EVIDENCE ON ACCESS TO ESSENTIAL MEDICINES FOR THE TREATMENT OF HIV/AIDS

A SUMMARY

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EXECUTIVE SUMMARY

The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) asked Charles River Associates (CRA) to review the evidence on the developments in access to antiretrovirals (ARVs) over the last 10 years in low- and middle-income countries, the factors which have contributed to progress and the lessons which this offers for the future.[1]

In order to set the context for the study, it is important to remember the situation at the beginning of the decade. As set out in UN Secretary-General Kofi Annan's call for a "war chest" to fight the epidemic, HIV/AIDS was seen as a continent-wide emergency, representing not only the primary cause of death in Africa, but also the biggest challenge to development.

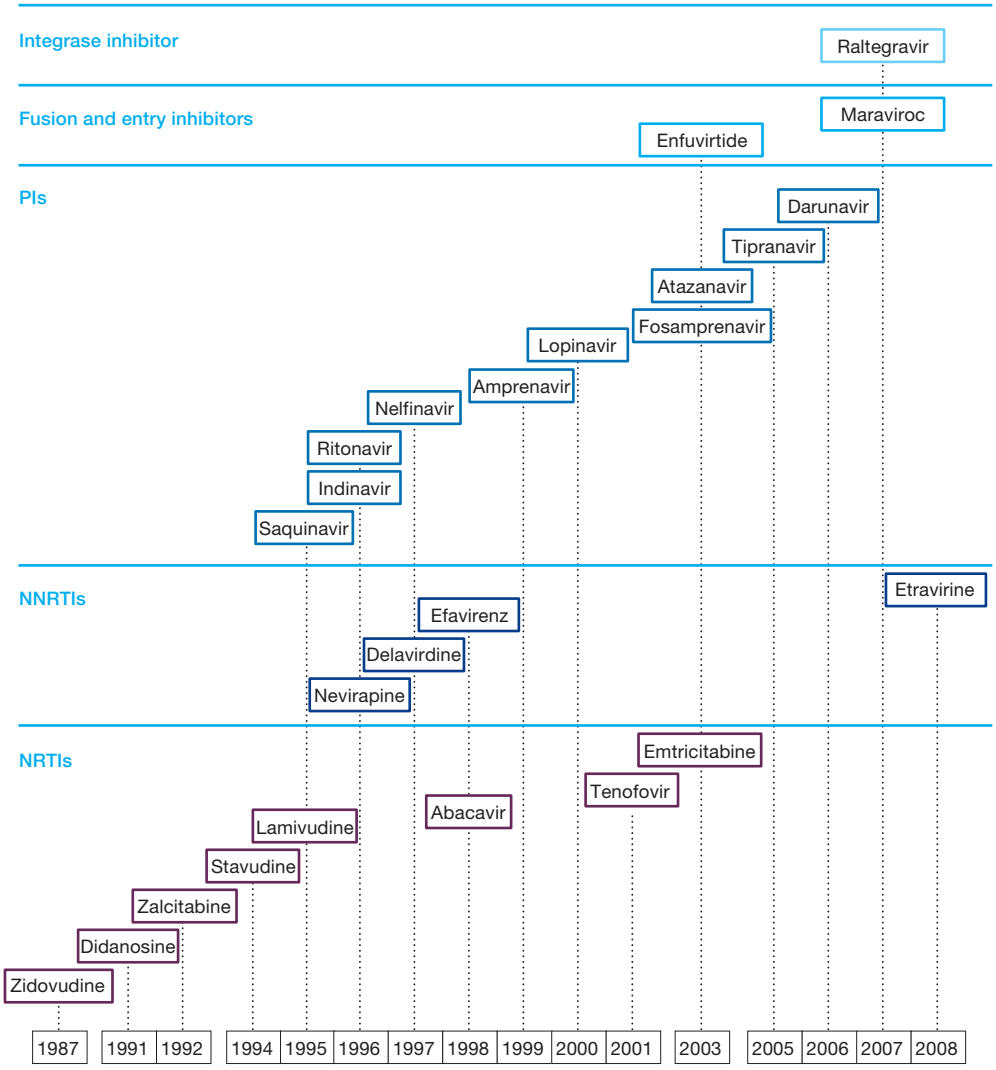
Access first requires innovation

A prerequisite for access is clearly innovation, so the starting point was to review how the industry has responded to the challenge of HIV/AIDS. While the first treatments for HIV/AIDS were developed in the late 1980s, the most significant developments toward current antiretroviral therapy (ART) standards were achieved in the mid-1990s with the launch of protease inhibitors (PI) and non-nucleoside reverse transcriptase inhibitors (NNRTI). These newer drugs have since been used for combination therapies, known as highly active antiretroviral therapy (HAART), resulting in reduced development of virus resistance to ARTs, one of the main limitations to the long-term efficacy of antiretroviral mono-therapy. As a number of new ARV medicines have become available, the set of treatment strategies available to patients has multiplied, offering increased tolerability, reduced side effects and simplified dosages. These new medicines expanded the treatments options in cases when resistance to first-line treatment is developed. This revolution in treatment options is illustrated in Figure 1 below. Given the significant innovation in treatments, the WHO recommended combinations of ARV drugs to be used as first- and second-line treatments have changed three times since the first WHO guidelines in 2002.

