *The Tuberculosis Treatment Timeline*, I-Base. [Online] <http://www.pipelinereport.org/2013/tb-treatment>, 21 July 2012.

29. *DR-TB drugs under the microscope: sources and prices for drug-resistant Tuberculosis medicines*, WHO. [Online] http://www.msfaccess.org/sites/default/files/MSF_TB_Report_UTM3rdEdition-2013.pdf, 2013.

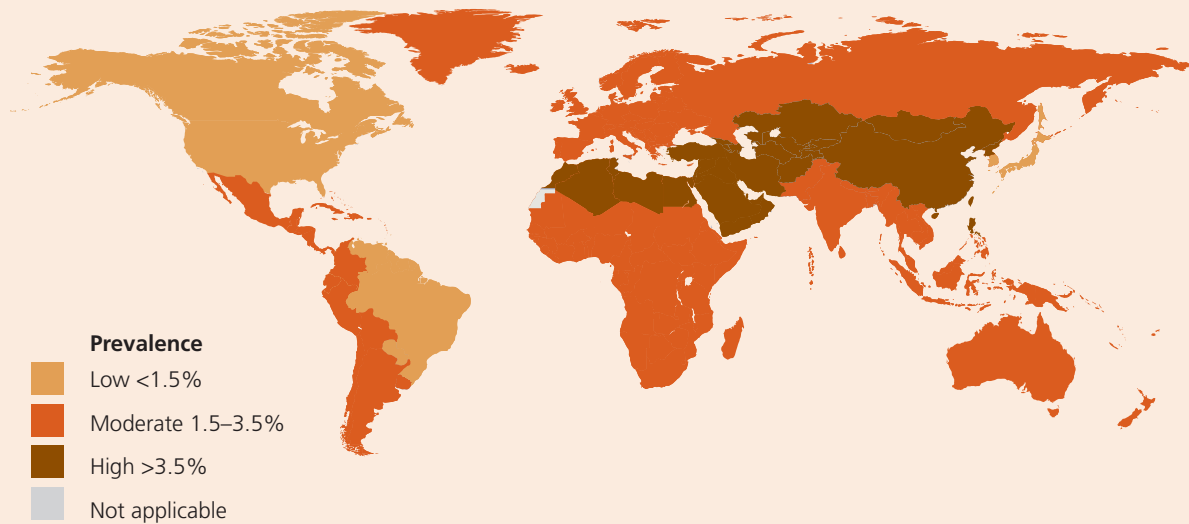
30. *Hepatitis, WHO fact sheet*. [Online] <http://www.who.int/mediacentre/factsheets/fs164/en/>, April 2014.

31. Momenghalibaf, Azzi. *Hepatitis C Treatment: Price, Profits and Barriers to Access*, Open Society Foundation. [Online] <http://www.opensocietyfoundations.org/sites/default/files/hepatitis-c-treatment-20130807.pdf>, 2013.

32. Erika Check Hayden, 'Activists sound alarm on tiered pricing' *Nature*, Issue 509, 22 May 2014, 412.

The global prevalence of HCV infection, 2005³³

FIGURE 3



Reproduced from Mohd Hanafiah K, et al. Anti-HCV prevalence by global burden of disease region, 2005. Reprinted with permission from MSF.

in MICs, which are largely excluded from the agreements, more action needs to be taken to address access in these countries.

The APPG recognises that Gilead has in many ways led the way in terms of delivering access to ARVs as the first company to sign up to the MPP. However, it is clear that there is potential for more to be done with HCV. Gilead's submission states that it is developing a treatment expansion programme to help ensure access to the drug in resource-limited settings, especially countries with a high HCV burden.

One way of ensuring access would be to include sofosbuvir in the MPP. Although HIV is predominantly a disease still situated in LICs and LMICs, over 70% of patients with HCV live in MICs. Therefore any MPP licence would need to include these countries. This will be explored in the next section of the report.

TRIPS FLEXIBILITIES

What can countries do to curb high drug prices using the Trade Related Aspects of Intellectual Property Agreement (TRIPS) flexibilities?

Where there is a public health imperative, countries can issue a compulsory licence to a generic manufacturer, on payment of a royalty to the owner of the patent. They can also apply a range of other public health safeguards and flexibilities to facilitate access to affordable medicines such as including a strict scope of patentability, the Bolar provision, parallel importation and pre-grant oppositions.

33. Mohd Hanafiah K, Groeger J, Flaxman AD, et al., *Global epidemiology of hepatitis C virus infection: New estimates of age specific antibody to HCV seroprevalence*, *Hepatology*, [Online] http://www.msfaaccess.org/sites/default/files/MSF_assets/HepC/Docs/MSF%20HCV%20landscape.pdf, 2012.

What more can be done to bring down prices?

The TRIPS agreement was a WTO agreement in 1995 to create minimum standards for the protection of IP for WTO members. In pharmaceuticals specifically, it led to the introduction of pharmaceutical product patent protection in many countries (such as India) that previously did not allow for product patents in pharmaceuticals. This created a public health problem as it meant that countries who had the capacity to make generic versions of drugs (like India) were unable to sell their drugs at cheaper prices to their own patients and to other developing countries that needed them most, including for HIV and AIDS.

The original intent of the TRIPS agreement was to retain safeguards for public health through a range of flexibilities to ensure patent monopolies did not prevent access to vital, low-cost, generic medicines. However, due to intense lobbying, this aspect of the agreement was largely annulled. Fortunately, this was later addressed by the Doha Declaration 2001. As outlined in *The Treatment Timebomb*, “the Doha Declaration of 2001 confirmed the legality of important flexibilities in (TRIPS) that allow countries to manufacture or import generic drugs.” This affirmation of the original intent of the WTO 1995 TRIPS agreement was an important landmark in the battle for affordable medicines in the developing world and has been used a number of times by different countries.³⁴

Compulsory licences have proved to be a useful tool; however, they are mostly a last resort with voluntary agreements the preferred option for the pharmaceutical industry. This often puts considerable pressure on governments not to issue compulsory licences. Submissions from civil society to the inquiry, including from STOPAIDS, highlight this pressure by pointing to the fact that India is on the US Trade Representative’s 301 Priority Watch List due to “inadequate protection of intellectual property”. This has been interpreted by some civil society groups as a response to India’s successful blockage of patents on a number of key drugs through Section 3d of its patent law which was introduced in 2005 to prevent “evergreening”. Evergreening is the process by which pharmaceutical companies file additional secondary patents (on new but very similar pharmaceuticals or other formulations or combinations) to delay generic entry to the market.

Another clear example of industry pressure is the case of South Africa earlier this year. South Africa is currently attempting to update its inadequate IP policy and legislation, one of the key levers for protecting generic competition and access to medicines. During our time in South Africa, the APPG met with the different departments involved in this process and uncovered a lack of cohesion within the government. The Department for Science and Technology were adamant that their patent system was adequate and reforming it would be too expensive and a pointless exercise, while the Department for Trade and Industry and Department for Health were fully supportive of the reforms.

Interestingly, prior to our visit, a leaked document outlining a lobbying plan for the Innovative Pharmaceutical Association South Africa (IPASA) – the representative body for pharmaceutical companies in South Africa – highlighted the industry’s plans to delay reforms.³⁵ The pharmaceutical industry has since distanced itself from these

34. *Access to Antiretroviral Drugs*, 2014.

