

## Non-Communicable Diseases 5



# Promotion of access to essential medicines for non-communicable diseases: practical implications of the UN political declaration

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Access to medicines and vaccines to prevent and treat non-communicable diseases (NCDs) is unacceptably low worldwide. In the 2011 UN political declaration on the prevention and control of NCDs, heads of government made several commitments related to access to essential medicines, technologies, and vaccines for such diseases. 30 years of experience with policies for essential medicines and 10 years of scaling up of HIV treatment have provided the knowledge needed to address barriers to long-term effective treatment and prevention of NCDs. More medicines can be acquired within existing budgets with efficient selection, procurement, and use of generic medicines. Furthermore, low-income and middle-income countries need to increase mobilisation of domestic resources to cater for the many patients with NCDs who do not have access to treatment. Existing initiatives for HIV treatment offer useful lessons that can enhance access to pharmaceutical management of NCDs and improve adherence to long-term treatment of chronic illness; policy makers should also address unacceptable inequities in access to controlled opioid analgesics. In addition to off-patent medicines, governments can promote access to new and future on-patent medicinal products through coherent and equitable health and trade policies, particularly those for intellectual property. Frequent conflicts of interest need to be identified and managed, and indicators and targets for access to NCD medicines should be used to monitor progress. Only with these approaches can a difference be made to the lives of hundreds of millions of current and future patients with NCDs.

### Introduction

Access to medicines and vaccines to prevent and treat non-communicable diseases (NCDs; mainly cardiovascular diseases, chronic respiratory diseases, diabetes, and cancer) is unacceptably low worldwide. Large disparities exist between high-income, middle-income, and low-income countries, and within countries, in access to medicines for NCDs and for infectious and acute diseases.<sup>1</sup> Mean availability of essential medicines in 36 low-income and middle-income countries was about 36% for NCDs versus 54% for acute diseases in the public sector, and 55% versus 66% (but at a much higher price) in the private sector.<sup>2</sup> The probability of patients receiving at least one medicine for secondary prevention of cardiovascular disease was 19·8% in low-income countries, 30·7% in low-income and middle-income countries, and 54·9% for upper-middle-income countries.<sup>3</sup> Why has substantial progress been made in global access to very costly medicines, such as antiretroviral drugs for HIV, but not for medicines for NCDs, which are largely off-patent and cheap to produce? What can be done to make essential medicines, irrespective of patent status, affordable for prevention and treatment for current and future patients?

We propose several measures to improve efficiency in medicine supply within existing budgets, increase financing for NCDs, integrate pharmaceutical management for such diseases with existing initiatives, and ensure access to new and future essential medicines.

Cross-cutting issues specific to NCD medicines are the management of frequent conflicts of interest and monitoring of progress. We refer to long-standing experiences with pharmaceutical policies for essential medicines in general and for antiretroviral medicines in particular, and apply the best experiences to NCDs. A particular issue is the insufficient access to controlled opioid analgesics for pain relief and palliative care (panel 1). Much of our report could apply equally to medicines for mental health, which should also be a priority for global action; however, they are not discussed in this Series.

### Access to essential medicines

Access to essential medicines is an important aspect of development. It was part of the Alma Ata Declaration of 1978, and is one of the six targets of Millennium Development Goal (MDG) 8 (develop a global partnership for development). This commitment was not confined to medicines for particular disorders, such as those specifically mentioned in MDG 5 (improve maternal health) and MDG 6 (combat HIV/AIDS, malaria, and other diseases). In 2007, the UN Secretary-General established the MDG Gap Task Force to consolidate information about progress towards MDG 8. In each of its four annual reports<sup>10–13</sup> of MDG 8 since 2008, the Task Force has noted the need for increased attention to access to medicines for NCDs. The 2008 report<sup>10</sup> contrasted the low level of support

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### Key messages

- Access to medicines is a core component of the right to health; this is especially relevant for long-term treatment of non-communicable diseases (NCDs). However, access to essential medicines and vaccines to prevent and treat NCDs is unacceptably low worldwide
- Efficiencies in improvement of access and affordability can be achieved within existing budgets. With the example of HIV, more medicines can be bought through generic policies, and better patient adherence to long-term treatment can be achieved with improved patient-centred care
- Prepayment and risk sharing through tax-based or obligatory health insurance are the most efficient ways to increase population coverage from domestic sources. Some low-income countries will need additional international financing to address NCDs
- Governments should ensure access to new, patented, and expensive NCD medicines through the full use of the flexibilities of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement
- Governments, intergovernmental organisations, and civil society need to aid and improve access to opioid analgesics for pain relief and palliative care
- Civil society advocates, treatment guideline committees, and patient groups should identify and manage their frequent conflicts of interest in relation to the pharmaceutical industry
- Specific indicators and targets are needed to monitor country progress towards access to essential medicines
- After 2015, access to medicines for NCDs should become a genuine priority in the development agenda, supported by resources, action, and systematic monitoring

that had been given to NCD medicines compared with that given to other diseases.

