

ASSESSING THE VALUE OF BIOPHARMACEUTICAL INNOVATION IN KEY THERAPY AREAS IN MIDDLE-INCOME COUNTRIES

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KEY FINDINGS

THE INTERNATIONAL FEDERATION OF PHARMACEUTICAL MANUFACTURERS AND ASSOCIATIONS (IFPMA) ASKED CHARLES RIVER ASSOCIATES (CRA) TO REVIEW THE EVIDENCE ON THE VALUE OF INNOVATION IN MIDDLE-INCOME COUNTRIES (MICS) AND TO TEST HOW THE EXPERIENCE OF THESE COUNTRIES COMPARES TO THAT OF HIGH-INCOME COUNTRIES (HICS)¹

We found that:

- For all five therapy areas investigated there is evidence that innovative medicines have delivered value to MICs (and HICs).
- Beyond the benefits to the patient, there is evidence of savings to the healthcare system and wider societal benefits from innovative medicines. However, there remains an enormous untapped potential to improve patient outcomes by adopting them more widely.
- The case studies illustrate the importance of national prioritisation and investments in healthcare infrastructure, as well as the value in building better epidemiological and cost databases to support the development of modern methods of evaluating the relative value of alternative therapies.

Methodology

The report focuses on five disease areas: coronary heart disease (CHD), depression, diabetes type II, HIV/AIDs, and rotavirus infections. These therapy areas were chosen because they have a high disease burden in MICs, represent both communicable and non-communicable diseases (NCDs) and are therapy areas where there are mature classes of medicines and where innovation is more recent. We adopted two different approaches: comparing across different MICs - this was the approach used for CHD, depression and HIV -, and comparing the value in a MIC directly to that observed in a HIC

- this was the approach used for rotavirus and diabetes type II.

We have classified value as falling into three general categories; the clinical benefit to patients, the impact upon health system costs and wider societal benefits.

From a methodological perspective the evidence base also consists of studies of different types: academic international comparisons, reports by organisations such as the WHO, reports derived from clinical research and analysis undertaken as part of the clinical or economic assessment of these medicines.

¹ The full report can be downloaded at http://www.ifpma.org/fileadmin/content/Publication/2014/value_of_innovation.pdf

Value of radical and incremental innovation in MICs

In all of the therapy areas considered there is evidence of value being delivered but it is clear that the quality of the evidence is weaker than in HICs. It is also the case, that the existing evidence for communicable diseases is stronger than for non-communicable diseases.

CHD: For MICs, CHD is a major issue in terms of mortality and the years of life lost due to premature death and disability. Looking at selected MICs, only Brazil, India and China have a national plan, and even these started only within the last three years. Therefore, it is still relatively early to assess their impacts. In terms of access, all the selected countries have included at least one molecule in each class, however, access depends on adequate primary care capabilities to diagnose, treat and monitor patients.

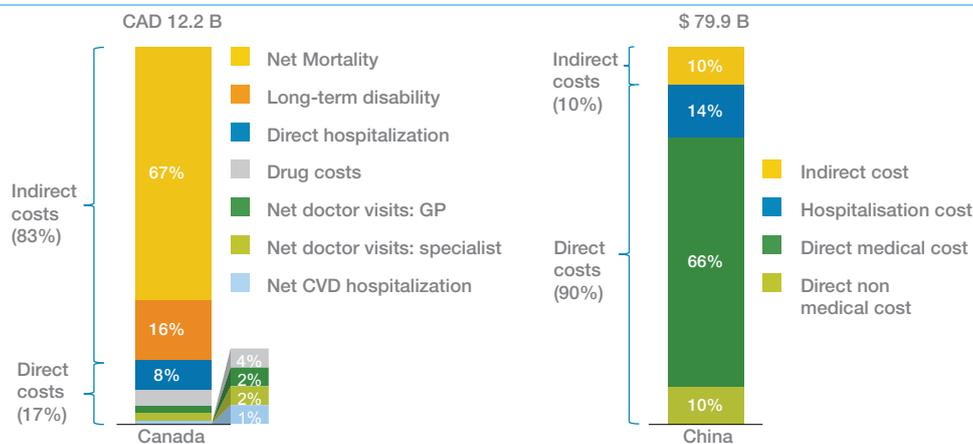
The evidence that the treatment for CHD has brought clinical and therapeutic benefits within the BRICS is mixed and it is difficult to determine how much of the reduction in CHD-caused mortality is attributable to access to medicines. Overall, there is evidence of value but there appears a significant opportunity for further health gains from the more widespread deployment of these innovative medicines from past decades.