35. Sarah Boseley, ‘South Africa pharma firms accused of planning to delay patent law reforms’, Guardian Online, [Online]. <http://www.theguardian.com/world/2014/jan/17/south-african-pharma-accused-delay-patents-law-reform>, 17 January 2014.

plans. The APPG would like to reiterate its recommendation from *The Treatment Timebomb* that IP reforms are encouraged and receive the extra support required from WHO, the United Nations Development Programme (UNDP) and WIPO to implement them effectively.

Threats to TRIPS flexibilities

Civil society organisations and UNITAID have highlighted concerns that the EU and the US are pushing for certain IP related provisions in the negotiation of Free Trade Agreements (FTAs) that would limit a country's ability to use its TRIPS flexibilities, known as TRIPS plus provisions. Given that the flexibilities are key to ensuring developing countries are still able to produce and sell generic medicines and that generic competition is the most effective way to bring down drug prices, the consequences for access to treatment could be very damaging.

One particular TRIPS plus provision of major concern is data exclusivity for clinical trial data generated for pharmaceutical products. This means that generic companies are unable to refer to clinical test data generated by the originator company, and submitted to drug regulatory authorities, for up to 10 years. Repeating these tests is extremely costly and unnecessary and is arguably only designed to delay generic companies from bringing a drug to market, thus preventing life-saving treatment from reaching the poorest when it is needed. This means that irrespective of the patent status of a medicine (including if a company does not have a patent in a particular country) data exclusivity prevents generic companies from securing marketing approval to market medicines unless they carry out time-consuming, costly and redundant tests.

The APPG recommends that WTO and WHO play a more active role in monitoring practices that suppress the use of TRIPS flexibilities in FTAs through TRIPS plus clauses with developing countries as TRIPS plus rules have a negative public health impact. In addition to receiving notification of FTAs from Member States, WTO should consider setting up guidance for FTA negotiations with the purpose of enabling developing countries to protect or safeguard the use of TRIPS flexibilities.



Student STOPAIDS campaigners carry out a publicity stunt on Westminster Bridge for World AIDS Day to raise awareness of the UK Parliament's role in improving access to medicines for people living with HIV.

FREE TRADE AGREEMENTS

A number of FTAs have been highlighted in the majority of submissions to the inquiry as cause for concern. UNITAID points out that “most, if not all FTAs involving the EU or the USA contain provisions on intellectual property rights that are ‘TRIPS-plus’ and have the potential and likely effect to hamper or prevent the use of one or more TRIPS flexibilities.”

Agreements of concern include the EU-India FTA (and potential FTAs with Thailand, Bolivia and Egypt), the Trans-Pacific Partnership agreement (TPP) between the US and 11 other countries through the Asia Pacific region and the Transatlantic Trade and Investment Partnership (TTIP), an FTA under negotiation between the US and EU. EU FTAs include a chapter on the protection, enforcement and promotion of IP rights.

In all these agreements, TRIPS-plus provisions are being negotiated and threaten the future stability of the generic drug industry and access to medicines as well as upsetting the balance established under TRIPS between protection of IP for medicines and promotion of public health and access to medicines for all.

UNITAID highlight that the TPP has been positioned as a “21st century agreement” by the United States, implying that other trade agreements might contain similar provisions going forward. MSF state in their submission that the TPP “is now the most damaging trade deal with respect to pharmaceutical access ever negotiated”. The Doha Declaration of 2001 must continue to be enforced and respected by all countries to ensure public health is prioritised over profits.

Local production – a potential solution?

Through this inquiry DFID and other contributors have suggested one possible medium to long-term solution to access problems created by more stringent TRIPS rules: a gradual shift towards a local production agenda. Given that LICs do not need to comply with TRIPS (until 2016), they could use this opportunity to develop their own pharmaceutical industry. This is already happening to a degree in South Africa and Uganda. Some attempts have been made to encourage local production in other LICs. Given the dominance of India and China over the generic ARV market, it is unlikely that LICs will be able to meaningfully compete in the near future. However, it is certainly a potential opportunity that should be explored by governments in LICs, the international community and the pharmaceutical industry.

A WHO policy brief on local production outlines some of the conditions required for investment in local production, including the capacity to manufacture products that would be both affordable and in demand.³⁶ It should therefore be noted that ARVs are not currently in short supply and that shifting supply would require considerable investment from international donors as well as the public and private sectors. Furthermore, it would require LICs to introduce a raft of industrial policy reforms

36. *Local Production for Access to Medical Products: Developing a Framework to Improve Public Health, Policy Brief*, WHO, 2011.

and would come with the considerable risk that, after said investment, LICs would lag considerably behind the Indian and Chinese generic industries. That is not to say that LICs could not take the lead on other related medical products and tools. Mark Dybul from the Global Fund reiterated this view point during the APPG inquiry oral evidence session when he stated:

“Now the problem comes when each country wants to do its own production. That is never going to be cost effective. So we’ve been talking with the countries in Africa. With their Heads of State work plan, they’re moving towards this regional production and even regional production by commodity so that there is a volume and cost benefit. But it’s not always the best place to do it. To be honest, a lot of this is being driven less by cost and production than jobs and creating jobs in their countries. And distribution systems create thousands and thousands of jobs.”

MARK DYBUL, GLOBAL FUND

Conclusions

Generic competition is still the best proven method to ensure sustainable price reductions of ARVs. It is still enabling greater access to medicines with significant price decreases in better quality first and second-line treatment since the last APPG report. More reductions could be made in second-line drugs and third-line still remains out of reach to the majority of LMICs. This is due in part to lack of viral load testing, which limits the demand for third-line drugs and in part due to pressure on countries with a strong generic industry (such as India) not to use TRIPS flexibilities and IP reform to enable greater pharmaceutical production.

Furthermore, many new second and third-line medicines are under patent protection in all key generic manufacturing countries, as many countries need to switch patients to new regimens. One potential solution to this problem is to encourage the local production agenda. However, given the considerable expertise and comparative advantage of India and China in producing generic ARVs, it is unlikely that this would be a viable solution in the immediate future. TRIPS plus provisions in FTAs with the US and EU are still a threat to treatment access. There is a historic opportunity with new drugs to treat two of the biggest HIV co-infections, HCV and TB but they are currently priced out of reach, in part due to patent protection worldwide.

Recommendations

- 1.** The MPP should examine the possibility of expanding to include drugs to treat hepatitis C and TB, and measure feasibility in part as to whether patients in MICs can secure access through voluntary licensing.
- 2.** More needs to be done to bring down prices of second and third-line drugs. Technical support to countries in using TRIPS flexibilities, complemented by IP reform should be fully supported by the international community, including DFID, in particular WHO, UNDP and WIPO who should collaborate more effectively together.
- 3.** WTO should support LDC members to make full use of TRIPS flexibilities in protecting public health, in particular that an LDC extension for pharmaceutical patents and related IP that affects medicines is extended or until LDCs graduate.
- 4.** WTO and WHO should play a more active role in monitoring practices suppressing the use of TRIPS flexibilities in FTAs through 'TRIPS plus' clauses with developing countries as such TRIPS plus rules have a negative public health impact. In addition to receiving notification of FTAs from Member States, WTO should consider setting up guidance for FTA negotiations with the purpose of enabling developing countries to protect or safeguard the use of TRIPS flexibilities.
- 5.** The UK government should take note of the concerns around FTAs and access to medicines, be explicit in what exactly it views as TRIPS-plus provisions and draw a red line with the EC on such issues.
- 6.** The Global Fund should assess the potential opportunity for it to show leadership in the financing of all HIV co-infections and opportunistic infections and move to intervene in the market to reduce prices, including for new hepatitis C treatment, as it has done effectively in the ARV market.