Although access to medicines for NCDs has formally always been part of the MDGs, in practice it has been neglected. For example, the target is entirely missing from the 2007, 2009, 2010, 2011, and 2012 official MDG reports (with access to treatment for HIV/AIDS, malaria, and tuberculosis reported as part of MDG 6). In the 2011 UN General Assembly Political Declaration on the Prevention and Control of NCDs,<sup>14</sup> states made several commitments relating to access to medicines, technologies, and vaccines, with additional commitments for strengthening of health systems, health-care infrastructure, budgetary allocation, and universal coverage. In the Rio+20 Outcomes Document,<sup>15,16</sup> state officials committed to promote affordable access to prevention, treatment, care, and support for NCDs, and called for further national and international cooperation to improve distribution and access to safe, affordable, effective, and quality medicines, vaccines, and medical technologies.

The right to the highest attainable standard of health was first endorsed in WHO's Constitution (1946),<sup>17</sup> and was later included and expanded upon in several international treaties, including the International Covenant on Economic, Social and Cultural Rights (1966)<sup>18</sup> and the UN Convention on the Rights of the Child (1989).<sup>19</sup> The UN Political Declaration on NCDs reaffirmed the right of everyone to the highest attainable standard of physical and mental health. Access to medicines is a core component of the right to health<sup>20</sup> and was recognised as such in UN General Assembly Resolution 64/25 to hold the high-level meeting on NCDs.<sup>21</sup> A rights-based approach to health can support national programmes for essential medicines to promote universal access.<sup>22</sup>

In 2008, domestic constitutional or legislative endorsement of access to essential medicines as part of the right to health became a WHO indicator to assess country progress.<sup>23</sup> In that year, 73% of the 186 national constitutions included provisions for the right to health, and 51% mentioned health facilities, goods, and services.<sup>24</sup> Such legally binding obligations on governments can be especially relevant for NCDs, for which access to treatment is still so often deficient. Patient-initiated court cases have resulted in governments including disadvantaged groups in their public services or nascent reimbursement schemes.<sup>25</sup> However, as noted in Latin America, excessive individual litigation can result in the allocation of resources to treat those with enough resources to start court proceedings,<sup>26</sup> undermining population-wide planning and resource allocation.

In May, 2012, the World Health Assembly adopted the global goal of a 25% reduction in preventable NCD deaths by 2025 (the 25 by 25 goal).<sup>27</sup> Access to medicines and vaccines is key to achievement of this goal. For example, a multidrug regimen based on opportunistic screening to prevent cardiovascular disease in high-risk individuals is estimated to result in prevention of almost 18 million deaths (a fifth from cardiovascular disease) in 23 low-income and middle-income countries in the next 10 years.<sup>28</sup> Investigators have suggested that in many middle-income countries, financing for scaling up of access to treatment is feasible from domestic sources, in view of the economic growth of these countries.<sup>29</sup> The so-called best-buy NCD strategies for countries include pharmacotherapy for secondary prevention of cardiovascular disease, glycaemic control for diabetes, provision of aspirin for acute heart attack, and the hepatitis B vaccine for prevention of liver cancer.<sup>27</sup>

What do countries need to do to improve access to medicines for NCDs to reach the 2025 target and to lay the foundations for progress after 2025? Because medicines are part of the six building blocks of health systems,<sup>30</sup> scaling up of access to medicines cannot be achieved in isolation,<sup>31</sup> but needs a comprehensive health system approach including, for example, pharmaceutical sector governance, appropriate pharmaceutical workforce

training, pharmaceutical management information systems, procurement planning, and sustainable financing of medicines.<sup>32</sup>

## Increase efficiency in selection, procurement, supply, and use to promote access to medicines within the existing health budget