1 The full report is available from the IFPMA website. http://www.ifpma.org/fileadmin/content/Publication/CRA_Research.pdf. The original report was published in October 2011

Figure 1: *Development of new ARV drugs over time by class*

SOURCE: CRA



Evidence not anecdote

To understand changes in access to these medicines, we selected seven countries (Botswana, Brazil, India, Mexico, Rwanda, South Africa, and Thailand) that are seen as having been relatively successful in improving access, but which represent a range of different economic, political, and demographic circumstances. For these countries, case studies were developed to illustrate some of the different approaches and strategies for combating HIV/AIDS. This allowed an analysis of the various strengths and weaknesses of the efforts undertaken in each these countries. Research for the case studies included interviews with local industry, academics, non-governmental organizations (NGOs), and, where possible, government officials involved in HIV/AIDS programs as who perform well as secondary research.

The insights gathered have been used to design a statistical analysis allowing us to test the relative importance of different factors in determining access to ART and prices of ARVs. This statistical analysis was performed using a wider set of low- and middle-income countries than the case studies, including those countries that have not had success improving access to ARVs. The statistical analysis provided a basis

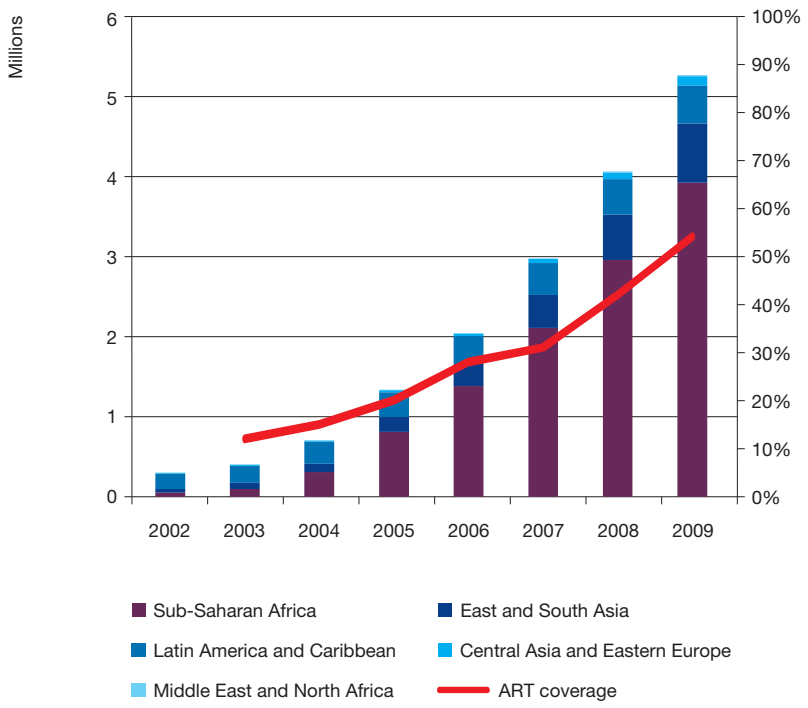
for quantifying the importance of the policy interventions that were identified as potential drivers for improving access to ARVs over the last decade.