The role of the Medicines Patent Pool

The Medicines Patent Pool (MPP) is a Swiss non-profit foundation established with UNITAID funding in 2010. It was set up to address intellectual property barriers to generic production as outlined in *The Treatment Timebomb*.

The MPP acts as a negotiator between originator and generic companies. Originator companies offer an ARV patent to the pool for a royalty from the generic companies who go on to use the patent to produce either generic copies or to develop the ARV into a fixed dose combination (FDC), which is both easier to use and cheaper to produce.

The MPP negotiates licences from a public health perspective, which means its agreements differ substantially from the bilateral commercial (and confidential) agreements that are also agreed in some cases by originators and generic companies. As a key innovative solution to some of the barriers created by patents in the developing world market, the MPP provides a useful focal point to look at potential resolutions to access problems.

How successful has the MPP been at improving access?

The MPP has, to date, approved licences on nine priority ARVs as well as negotiating a price agreement on a medicine for an opportunistic infection. The licences cover the main first-line drugs for children over three years old and for adults, one of the main second-line medicines, the most recent single tablet regimen (TDF/FTC/EVG/COBI³⁷) and for the two most promising new medicines dolutegravir (DTG) and tenofovir alafenamide (TAF). According to the MPP, the impact of their first licences with Gilead are already materialising with over US\$40 million in savings since early 2012, this impact will grow exponentially. However, it is important to note the time-lag from the period when a licence is agreed and the two-three years it takes for a generic manufacturer to develop the new drug. Given that the MPP was only established four years ago, most licences were agreed in the past two years. The main impact of their recent licences will therefore materialise over the next few years.

How effective is the MPP in encouraging innovation in paediatric ARVs?

According to UNITAID's *Strategic Review* "the MPP is a unique and relevant institution, and an important 'part of the solution' for unblocking patent-related barriers to access HIV medicines." This is echoed by WHO in their recent publication, where they state: "Voluntary licences, in particular through the MPP, are enhancing access to newer patented ARVs in a large number of LMICs".³⁸

37. Tenofovir/emtricitabine/elvitegravir/cobicistat.

38. *Access to Antiretroviral Drugs*, 2014.

The UNITAID review, however, also recognises that in some areas progress still remains to be seen. For example, the MPP was originally created to enable innovation in previously neglected areas, such as the development of paediatric HIV medicines that are better suited to certain age groups. This is very much in the initial stages. This is because the development of paediatric formulations takes time, requires clarity on which formulations and dosages are needed, and needs a market to incentivise manufacturers to develop them. Without a developed world market for the drug, the incentives are seldom there. Therefore, unless the MPP is accompanied by other partners, its role as facilitator of new paediatric HIV medicines will be difficult to realise.

This has been recognised by UNITAID and the MPP who have recently launched the Paediatric HIV Treatment Initiative in partnership with the Drugs for Neglected Diseases Initiative (DNDI) and recently joined by the CHAI. DNDI initiates and coordinates R&D projects in partnership with private industry, public institutions, academia and NGOs and is playing an important role in addressing gaps in paediatric ARVs. However, as we have already explored, HIV treatment for children still lags considerably behind adult treatment, thus the R&D issue remains a priority area for concern. This is discussed in greater detail later in the report.

Critiques and appraisals of the MPP

Another limitation of the MPP pointed out by UNITAID is that “the existence of previous bilateral licences/ generic production for some of the MPP licenced compounds (e.g. with Gilead for existing ARVs, and with ViiV for abacavir (ABC) and dolutegravir (DTG) reduces its potential impact”. This is something the APPG found to be true when talking to the drug companies in India. Most of them had already agreed licences with either ViiV or Gilead on their latest drugs. However, in the APPG inquiry oral evidence, Denis Broun, who represented Cipla (one of the most respected Indian generic companies) stated that the MPP licences were much better than previous licences agreed directly with the originator companies in that they had a broader scope and were more transparent:

“For generic companies negotiating directly with originators has been the rule for a time and what you find now is that the licensing agreements negotiated under the patent pool are a lot better. There are more advantages and they are more transparent.”

DENIS BROUN, CIPLA

Despite this potential limitation the MPP still functions as an important public health broker between originator and generic companies and has the potential to expand the generic market further and contribute to bringing down the price for new patented ARVs in many LMICs. The recent round of seven new sub-licences agreed by the MPP is testimony to this, particularly with regard to licences for the promising new drugs TAF (tenofovir alafenamide) and DTG (dolutegravir).³⁹ In the past it has taken between five and 10 years for new ARVs to become available through quality assured generics in developing countries. The MPP should be able to reduce

39. The medicines patent pool signs a record seven new sub-licences to speed the availability of generic HIV medicines to developing countries, Press Release, Medicines Patent Pool. [Online] <http://www.medicinespatentpool.org/the-medicines-patent-pool-signs-a-record-seven-new-sub-licences-to-speed-the-availability-of-generic-hiv-medicines-to-developing-countries/>, 17 July 2014.

this time-lag to two to four years. Civil society organisations in India (such as the Lawyers Collective) highlighted concerns that the MPP currently allows originator companies to dominate negotiations with no standard set of terms and conditions. Furthermore, they are particularly concerned about the exclusion of some MICs from licence agreements particularly where there is a strong generic manufacturing base such as in Thailand and Brazil.

Executive Director of the MPP, Greg Perry responded to this criticism stating that the MPP does have a set of norms for innovator companies and tries to achieve the highest geographical scope and number of sub-licences possible. He also indicated that MPP adult licences cover countries that account for between 88% and 93% of adults living with HIV in LMICs, as well as covering countries which account for 98% of all children living with HIV globally.

Furthermore, the agreements have generally included over 70 MICs. The MPP has since pointed out that Brazilian and Thai manufacturers can take out sub-licences if they wish but have not done so to date. However, Greg Perry also recognised that innovator companies are not willing to negotiate on voluntary licences for several UMICs. This means these countries have the option to purchase the originator product (e.g. at a tiered price), challenge the patent or issue a compulsory licence.

The issue of access to affordable generic medicines in UMICs is one of the major points of contention in the access to medicines debate currently. The question is who should take responsibility for ensuring access in UMICs where GNI is considerably higher than in LMICs and LICs? Is it the responsibility of the MPP to negotiate broader licences despite pharmaceutical opposition and the voluntary nature of the programme? Should the Global Fund and other international donors re-think their decision to pull out from these countries given that their decisions have been based on an outdated World Bank measure of development? Or is it the responsibility of the governments in UMICs to meet their own public health needs? The answer is a combination of all three.

What is required is some form of needs assessment (health, governance, inequality and other development indicators) to ensure that countries with a high GNI but very underdeveloped health systems for example, are not left behind. As indicated earlier, the Global Fund is currently in the process of creating a new measure of development (other than GNI) to facilitate this. At the very least there needs to be some form of acceptance from the global community that access to medicines in UMICs needs to be addressed and consensus achieved between the pharmaceutical industry, civil society, governments and the multilateral donors.

What about tiered pricing?

Pharmaceutical companies such as Gilead, ViiV and Janssen argue that tiered pricing (where the price of drugs is segmented according to the market in different countries and within countries) has also increased access considerably. Conversely civil society argues that tiered pricing is a commercial strategy, not an access scheme, designed to give pharmaceutical companies maximum profits in LMICs. While it is clear that tiered pricing is better than nothing, it is not the most effective mechanism for bringing down the price of drugs as highlighted by global-health researchers such as Suerie Moon at the Harvard School of Public Health in Boston, Massachusetts. "We have 10 years of experience that shows that tiered pricing is going to lead to higher pricing".⁴⁰

40. 'Activists sound alarm on tiered pricing' *Nature*, 2014.