### Generic policies

Data from several countries show that access to medicines for NCDs can be substantially improved within existing budgets for pharmaceutical medicines by optimisation of the selection, procurement, supply, and use of medicines. For example, legislation can promote generic market entry and substitution, which are further facilitated by quality assurance systems to reassure prescribers and the public, price information promoting the financial advantages of generics, and reimbursement schemes promoting generic substitution and reduced patient copayments for generic products. Policies that promote generic medicines can generate large savings; in France, implementation of a general generic substitution strategy saved nearly US\$2 billion in 2008 alone.<sup>29</sup> Policies promoting the use of safe, affordable, effective, and quality generic medicines should address the effect of mark-ups and of poor purchasing practice, and any perception that low price equals low quality.<sup>33,34</sup>

### Rational selection

Selection of suitable medicines can also support generic products. In 2009, the Kyrgyzstan Government spent 57% of its insulin budget on patented analogue insulins, which were used by only 13% of patients with diabetes.<sup>35</sup> In 2011, WHO concluded that analogues had few advantages compared with generic human insulin and did not add them to its model list of essential medicines. If these patients were put back on generic insulin, twice the number of patients with diabetes could have been treated in Kyrgyzstan with the same budget. Hence, careful selection of medicines financed by public or private financing schemes is crucial to ensure efficient procurement and use.

Most NCDs can be treated with a small range of off-patent medicines, such as analgesics, antihypertensives, cardiovascular drugs, statins, antiasthmatics, and some common anticancer drugs. However, some generic medicines are so cheap that they are no longer commercially appealing and might stop being produced (panel 2). WHO's model list of essential medicines and global model evidence-based clinical guidelines for the prevention and treatment of NCDs are periodically updated through assessments of potential new essential medicines.<sup>37</sup> The list is a guide for national committees that are responsible for identification of the most cost-effective medicines at country level for procurement, reimbursement, and treatment decisions, and helps to focus national efforts towards universal coverage. A

### Panel 1: Access to opioid analgesics

With increased attention to medicines for prevention and treatment of NCDs, priority should also be given to opioid analgesics for pain relief and palliative care. For access to opioid analgesics, disparity between high-income and low-income countries is especially high. The International Narcotics Control Board estimated that in 2009, more than 90% of the global consumption of opioid analgesics was in Australia, Canada, New Zealand, the USA, and some European countries, with less than 10% of global quantities used by the other 80% of the world's population. The major barriers have long been known, and can be overcome. These barriers include insufficient training of health-care professionals for the prescription and administration of opioids; misperceptions of health-care professionals, policy makers, and patients and their families about the safety of opioids; exaggerated fears about the development of dependence; overly restrictive laws and regulations that exceed the requirements of the UN Single Convention on Narcotic Drugs for the trade, distribution, and use of opioids; and unduly harsh sanctions for unintentional mishandling of opioids by health workers.

Substantial international developments have laid the groundwork for coordinated global action between governments, intergovernmental organisations, and civil society, including two resolutions of the UN Commission on Narcotic Drugs,<sup>4,5</sup> the Political Declaration's recognition of palliative care, and major UN reports.<sup>6-8</sup> Progress has been made in many countries, including Uganda, Kenya, and Nigeria, through the joint efforts of ministries of health, health-care workers, national palliative-care associations, regional networks, international non-governmental organisations and supporters, and the WHO Collaborating Centre, the Pain and Policy Studies Group.<sup>9</sup>

study<sup>38</sup> of 13 sub-Saharan African countries showed that only 38% of national lists were updated in the past 5 years. The investigators noted that antihypertensive drugs on national lists were substantially cheaper than were those not included, underscoring the role of the national list in ensuring financial accessibility.

### Quality assurance

Assurance of medicine quality is crucial to protect the population from potentially harmful medicines and reduce waste of resources. Because of inadequate regulation and insufficient penalisation, substandard medicines are common in developing countries.<sup>39,40</sup> Medicines for NCDs are no exception, as shown by the tragic incident in Pakistan in 2011, when contamination of isosorbide mononitrate led to more than 100 deaths.<sup>41</sup> In Rwanda, 20% of hypertensive medicines purchased on the market were of substandard content and 70% were of insufficient stability.<sup>42</sup> Although regulation of safe, quality medicines is a necessary investment by

### Panel 2: Scarcity of access because medicines are not profitable enough

In some cases access to essential medicines is compromised because products are so cheap and demand so volatile that pharmaceutical companies might consider the sales not sufficiently profitable to be maintained. Examples for NCDs are thiazide diuretics and morphine. However, producers of aspirin in the USA and elsewhere have been able to survive on narrow margins when demand is predictable. Paediatric antiretroviral drugs are an example of how a small, fragmented, and unprofitable market can be stabilised: the Clinton Foundation with funding from UNITAID stabilised the market through global pooled demand, generation of uptake at programme level, and donor funding for the drugs. Production can also be threatened when global companies acquire high-end generic companies in India then shift production capacity towards more expensive products for the Indian market and for export to industrialised countries.<sup>36</sup>

society to protect the public and support the domestic pharmaceutical industry, only about one in three regulatory agencies in Africa function adequately.<sup>43</sup> Some manufacturers take advantage of this unfortunate situation by exporting substandard medicines to other countries while being regulated for domestically marketed products.<sup>40,44</sup>