Significant progress has been made, but there remains much to be done

The most widely used measure of access is the ART coverage rate — this is the fraction of people eligible for ART that effectively receive treatment.[2] As shown in Figure 2, in the past 10 years, there has been a substantial improvement in access to ART, and approximately 50 % of the HIV-infected population eligible for ART now has access, which represents an estimated five million people being treated.[3]

Figure 2: *Patients receiving ART in developing countries by region*

SOURCE: BASED ON WHO PROGRESS REPORT 2010 AND WHO DATA (EXTRACTED FROM HTTP://WWW.AIDSINFOONLINE.ORG/)



This picture of progress was also illustrated by each of the case studies (summarised in Table 1).

2 This is also complicated as over the past decade we have seen changes in the clinical criteria for commencing ART treatment based upon diagnostic testing of the CD4 cell count. We have based out analysis on measures reflecting the older threshold of 200 cells/mm³. This was raised to 350 cells/mm³ by the WHO in the 2010 HIV/AIDS guidelines. Using the older threshold allows more consistent data over time. However, it is important to note that access as measured by the new threshold is substantially lower.

3 The figures are obviously less positive if we were to use instead the new WHO recommended threshold for ART initiation. The change in the threshold, which now recommends ART to be initiated at an earlier stage of disease, increased the number of eligible patients in low- and middle-income countries by 45 %, from 10.1 million to 14.6 million. In spite of continued progress, according to the new guidelines only 36 % of patients in need of ART's in low- and middle-income countries currently have access to it.

Table 1: *Overview of case studies*

SOURCE: CRA ANALYSIS

		Botswana	Brazil	India	Mexico	Rwanda	South Africa	Thailand
Category	Region	Africa	Latin America	Asia	Latin America	Africa	Africa	Asia
	Income group as at 2000*	Upper middle income	Upper middle income	Lower middle income	Upper middle income	Low income	Upper middle income	Lower middle income***
	Type of epidemic	Generalised	Concentrated	Concentrated	Concentrated	Generalised	Generalised	Concentrated
Political Will	Year of HIV universal service	1999	1996	2004	2003	2002	2004	2000
Spending	Share of HIV spending on treatment (including infrastructure, staff, drugs, etc.)	48.6% on treatment	83.9% on treatment	37.2% on treatment	74.8% on treatment	40.3% on treatment	Not available	76% on treatment
	Involvement of the international community	67.3% domestic funded, ACHAP a significant component	99% domestic funded	16.5% domestically, Global Fund a significant funder	99.4% domestic funded	8.2% public funding, with the rest through Global Fund and bilateral funding	72.7% public funding, with the rest through bilateral funding	90% public funding, with the rest through Global Fund
IP	Local generic industry	No	Yes	Yes	No	No	Yes	Yes
	Government own manufacturer	No	Yes	No	No	No	No (under debate)	Yes
	Use of compulsory licensing	No	Yes	No	No	No	No	Yes
	Use of Paragraph 6	No	No	No	No	Once	No	No
Access	ART coverage 2004**	46%	83%	5%	46%	13%	5%	27%
	ART coverage 2009**	95%	80%	41%	71%	95%	56%	76%

NOTES:
* World Bank categorisation
** ART coverage according to 2006 WHO guidelines
*** Changed in 2011

Case studies in Sub-Saharan Africa (SSA): In Botswana the number of patients with HIV/AIDS who receive ART has increased by a factor of four between 2000 and 2005. By 2009, 87 % of the population in need of treatment was able to receive it. Similarly, Rwanda has one of the highest rates of ART coverage of any country in Africa, almost 90 % by the newest WHO guidelines. Progress in South Africa has been slower but it has the largest ART program in the world. However, at is also has the largest population of people with HIV/AIDS, access to treatment remains relatively low compared to other middle-income countries, although above the average

in Sub-Saharan Africa: 66 % of people needing treatment actually received it in 2009 according to 2006 WHO guidelines (37 % according to 2010 WHO guidelines).

Case studies in Asia: India has improved access to ARTs over the last decade, but there remains a significant challenge. In 2004, only 28,000 people were receiving ART, out of a population of 622,222 who needed it (4.5 % coverage) as defined by the 2006 WHO Guidelines. According to 2006 WHO Guidelines, 780,668 people required ART in 2009 and 41 % of them received it. Even faster progress is observed in Thailand with the number of HIV/AIDS patients receiving ART increasing steadily over the last decade. In 2002, only 2,000 patients were treated but this has grown to more than 200,000 patients receiving ART in 2009. The level of ART coverage was slightly below 80 % using the 2006 WHO guidelines, and slightly above 60 % using the new 2010 guidelines.