While it is clear that the MPP needs to maintain dialogue with the pharmaceutical companies to encourage more to sign up to the pool, an alternative for UMICs should also be explored and access to medicines closely monitored by multilateral agencies, WHO, UNAIDS and UNITAID. The recent MPP licence on dolutegravir involved new strategies such as tiered royalties and market segmentation to increase access in more countries. This could be further developed to enable the inclusion of additional countries in the licences. Other potential incentives could also be explored. The MPP should ensure it continues to expand the number of generic companies it works with alongside innovator companies, to enable smaller companies to grow.

Conclusions

The MPP plays an important role in potentially improving access to medicines through generic competition. The transparent nature of MPP licences with their public health-oriented terms and conditions are preferable to private bilateral voluntary licence agreements and are helping to establish new norms in voluntary licensing. Although innovator companies that have signed up the Pool (Bristol Myers-Squibb, Gilead Sciences, F. Hoffmann-La Roche, the US National Institutes of Health and ViiV Healthcare) have in some cases maintained private voluntary licences as well as licences with the MPP, the Pool’s primary function to expand access has not been hindered.

Limitations of the MPP are down to its voluntary nature and lack of additional incentives or leverage to expand access. It will only succeed if sufficient innovator companies are willing to pool their patents. Similarly, if the innovator companies refuse to negotiate on access in MIC and UMICs, the scope of the MPP will be restricted.

Recommendations

1. The MPP on its own does not provide an answer to gaps in R&D for paediatric treatment and must be accompanied by greater investment in R&D.
2. More pharmaceutical companies need to be encouraged to sign up to the MPP as one of the most effective methods of addressing access problems in LMICs, particularly those companies that currently hold patents on priority drugs.
3. Access in some MICs needs to be closely monitored as aid is withdrawn and an alternative solution to bring down prices must be found by the national governments, civil society, multilateral agencies and donors such as UNITAID, UNAIDS, WHO and the Global Fund.

Section 3

Underlying causes and solutions to other barriers to access

As has already been explored, price is often the major barrier to access of ARVs in LMICs. However, it is not the only factor preventing medicines getting to the people who need them most. This section will look at issues such as drug registration, corruption and the impact of weak health and procurement systems on access to treatment.

Drug registration, quality assurance and corruption

Every generic company the APPG spoke to in both South Africa and India highlighted that drug registration is a major barrier to delivering ARV access. In South Africa in particular, the companies stated that the archaic system used by the Medicines Control Council (MCC) was putting small and medium-sized companies out of business due to the arbitrary and slow nature of drug registration.

DFID in South Africa spoke to the APPG about a project they are currently rolling out with CHAI to improve South Africa's drug registration processes. They hope the new system, called the South African Health Products Regulatory Authority – which will take over from the MCC – will be established in April 2015. However, DFID funding is due to be withdrawn from South Africa and this may affect implementation and therefore should be closely monitored by DFID.

Drug registration and quality assurance have long been recognised as key issues to address in ensuring access to medicines in LMICs. Current projects to address the issue are going some way to help overcome the problem. The WHO's Prequalification Programme (PQP) for example, was designed to speed up registration with the added benefit of a quicker and more efficient drug approval process, by providing quality assurance for generic drugs from an independent, recognised global institution. Another WHO collaborative procedure with national medicines regulatory authorities was launched in 2012 to fast-track WHO prequalified medicines into countries where the medicines are needed.

Other attempts to address the issue of drug registration have been at the African Union level with the African Medicines Regulatory Harmonization (AMRH) Programme and the East African Community Medicines Registration Harmonisation initiative. Though these projects are an important step in the right direction, the APPG inquiry highlighted that one of the biggest barriers to improving these systems is corruption within national governments.

Key donors such as DFID are already doing considerable work in this area. DFID has provided £3 million over three years (2013–2015) to various donors. Initial results have shown significantly accelerated market approval of five essential medicines in the East African Community (EAC), through the first ever experience of work-sharing and joint assessments in the EAC. The programme is looking to scale up to other parts of Africa, especially Western and Southern Africa, which have shown strong political commitment to this work.

The UK government also agrees that corruption within the medicines sector is an issue and has adopted a zero tolerance approach to fraud and corruption. It is working on health systems strengthening and ways of reducing incentives for corrupt behaviours. DFID has supported the Medicines Transparency Alliance (MeTA) and other initiatives to increase transparency within the medicines sector and continues to explore the best ways of raising transparency and reducing the scope for corruption. The APPG applauds the UK for taking a strong leading role in tackling corruption and assisting the streamlining of drug registration processes. We urge DFID to continue and expand this important work.

Poor supply chain management leads to stock-outs

Supply chain management has been highlighted by a number of organisations in submissions to the inquiry including DFID, WHO, Professor Paul Lalvani from the Empower School of Health and both generic and innovator pharmaceutical companies. Problems related to supply chain management include fraud and corruption (as described above), poor supply chain information management systems, low levels of transparency, the inability to undertake effective demand forecasting, huge fragmentation in supply chains due to the multitude of different actors involved and finally, a lack of professionalism and decent wages in the supply chain management workforce to promote incentives for better results. The list could go on. Due to time constraints this report will focus on two examples of poor supply chain management from the APPG's visits to South Africa and India.

In India one of the biggest problems highlighted to the APPG was the failure of the Indian government to pay generic companies for medicines on time and the complicated tender process, which is a real disincentive for Indian companies to do business in India.

In South Africa, a major problem is the government-run procurement process. The South African government procures medicines for the whole country and then transports the drugs to regional depots. For this system to work there needs to be a well-functioning data collection system whereby drugs are recorded well before they have run out; in addition systems need to be flexible enough to manage regime changes. This, unfortunately, is not the case in South Africa and is a common problem throughout the whole of Africa. Corruption was also highlighted as an issue with drugs frequently being sold to the private market or left to go out of date.

The consequence of these inefficiencies is stock-outs, which in turn leads to patients dropping off treatment or developing resistance to drugs. In South Africa, MSF highlighted that this is currently the biggest challenge for the organisation. As pointed out by WHO:

“The Coordinated Procurement Planning (CPP) Initiative, which monitors the supply situation for ARVs in 22 countries, consistently reports around half of its client countries on red alert for imminent stock-out. It should therefore come as no surprise that in recent years between 30–45% of LMICs annually reported ARV stock outs.”

Role of the Global Fund and procurement agencies

In the past, the Global Fund has focused on procurement of health commodities at a national level and then used third parties, such as NGOs to distribute at a local level. In oral evidence to the inquiry, Executive Director of the Global Fund, Mark Dybul explained why their approach has shifted towards a focus on end-to-end distribution. According to Dybul, the use of third parties was extremely expensive and not particularly functional, as systems were often replicated at a local level. The Global Fund is therefore now working on developing the distribution chain as well as purchasing medicines. They are currently developing an online tool to assist countries in procuring their own medicines. The e-market will enable governments’ to compare shipping costs, reference prices and other costs associated with distribution to enable them to make the most efficient choices and take ownership of procurement, which is more sustainable in the longer term.