Depression: Depression is a common mental disorder that has significant consequences for the patient's quality of life and at its worst, can lead to suicide. There are several classes of antidepressants with different mechanisms of action. Regarding access, very few MICs have national strategies targeted specifically at depression. Most of the MICs studied – Brazil, Russia, India, and China – only

have national mental health policies, which are geared more towards psychotic conditions than depression. However, there are exceptions such as Chile which has a program specifically aimed at depression. In terms of value, there is evidence that the treatment for depression delivers clinical and therapeutic benefits, however, there clearly remains a significant issue associated to awareness and the extent of resources allocated in the health system. There is more limited evidence regarding the link between the use of antidepressants and non-clinical benefits.

Diabetes type II: The improved economic status and the adoption of western life styles across society in MICs, notably poor diets and lack of exercise, is driving the incidence and prevalence of diabetes to unprecedentedly high levels.

Figure 1: Burden of Diabetes in HICs and MICs



Source: CRA analysis using Canadian Diabetes Association (2009), 'An economic tsunami the cost of diabetes in Canada' and Wang et al (2009), 'Type 2 diabetes mellitus in China: A preventable economic burden', The American Journal of Managed Care, 15,9; Note: CAD – Canadian dollars

There has been considerable advance in the medicines available for treating diabetes. Whilst, diagnosis, treatment and management of diabetes are very well defined in HICs, access to treatment in MICs appears significantly less complete. Diabetes care in China has limited infrastructure, and the delivery of healthcare varies considerably by location. However, we found evidence diabetes treatments have also yielded clinical benefits in China when they were used, and there is evidence that effective treatment results in savings to the health system. Treatment has also been shown to reduce lost productivity among diabetics in China, although since indirect costs were a smaller portion of the societal cost of diabetes in China compared to HICs, the savings per person are not as large.

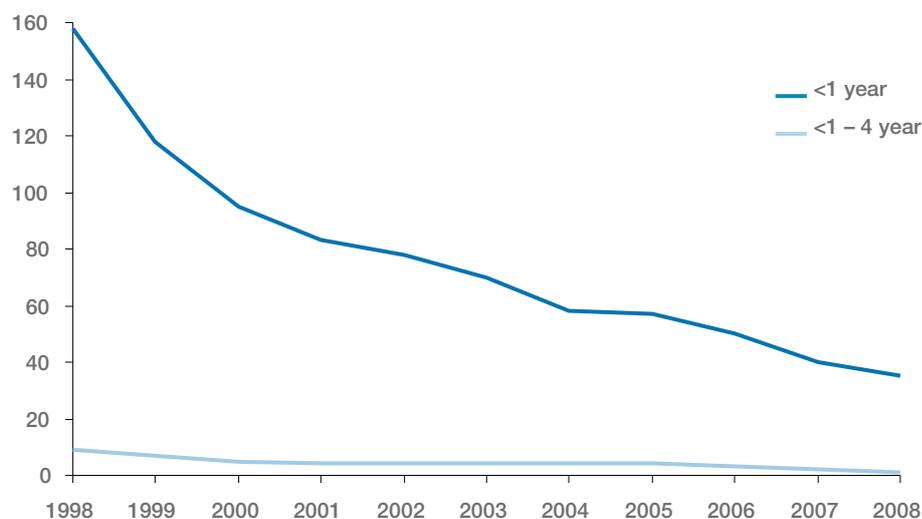
HIV/AIDS: HIV/AIDS is a severe disease and addressing it became a national priority during the 1990s and early

2000s. It is evident that access to ART (anti-retroviral treatment), in combination with improvements in prevention and diagnosis, has played a significant role in fighting this disease. Access to improved fixed dose combinations is likely to have had a positive impact in markets where they are available, due to increased adherence. This represents both radical and incremental innovation. In addition to clinical and therapeutic benefits, there is also evidence that the introduction of these policies and access to ART is beneficial economically, through a reduction in other healthcare costs (such as hospitalisations), and socio-economically, through a reduction of absenteeism and improvements in HIV/AIDS patient quality of life.

Rotavirus: Diarrhoea is a leading killer of young children worldwide, and rotavirus is the most common cause of severe diarrhoea. Two vaccines

against rotavirus were launched in 2006 and 2008. Rotavirus vaccination programs have been shown to bring a wide range of benefits within both HICs (as illustrated by Australia) and MICs (as illustrated by Brazil). In Australia, the biggest benefit we observed was related to the reduction in hospitalisation costs, while in Brazil we observed clinical and therapeutic benefits as well as those related to hospitalisation costs. In particular, the rotavirus vaccine has led to a dramatic reduction in gastroenteritis-related deaths in Brazil. These results reflect the fact that rotavirus-related mortality is almost non-existent within HICs while it is still significant within MICs. Rotavirus therefore provides a case study where both HICs and MICs clearly benefit from the introduction of an innovative medicine but where MICs are likely to receive a wider variety of benefits than HICs.