Case studies in Latin America: Coverage rates in Brazil have been stable, but at a high level, between 80 % and 85 % from 2004 to 2009, the period for which the WHO provides records. Whilst in Mexico, the number of HIV/AIDS patients receiving ART has increased steadily over the last decade. By 2009, Mexico has been able to offer ART coverage to 71 % of HIV/AIDS patients with a cell-count below 200 cells/mm^3 and to 54 % of patients below 350 cells/mm^3.

Factors contributing to improvements in access to ART

From both the case studies and the statistical analysis, a number of conclusions can be drawn (summarised in Table 2). The date when the universal ART programmes were initiated is clearly important and this reflects the relevance of political will and commitment. It is hardly surprising that programmes starting earlier-in Brazil and Botswana-have been the most successful in achieving high levels of access to ARVs. Political commitment to HIV/AIDS, encouraged by civil society and NGOs, has played a significant role in changing attitudes, committing domestic resources, and encouraging the industry to increase its contribution. However, the speed at which it has been possible to improve access depends on the development of the domestic health infrastructure and associated programmes to address stigma. Building up necessary infrastructure takes time. It is one of the primary reasons that countries struggle to raise levels of access at an accelerated rate.

The substantial increase in the resources from the international community that have been dedicated to promoting health over the last several years has begun to change the trajectory of the HIV/AIDS epidemic in the poorest countries, as evidenced by the case studies of Rwanda, Botswana, and South Africa. Only once the Global Fund, the President's Emergency Plan for AIDS Relief (PEPFAR), the Gates Foundation, and UNAIDS focused resources did access start to improve for the poorest countries. Middle-income countries have mostly funded their own programmes although they have also been able to leverage the experience of multilateral agencies to their benefit.

The role of the pharmaceutical industry has been important. The innovative industry has contributed to the affordability of ARVs through differential pricing, which emerged as a common practice at the beginning of the decade, and more flexible licensing opportunities. Voluntary licence agreements have played a sig-

nificant role in the development of generics, particularly in South Africa, and are increasingly important to the provision of second-line medicines by Indian generics. Last, but not least, generic manufacturers have been important in the great majority of the case studies. In Brazil, Thailand, India, and South Africa, domestic suppliers have played an important role for first-line ARVs. In Botswana and Rwanda, Indian generics have played an important role through pooled and direct purchases. This has been clearly the case for first-line treatments, and they will play a similar role for second-line treatments in the future.

Neither the case studies or the statistical analysis suggest that the use of compulsory licensing or provision of generics through using Paragraph 6 have played a significant part in improving access. Very few products have been compulsory licensed (and even fewer have used Paragraph 6 provisions).

Instead the analysis the supports the value of partnership between different stakeholders, whether represented by the Global Fund itself or through partnership programmes, such as the Accelerated Access Initiative (AAI), or the African Comprehensive HIV/AIDS Partnerships (ACHAP).

Table 2: *Overview of key factors affecting access in the case studies*

SOURCE: CRA ANALYSIS

	Rwanda	India	Thailand	Brazil	Botswana	Mexico	South Africa
Political will	***	*	***	***	***	***	**
Overcoming stigma	**	*	Unknown	***	**	Unknown	**
Domestic healthcare capacity	**	*	**	**	***	***	**
International funding	***	**	*	*	**	*	**
Negotiation and procurement	***	*	*	*	*	**	***
Generic manufacturers	***	***	***	***	**	*	***
Compulsory licensing	*	N/A	*	*	N/A	N/A	N/A
Partnerships	***	**	**	*	***	*	**

NOTES:
*** represent a significant factor in raising access to the current level
* represent a minor factor in raising access to the current level

Conclusions

There has been substantial progress in providing access to HIV patients over the last ten years. ART coverage in low- and middle-income countries has increased from 12 % in 2003 to 54 % in 2009, measured according to the 2006 WHO guidelines. This is due to many different factors working together. However, given many challenges clearly remain and there is still a large under-served population, it is vitally important the lessons from the progress that has been achieved are built on in the future.

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