This approach seems to chime with the APPG’s findings, that while the price of medicines is crucial, it is also necessary to invest in distribution and supply chain systems. However, it should be noted that although the Global Fund has started to broaden its approach to funding, it still remains a key purchaser of ARVs, alongside UNITAID, PEPFAR and UNICEF. The Fund’s submission to the inquiry states that “at the end of 2103, it was estimated that of the estimated 11 million people on ARVs, six million were financed by the Global Fund.” With this in mind, it plays an important role in market shaping and enabling bulk procurement of cheap medicines for the developing world.

Generic companies in India and South Africa complained that procurement forecasting from donors such as the Global Fund was not always accurate and that this creates too much risk. The Global Fund argues that it has made great strides to improve forecasting (by working together with other donors to achieve greater price reductions and accuracy), and that the focus on end-to-end distribution is all part of the process to enable this.

Conclusions

Poor management of supply chains, weak health systems, inadequate drug registration systems and corruption within these systems present considerable barriers to access and should continue to be addressed alongside any attempts to reduce drug prices.

The Global Fund has started to address distribution as well as procurement in its programmes which should help to improve forecasting in the future. DFID’s work on “market-shaping” is helping to address bottlenecks in supply chains (such as in South Africa), however removal of funding from MICs could hinder progress in this area considerably.

Whilst the gains made through the WHO PQP for generic drug quality assurance are clearly huge, they should not be taken as a given. Without continued investment in the PQP programme we risk losing this vital programme that has delivered so much for people living with HIV.

Recommendations

1. Barriers to access, including weak distribution networks and inadequate supply-chain management should continue to be addressed alongside market-shaping policies by funders such as DFID and the Global Fund.
2. DFID, international donors and WHO should continue to put pressure on governments in Africa to implement regional drug registration processes (EAC, SADC and ECOWAS have already made formal commitments to harmonisation of drug registration processes) to enable quicker registration of drugs. This should be prioritised by all donors in a coordinated effort.
3. DFID and other international donors should provide financial support to WHO’s PQP to ensure its continued operation and expansion to other priority health products. Increased financial support will enable PQP to continue its invaluable technical assistance and support to quality assurance at a country level, and to continue to build long term capacity through technically supporting regional harmonisation initiatives. This will have a direct and immediate impact on people living with HIV.
4. Corruption within health systems needs urgent attention. International donor government’s such as the UK should use their influence to encourage recipient governments to increase vigilance and accountability in their national health systems.
5. The UK should lead the international development community by example by committing resources and taking urgent action to address the gap in funding for treatment in countries graduating from LIC to MIC status.

Section 4

Filling the gaps in research and development

Gaps in research and development (R&D) for paediatric HIV drugs have been well documented by NGOs, pharmaceutical companies, UN organisations and international donors. The challenges are well known. The commercial incentives are simply not there for paediatric ARVs given that HIV in children is largely a developing world issue. The problem is the same for a number of co-infections, particularly TB and other neglected tropical diseases which are not covered in this report. The problem is widely understood and the evidence indisputable. However, only 647,000 of the 3.4 million children living with HIV are able to access ARVs. The current solutions have only partially addressed the issue and the gap remains substantial.

During the inquiry, this issue proved to be highly contentious with strong, and at times emotive stances coming from both sides: the private sector and NGOs. Ultimately, the purpose of this report is to bring together the best from both sides of the equation to enable a positive vision and way forward in one of the most critical areas of global health policy today.

What has changed since 2009 in R&D when The Treatment Timebomb report was published?

The Treatment Timebomb identified that more fixed dose combinations (FDCs) are needed in resource-poor settings because they are both easier to take and are cheaper to manufacture. Adherence can be a major problem for people taking medicines, including in developing countries. Therefore, the simplification of ARV treatment was identified as an important area of focus in R&D.

One potential solution to this problem and the lack of investment in paediatric drugs that featured in the APPG's previous report, was the MPP. However, as noted earlier, the MPP cannot resolve the problem of the unwillingness from both industry and other funders to invest in drug development on behalf of neglected patients. Patents are available through the Pool, but the fundamental lack of a lucrative sales market will always undermine progress in this area until an alternative solution is found.

Another area that was marked for R&D was in diagnostics. In 2009, the report recommended that a CD4-based diagnostic process is developed as well as a simple point of care viral load test. Both of these innovations have come to fruition with the development of dried blood spot tests, which are a cheap and easy way to transport samples to central laboratory facilities for viral load tests.

Point of care tests are now also available in settings with poor infrastructure and can be carried out by nurses or community health workers. CD4 tests have come to be considered much less accurate than other tests, however due to the greater simplicity of CD4, it is still currently used more widely than viral load testing. The

technology exists, but market barriers and a lack of prioritisation by governments and international donors, continue to impede more widespread uptake.

Progress has also been made in TB diagnostics. DFID has played a significant role in supporting the product development, policy development and scale up of a new rapid diagnostic test for tuberculosis and rifampicin resistance Xpert MTB/RIF, a rapid molecular diagnostic test. According to DFID's latest policy review, "evidence to date has shown that it could double the number of HIV-associated TB cases diagnosed in areas of high rates of TB and HIV".⁴¹ It is clear therefore, that since 2009 progress has been made in some areas but in paediatric ARVs there remains a considerable R&D gap.

We are still some way off the discovery of a vaccine that will definitively end the AIDS epidemic and there are major concerns about the UK's reduction of funding by more than 80% for the period 2013 to 2018. It is important that this particular area of R&D is not neglected due to the need for governments like the UK to demonstrate short-term deliverables.

It must be recognised that DFID completely fulfilled their previous commitment of £40 million to the International AIDS Vaccine Initiative (IAVI) between 2008 and 2013. However, it should also be noted that the new grant for the next five years has reduced to only £5 million. Current DFID spending on HIV vaccine research is therefore one eighth of its previous level.

Across the board, funding for the development of new prevention technologies has also been reduced. According to a DFID written⁴² answer, the department invested a total £171m in Product Development Partnerships (PDPs) over the five years from 2008 to 2013. Over the next five years, the equivalent figure will be £138m. In the case of AIDS-related research (IAVI plus IPM) a total of £60m was invested from 2008 to 2013, compared to £20m over the coming five years. This continued support is important and welcome however, it is clear that investment in this area has reduced considerably.

After years of generous and consistent support for AIDS vaccine research, the APPG remains concerned with the decision to reduce funding and feel it is inconsistent with the government's overall strong commitment to fighting AIDS, supporting vaccines and promoting treatment roll-out. Equally, the APPG feels that long-term investment is often the most effective use of funds and DFID should not lose sight of this fact.

What works?

The problem with the current system of R&D is that it is incentivised by the potential profits a new medical product could generate through sales under a monopoly created by the granting of a patent. The reward of innovation is one of the basic tenets of a capitalist society and has, for most part, generated progress and efficiency in the pharmaceutical industry. However, predictably this system does not always cater for the most vulnerable in society. In other words, Adam Smith's "invisible hand" does not always self-regulate the market to ensure that where there are no large-scale profits to be made, medicines are still developed.

41. *Towards Zero Infections*, 2013.

42. House of Commons Hansard, [Online] http://www.publications.parliament.uk/pa/cm201314/cmhansrd/cm130910/text/130910w0002.htm#130910w0002.htm_spnew6.

This has been recognised by academics, multilaterals (like WHO), governments, NGOs and the pharmaceutical industry alike who are working together to try and find a solution. Some policies have had greater success than others. This report will not cover those policies extensively (see the APPG on Global Tuberculosis report on Global R&D for more detail).⁴³ As highlighted in the first *Treatment Timebomb* report, suggested models of encouraging innovation in HIV and neglected diseases can broadly be divided into “push” and “pull” mechanisms.