Figure 2: Gastroenteritis-related deaths by age group, Brazil, 1998-2008



Lanzieri et al (2011), 'Impact of rotavirus vaccination on childhood deaths from diarrhoea in Brazil', International Journal of Infectious Diseases, 15, 3

Policy implications

Learning from the case studies, we draw five policy conclusions:

1. Ensuring that the widest population receives the value of innovative medicines often requires a national programme to increase awareness and overcome cultural challenges

If we consider the therapy areas where there is the clearest evidence of value being delivered in MICs, this typically occurs once this has been recognised as a priority area at the national level. HIV/AIDS and, to a less extent, rotavirus have been a major focus of governments in the case study countries. For NCDs, political prioritisation also appears important, particularly, where the main limitations that are preventing the benefits of innovative treatments from being brought to MICs are the healthcare infrastructure and cultural barriers. Only in recent years, have we seen CHD, depression, diabetes being given significant attention and therefore it is not surprising that the evidence on benefits today is limited.

2. For medicines to deliver value, there needs to be appropriate healthcare infrastructure, this works best when integrated programmes are used to ensure diagnosis, testing, access to medicines and maintenance of patients on a course of treatment

For CHD, diabetes or depression, for example, the main barrier to treatment is that patients suffering or at risk of suffering from these diseases are not always diagnosed. It is evident that the necessary health system, clinical infrastructures for diagnosis, treatment and follow-up needed to extend access or distribution systems do not always exist. The largest benefits have been achieved in those therapy areas where the infrastructure required to introduce innovation is smaller or where it has been seen as a priority (and hence significant investment in infrastructure undertaken). This requires adequate healthcare resources and government capital and revenue funding being consistently allocated to building these infrastructures over time. Capturing the value of innovative medicines, especially for NCDs, requires an integrated policy developing the infrastructure to diagnose and manage patients, as well as access to innovative medicines.

3. The healthcare system needs to incorporate both incremental and radical innovation

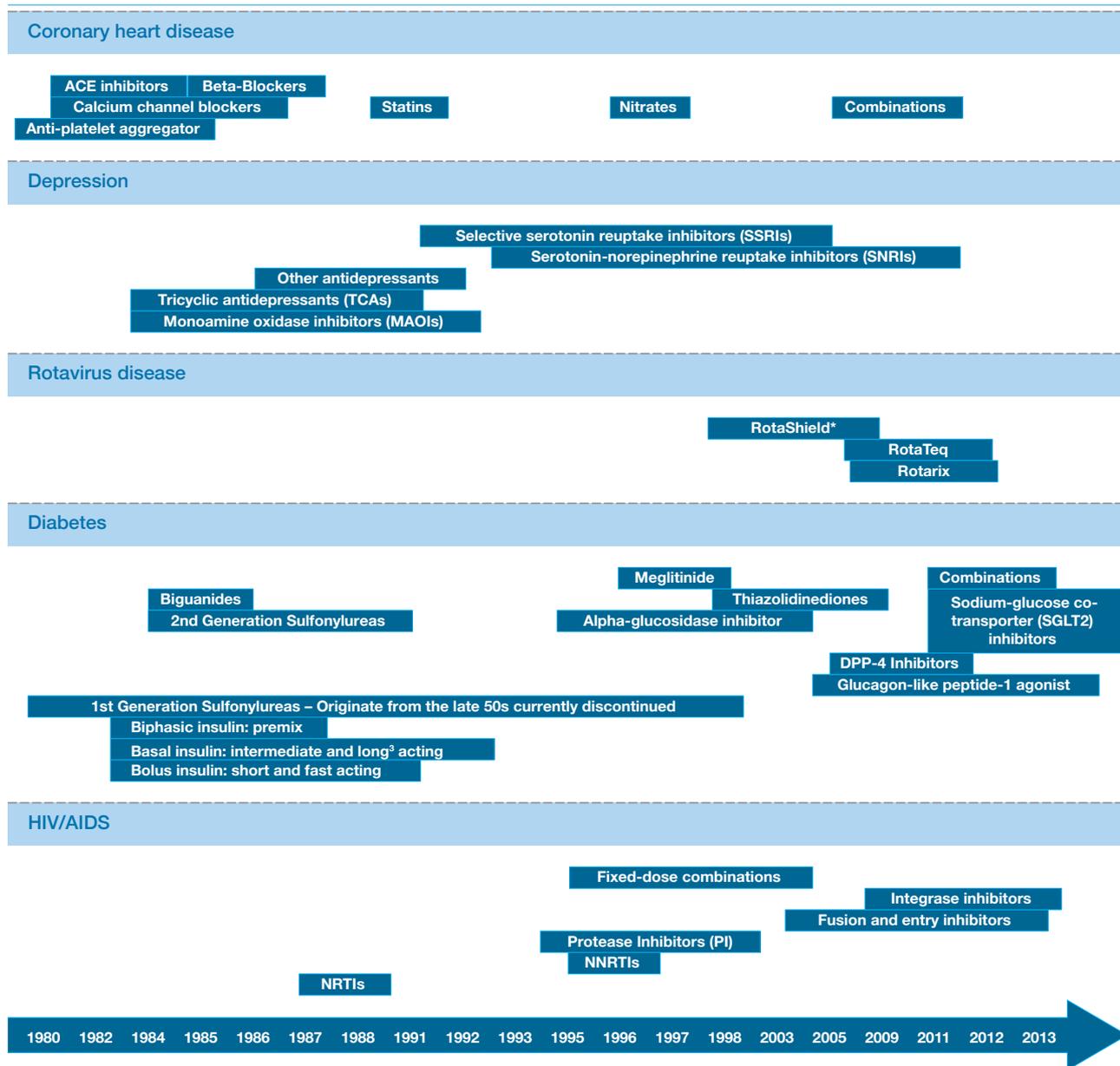
The benefits from innovative treatments have been delivered through different types of innovation. We find that whether the innovation