Push mechanisms reduce the risks and costs of investment in R&D. They include direct funding of research, and tax credits, both of which have been used by the UK government. The main drawback to ‘push’ mechanisms, such as direct funding, is that they require funders to make a judgement about which research bodies are most likely to achieve the needed results, and sometimes the recipients of funding do not deliver.

Pull mechanisms in contrast, create an extra incentive to achieve the result (such as a new medicine) with the benefit only delivered on achievement. Examples of such mechanisms include prizes for the first researchers to come up with a specified innovation, advanced market commitments or tax credits on sale of a certain product which is yet to be developed.

SUCCESSFUL POLICIES

Product Development Partnerships (PDPs) are one part of the solution and have, according to STOPAIDS, delivered considerable improvements. PDPs involve the harnessing of diverse entities, including government, NGOs and the private sector. The Drugs for Neglected Diseases Initiative (DNDI) is doing this in paediatric ARVs, alongside other neglected areas. They are able to operate on much smaller budgets than big pharmaceutical companies, given the not-for-profit nature of the business. The limitation however, as always, is funding and sustainability.

Other successful approaches include **Socially Responsible Licensing (SRL)** which involves policies such as the non-enforcement of IP in certain countries and royalty-based production of generic drugs. A number of big pharmaceutical companies have introduced SRL policies, including those who have participated in this inquiry, Gilead, ViiV, Janssen and Boehringer. SRL is proven to be both effective at improving access without affecting stock value and is the basis for the MPP. It is, however, voluntary and therefore dependent on the good will of pharmaceutical companies, which as has been demonstrated by the MPP, does not necessarily always lead to filling the gaps in R&D for neglected areas such as paediatric HIV treatment without other mechanisms and incentives being in place. The recent Paediatric HIV Treatment Initiative will likely be an important contribution to addressing this challenge.

Direct government funding and grants have also had considerable impact on the R&D agenda. However, their benefits have not been fully capitalised by governments to progress the public health agenda. Seventy-five per cent of new molecular entities that have been registered over the last 20 years can trace their origins, not to private sector labs, but to publicly funded labs or to national institutes of health in the US, the British Medical Research Council and other similar entities around the world.⁴⁴ The drawback with this system however is that the IP for the molecular entities is most often sold to the pharmaceutical companies that invest in developing the drug. The drug development is the costly and risky exercise, which up until now

43. *Dying for a Cure: Research and development for Global Health*, APPG on Global Tuberculosis, [Online] <http://appg-tb.org.uk/images/reports/Dying%20for%20a%20Cure%20-%20Research%20and%20Development%20for%20Global%20Health.pdf>, July 2014.

44. STOPAIDS oral evidence to the APPG.

has been largely undertaken by big pharmaceutical companies unless subsidised by a philanthropic organisation. Today, the public sector plays an increasingly significant role in subsidising drug development.

LESS SUCCESSFUL POLICIES

Tax credits are one way of stimulating research and are currently used in the UK; however, they have not been shown to stimulate innovation in line with public need as they don't allow the government to direct the research agenda. They are also an expensive way to invest in research.

Another policy which is favoured by the pharmaceutical industry is the **extension of patents** to offer a greater financial incentive. The patent system has failed in the area of neglected diseases thus far and a further extension is unlikely to change the current outcome.

Bold ideas for the future – a global R&D fund

As the report demonstrates, the current system has its flaws. In HIV, these weaknesses are highlighted by the lack of paediatric treatment options. As human beings our natural instinct is to protect and nurture the child. Conversely however, the rules of the marketplace dictate precisely the opposite. Clearly, efforts have been made to balance out the quest for profit over the need for quality paediatric medicines. But, are those efforts sufficient or does the State need to play a stronger role to ensure the poorest and most vulnerable are cared for?

Chair of the APPG, Pamela Nash MP, at the Naz Foundation Orphanage for children living with HIV either orphaned or abandoned by families, in Delhi, India.



Civil society are calling on governments to take a more decisive role in deciding the fate of people living with neglected areas of disease by de-linking the cost of R&D from the demands of profitability to enable research to be steered by public health need rather than profit. In theory, the idea makes sense, not just in HIV but across the board.

The proposal is to create a global R&D fund which would operate through a variety of grants, mile-stone prizes, end-goal prizes, and if based on an open innovation approach, could reward all entities who have contributed to the development. STOPAIDS and MSF have suggested that governments set aside 0.01% of GDP to finance the fund, however other methods of innovative finance could also be researched.

IS IT POLITICALLY FEASIBLE?

The idea originally stems from WHO, as part of the recommendations which came out of the Consultative Expert Working Group on Research and Development (CEWG), set up by WHO in 2010. To date however, it has not succeeded in gaining widespread international support. The UK government (as part of the EU) has actively lobbied against the idea leading to the postponement of discussions until 2016. At the moment the aim, as recommended by the CEWG, is to negotiate a binding convention on R&D, a Global R&D Treaty, which would, in theory, also provide the best framework to implement a global R&D fund.

EXAMPLES OF "DE-LINKAGE" APPROACHES

We have seen success in delinking R&D costs through the efforts of the **meningitis A vaccine initiative**. This developed an adapted meningitis A vaccine through collaborative research including the National Institutes of Health and the Serum Institute of India, a private vaccines company. The cost of the vaccine is approximately 50 cents a dose.

MSF have reported to the APPG that any **drug or vaccine to emerge to treat or prevent Ebola**, is likely to be as a result of a partially or fully de-linked R&D model, especially since nearly all funding for the development of such products will come from the public sector and philanthropies. The lack of treatments and vaccines for Ebola also reflects the failure of the patent system to create incentives for the private sector to develop appropriate medical tools that can assist in preventing, diagnosing and treating Ebola (as well as other neglected diseases).

Finally, de-linked models of R&D are seriously under consideration for the **development of new antibiotics**, in particular because there are no incentives for industry to develop products that are meant to be both affordable and conserved or tightly managed. A number of recent news stories and government press releases highlight that the UK Prime Minister is already seriously considering how to address market failures, particularly in the areas of new antibiotics and dementia. The government's announcement in July that it has "commissioned a wide reaching independent review, led by the internationally renowned economist Jim O'Neill and co-funded and hosted by the world's second largest medical research foundation, the Wellcome Trust, to explore the economic issues surrounding antimicrobial resistance", is a positive sign that the UK government is looking innovatively at how to address to market failures in neglected areas of research.

It was noted with interest that in his oral evidence Gilead's Greg Alton was explicit in rejecting the traditional industry justification for high prices – that they are necessary to cover the high costs incurred in the research and development of new medicines.

When asked to explain the high price of their hepatitis C treatment sofosbuvir he replied: "The cost of R&D and the actual price of the product – I don't think, you're going to find a connection between the two." This illuminating exchange undermines the long standing case made by others in this sector around high prices and R&D costs. NGOs argue that in reality pricing is determined by what the market will bear rather than the high costs they have incurred. Furthermore it has long been asserted that the amount pharmaceutical companies claim to invest in R&D is much higher than the reality of the costs incurred. Greater transparency is needed from industry so that society can make informed judgements about the costs.

Obviously, the UK government is more focused on diseases that impact on the UK population rather than the developing world. However, DFID could take the lead in pushing this agenda, by calling for the UK government to commission an economic paper to assess the potential cost-benefits of shifting towards a state-funded (partially or fully, as appropriate) approach in neglected areas, both as an international development priority (DFID) and for neglected areas of research in the UK under the Department of Business, Innovation and Skills (BIS). The aim of the study would be for the UK government to come to an informed decision on the most effective ways of creating incentives to encourage investment in R&D, and more broadly to look at the benefits and challenges with different approaches to drug development.

More generally, the UK government and others should consider whether incentives can be better delivered for neglected public health needs through patents and high prices for medicines or through a combination of push and pull incentives. These can create incentives for substantial private sector investment into R&D for neglected areas of need, while ensuring that end products are affordable and appropriate.

How effective is a Global Treaty?

At the moment it is difficult to say whether the idea of a Global R&D Treaty would have any traction, particularly in the short time-frame before 2016. This inquiry has shown some promising signs that agreement at least between civil society and the private sector may be possible.

The various multilateral organisations and drug companies that participated in the inquiry oral evidence sessions did express sympathy with the concept, however they were equally cautious about the lack of international support and need to ensure that financial incentives for the pharmaceutical industry are protected.

This report is not suggesting that private sector investment into R&D should be in anyway discouraged. In fact de-linkage is intended to create incentives that encourage and reward private sector investment into R&D for neglected health needs through a combination of push and pull incentives. Nor is the report suggesting that de-linkage is the only solution to the problems we currently see in neglected areas of disease.

The APPG however would encourage the UK government to look at the proposals more closely and to open up dialogue on the issue. Although the idea of a binding Global Treaty has met strong resistance from many governments who fear the consequences for trade and private sector investment, the UK has the power to

galvanise international support and could lead the way in designing a Treaty that could both protect and even enhance pharmaceutical innovation and address the market failures of the current patent system.

FRAMEWORK CONVENTION FOR TOBACCO CONTROL

WHO's framework on tobacco control is an example of a globally binding treaty on a public health issue, which could be used as a model for the future. Although the treaty has been criticised by DFID as "binding but not effective", a number of other key organisations believe it has had a considerably positive impact.

The Bill & Melinda Gates Foundation website states: "with 176 signatory countries the Framework Convention for Tobacco Control (FCTC) has led to stronger tobacco control policies in many parts of the world." The impact of the Convention is also easily visible from the changes which have been implemented here in the UK through the introduction of key FCTC recommendations such as:

- tobacco taxes that raise the price of cigarettes for the consumer
- comprehensive bans on tobacco advertising
- graphic health warning labels on cigarette packaging and plain cigarette packaging
- indoor smoking bans.

Conclusions

The gaps in R&D for HIV have been filled to some degree since 2009, particularly in diagnostics. However, there is still considerable concern about the lag in development of paediatric treatment and neglected co-infections such as TB. Some policies, such as PDPs, direct grants and Socially Responsible Licensing have led to considerable improvements; however concerns remain around the sustainability of financing and the limited scope of these policies.

A bold idea for the future which is currently supported by civil society and has the sympathy of the pharmaceutical industry would involve de-linking the cost of R&D from the sale of the product through the creation of a state funded Global R&D Fund that would deliver new pull incentives such as prizes, patent buy-outs and purchase commitments, complemented by push funding (and of course many such push funding initiatives, including the European Developing Country Trial Partnership, already exist). The idea does not have widespread international support but more research into the cost-benefits of such a fund and negotiation between governments, civil society and the private sector could enable this idea to come to life in the not too distant future.

Recommendations

- 1.** DFID should continue to support R&D through Product Development Partnerships, stipulating a commitment to open access, generic production and a non-patent monopoly based approach.
- 2.** The APPG supports the Global TB APPG report recommendation that the UK should commission an economic paper to contrast the total costs of developing and purchasing medical tools using the current R&D model with the costs of a de-linked model.
- 3.** The UK government should initiate dialogue with the pharmaceutical industry and civil society to reach agreement over a possible R&D Treaty in the run up to the World Health Assembly in 2016.
- 4.** The UK government should re-assess its decision to cut funding for the development of an AIDS vaccine as part of a larger review of the scale of investment the government is making to ensure we have the pipeline of new medical tools the world needs.

“We live in a completely interdependent world, which simply means we cannot escape each other. How we respond to AIDS depends, in part, on whether we understand this interdependence. It’s not someone else’s problem. This is everyone’s problem.”

BILL CLINTON

Conclusion

As Bill Clinton asserted “we live in a completely interdependent world”, unless we understand our global interdependency we will not be able to combat the HIV epidemic. We are all reliant on each other: patients rely on pharmaceutical companies to develop drugs; the pharmaceutical companies depend on the generosity of governments to fund research and then to have the purchasing power to buy their drugs; civil society rely on the willingness of governments to act on their behalf; and people living with HIV rely on civil society to push governments to meet their needs. It is this interdependency that gives us the leverage to make change happen where it is needed. If we all need each other, then there is always scope for negotiation, compromise and new agreements.

As we approach the final year of the Millennium Development Goals it is time to look at what change is needed for the future. Access to treatment continues to be denied to too many people living with HIV. Children rely on adults to speak up for their needs. Unfortunately they continue to be a neglected population in access to HIV medicines. It is time to prioritise the needs of children so that vital medicines are developed at affordable prices despite the market barriers to achieving this. Governments globally must prioritise R&D in neglected areas and find new, sustainable ways of tackling this fundamental flaw in the current model. Governments should introduce and implement alternative incentive mechanisms that de-link the cost of R&D from the price of drugs and diagnostics.

Marginalised populations are also dependent on the willingness of governments to listen to their needs. However, they are “marginalised” for this very reason, governments are often shut-off from their concerns. The very nature of the AIDS epidemic makes marginalisation a dangerous threat to bringing the disease under control. Governments need to recognise this and where they don’t the international community has a responsibility and ultimately a special interest in ensuring these people receive the treatment they need.

The simplicity of ending aid when a country reaches middle income status completely negates this reality. If aid stops, the international development community must invest in ensuring the ability of people in those countries to access and pay for medicines through market shaping policies. Access to medicines should be a target for all diseases of public health importance, and as argued by MSF, “should know no borders according to a country’s level of socioeconomic development ... governments should define their relevant public health priorities.”

Getting patients on treatment, with an undetectable viral load should be the next goal for ending HIV and AIDS. That means investing in viral load testing, scaling up treatment to start much earlier and identifying and maintaining patients on a closely monitored treatment programme. Without viral load testing, resistance to ARVs will continue to increase.

Cheaper and easier to use technologies are available; governments across the developing world must prioritise these if they are serious about bringing the epidemic under control. Second, and particularly third-line treatment remain largely unaffordable in the developing world. Pharmaceutical companies and the world's multilateral organisations (WTO, WHO, UNITAID, MPP) must work together to ensure generic competition is able to flourish so that prices can be brought down. Equally, we must commit to finally ending the epidemic which means maintaining our investment in vaccines.

Finally, it is vital that price decreases are accompanied by improved distribution networks, supply chains and health systems. Corruption must be acknowledged and challenged where it is happening. Donor governments have an important role to play in using their soft power to stamp it out. Price decreases and the strengthening of systems go hand in hand and should not be separated by donors. Both priorities must be addressed with equal importance and emphasis.

We must be bold with our ambitions for the future. In a post Millennium Development Goal framework, we should endeavour to bridge the gaps which have to date prevented the AIDS response from reflecting the best parts of an interdependent world. R&D needs to work for people as well as profits, paediatric medicines must catch up with adult treatment. Second and third-line drugs must be affordable for all people living in LMICs, viral load testing should become the gold standard of treatment for **everyone** and health and drug distribution networks must be strengthened to ensure the long-term sustainability of any aid-assisted development. We are all dependent on these steps being taken. This is not someone else's problem. This is everyone's problem.