is perceived as radical or incremental is not associated with the value achieved. Most would characterise rotavirus and HIV/AIDS as involving radical innovation. However, it is clear that the development of classes of medicines for HIV, fixed dose combinations and targeting the medicines on new patients groups has brought significant value to patients and society more generally.

4. There is not a simple relationship between whether we can observe value and the current intellectual property protection of the medicines

Based on the case studies chosen for this project, we found that the current status of patent protection does not inhibit the value of the innovation to society. The study shows value to society being delivered by both patented and off-patent medicines. Indeed, in the therapy areas where there is the clearest evidence that treatments have brought the greatest value, rotavirus and HIV/AIDS, the medicines used are still protected. In contrast, in therapy areas where the existing treatment has been on the market since the '80s and is now off-patent, and low-cost drugs are available – depression and CHD – only limited benefits have been realised and there is still significant value to be extracted.

Figure 3: Development of innovative treatment in the selected therapy areas



Source: CRA analysis

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5. In MICs, as in HICs, value can be delivered directly to patients, in terms of cost savings to the healthcare system and to wider society. This needs to be reflected in how medicines are assessed.

Innovative medicines have delivered a broad range of benefits to patients but also to

the healthcare system and the society in general. Evidence shows that the full range of benefits can be achieved in both HICs and MICs and for some therapy areas a wider variety of benefits is achieved in MICs than HICs. There is considerable scope over the long term for MIC health authorities to refine their

approaches to assessing the value of modern medicines from a national perspective through building better epidemiological and cost databases to support the development of modern methods of evaluating the relative value of alternative therapies.

Conclusion

The purpose of this paper was to set out the evidence that innovative medicines deliver value in MICs and to compare this to evidence from HICs. We find innovative medicines deliver value to patients but also through a reduction in healthcare costs and to wider society in MICs and HICs - the categories are often the same, even if, the composition of this does vary in MICs compared to HICs. In some cases, medicines offer greater benefits in MICs and in some cases less.

The extent of access to medicines is a significant factor in the value they deliver. The cost of

medicines has an impact on how widely they are used, but we have found that the value delivered by innovative treatment in MICs depends on several other elements: whether governments have chosen to prioritise that particular therapy area and the availability of the appropriate infrastructure to implement the innovation.

It is also clear that value of medicines occurs through both radical innovation, offering a treatment where none previously existed but also through incremental innovation, reducing side effects, expanding

choice of treatments or widening the patient population. This brings value to MICs, just as it does in HICs.

In summary, the case studies illustrate well the remarkable range and diversity of biopharmaceutical innovations which have added value across all MICs to some degree. It also reinforces the message that there remains enormous untapped potential to improve patient outcomes by adopting them more widely. In some cases less than 10-20% of the relevant population currently have access to these important advances in therapy.

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