Abbreviations and acronyms

AMRH	African Medicines Regulatory Harmonization	LMICs	low and middle income countries
API	active pharmaceutical ingredient	MCC	Medicines Control Council
APPG	All Party Parliamentary Group	MDR-TB	multi-drug resistant TB
ART	antiretroviral treatment	MeTA	Medicines Transparency Alliance
ARVs	antiretroviral drugs	MPP	Medicines Patent Pool
BIS	Business, Innovation and Skills Department	NGO	non governmental organisation
CEWG	Consultative Expert Working Group on Research and Development	PDPs	Product Development Partnerships
CHAI	Clinton Health Access Initiative	PMTCT	prevention of mother-to-child transmission
CHIVA	Children's HIV Association	pppy	per person per year
DFID	Department for International Development	PQP	Pre-qualification Programme
DNDI	Drugs for Neglected Diseases Initiative	R&D	research and development
EAC	East African Community	SADC	Southern African Development Community
EC	European Commission	SRL	socially responsible licensing
EID	early infant diagnosis	TB	tuberculosis
ECOWAS	Economic Community of West African States	TPP	Trans-Pacific Partnership
FDC	fixed dose combination	TRIPS	Trade-Related Aspects of Intellectual Property Rights
FTA	Free Trade Agreement	TTIP	Transatlantic Trade and Investment Partnership
GNI	gross national income	UMIC	upper middle income country
HCV	hepatitis C virus	UNAIDS	United Nations Programme on AIDS and HIV
IAVI	International AIDS Vaccine Initiative	UNDP	United Nations Development Programme
IPASA	Innovative Pharmaceutical Organisation South Africa	WHO	World Health Organization
IP	Intellectual Property	WIPO	The World Intellectual Property Organization
IPM	International Partnership for Microbicides	WTO	World Trade Organization

Organisations that contributed to the APPG inquiry

Developing country based charities

Treatment Action Campaign (TAC) (South Africa)
Delhi Network of Positive People (DNP+)
Lawyers Collective (India)
Naz Foundation (India)
Médecins Sans Frontières (MSF) (India)
India HIV/AIDS Alliance
CHIVA Africa
International HIV/AIDS Alliance (South Africa)
SWEAT (Sex Workers Education and Advocacy Task Force)
Desmond Tutu HIV Foundation Youth Centre Section 27 (South Africa)

Other charities

CAFOD
Oxfam
Tearfund
STOPAIDS
International HIV/AIDS Alliance
Médecins Sans Frontières
Harm Reduction International
DSW (Germany)

Private sector

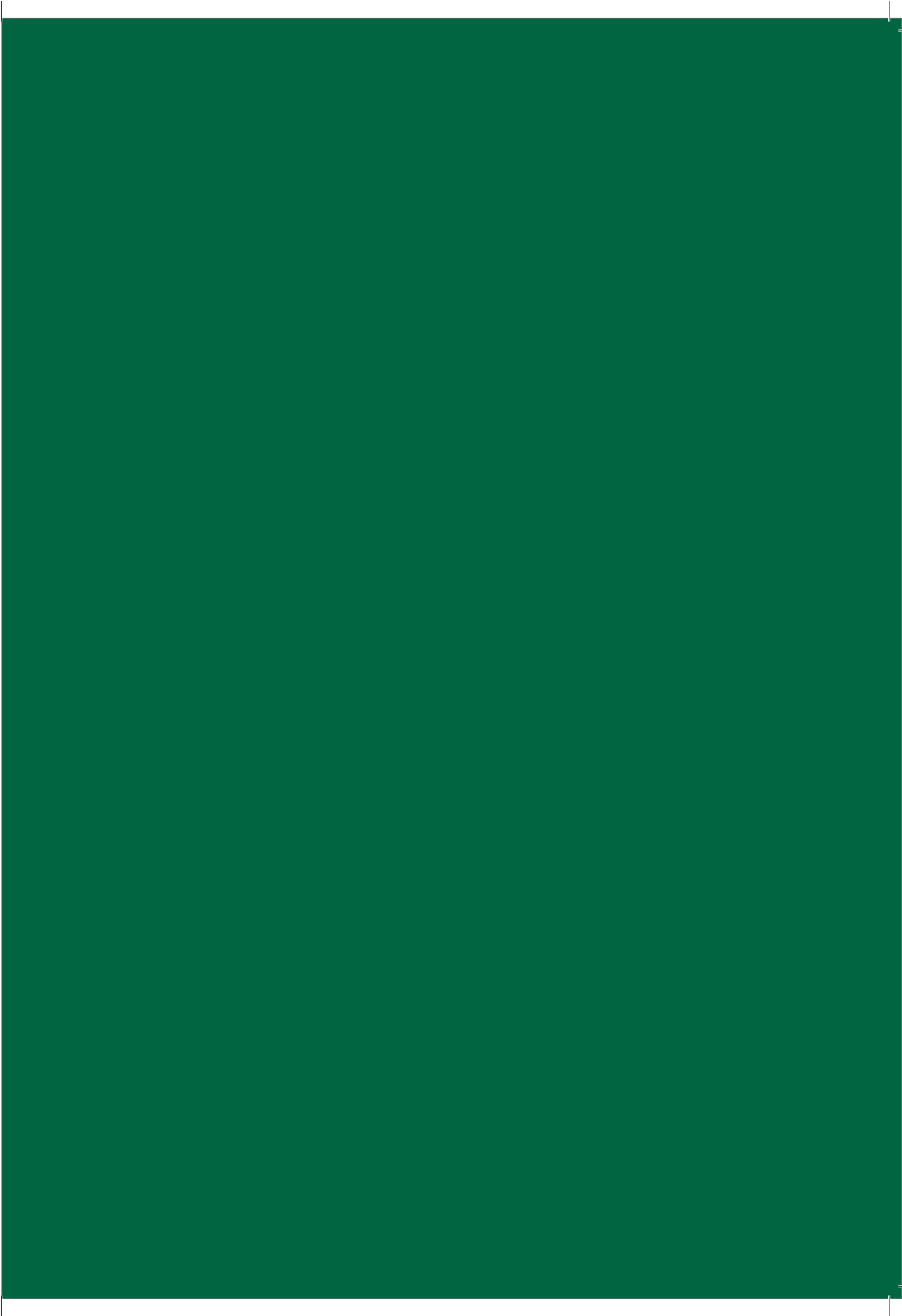
Gilead
ViiV Healthcare
Janssen
Boehringer
Cipla
Aspen
Aurobindo
Mylan
Hetero Labs

Other

Clinton Health Access Initiative
Global Fund for AIDS, Tuberculosis and Malaria
International AIDS Vaccine Initiative (IAVI)
Wellcome Trust
Medicines Patent Pool
Universities Allied for Essential Medicines (UAEM)
The National Association of Pharmaceutical Manufacturers (NAPM) (South Africa)
Partnership for Supply Chain Management
Empower School of Health (India)

Government and international governmental organisations

Department for International Development (DFID)
World Health Organization (WHO)
Joint United Nations Programme on HIV and AIDS (UNAIDS)
UNITAID
National AIDS Control Organisation (India)
Department for Science and Technology (South Africa)
Department of Health (South Africa)
Department of Trade and Industry (South Africa)





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