The most effective long-term solution is that national medicines regulatory authorities receive increased political support and resources to protect patients. Worldwide, the success of the WHO programme to prequalify HIV/AIDS, tuberculosis, and malaria products for UN procurement cannot easily be extended to NCD medicines for which the market is so fragmented. Prequalification works only when large global funds and procurement programmes or large national procurement agencies are interested in using global assessment reports of important products of which the quality, safety, and efficacy is doubtful or unknown. For NCDs, the most likely candidate for inclusion would probably be generic human insulin, for which few international suppliers are available and for which difficulties exist for low-resourced regulators to assess quality. For other NCD medicines, the best solution might be for national procurement agencies to follow the well established quality assurance policies of the Global Fund to Fight AIDS, Tuberculosis and Malaria. This approach could be supported by the establishment of an independent system for the support, assessment, and endorsement of national and international procurement agents and distributors,<sup>45</sup> or by the strengthening of a few effective regulatory authorities to regionally collaborate with countries with less capacity. Governments need to address the many political and financial barriers to implementation of these strategies.

### Monitoring of availability

Good monitoring systems for stock levels and use are crucial. Innovative use of communication technology, such as mobile telephones and short message service (SMS) messaging, could increase procurement efficiency and monitoring. Community volunteers can track the availability of medicines in local facilities, and their SMS messages can feed into a website that helps to identify underperforming districts and start corrective action.<sup>46</sup> Similar approaches for first-line antimalarial drugs have resulted in a 50% decrease in facility stock-outs.<sup>47</sup> Such initiatives, if successful in the medium term, need to be scaled up.

### Rational use

Distribution challenges are often referred to as being the transport problem of the last mile, from district centre to village facilities. However, in practice the largest economic and public health losses, estimated at up to 50% of the cost of medicine, often take place in the last metre—ie, in the interaction between the prescriber and patient and the direct purchase of medicines by consumers. Approaches to improve the use of NCD medicines through prescription or over-the-counter use are the same as are those for other essential medicines.<sup>48,49</sup> Such approaches include the strong recommendation to establish a dedicated national body to promote prescribing guidelines, monitor medicine use, and provide education and independent information to prescribers, patients, and consumers, as is done in several countries. Examples are the National Prescribing Centre in the UK, the Belgian Centre for Pharmacotherapeutic Information, and the Rational Use Directorate of the Sultanate of Oman. A particular issue with NCDs is the need to promote patient adherence to long-term treatment, as discussed later in this report.

### Increase financing for NCD medicines through domestic funding and international support

In low-income and middle-income countries, out-of-pocket payments for medicines account for the largest proportion of household health expenditure.<sup>29</sup> For example, in Ghana, the lowest paid government worker will use 15 days' wages to pay for 1 month of the lowest price hypertension and diabetes treatment from a private pharmacy.<sup>30</sup> Household surveys have shown that 41–56% of households in low-income and middle-income countries spend all their health-related expenditure on medicines; poor households in these countries spend up to 9·5% of their household expenditure on medicines compared with 3·5% by poor households in high-income countries.<sup>31</sup> Reliance on direct out-of-pocket financing for chronic disorders needing daily treatment is a real economic threat to individuals and society as a whole, and is a substantial obstacle to increasing access to medicines for poor populations.

Prepayment and risk sharing through tax-based or obligatory health insurance are the most efficient and



equitable ways to increase population coverage and promote equity.<sup>29</sup> Improved financial protection for families against large medical bills reduces their risk of financial ruin and increases security of their assets and savings; when many families benefit, increased economic activity can stimulate improved economic development.<sup>29,52,53</sup> Financing of access to medicines through universal health coverage, including for NCDs, is a top priority of the policy agenda in India. This agenda includes ensuring of domestic public and private financing, strengthening of the public sector, and ensuring of oversight in the private sector in which all initiatives should enhance equity and rational use.<sup>54</sup>

What will it cost to provide access to medicines for NCDs? A WHO study<sup>55</sup> estimated a cost of \$1 per person per year in low-income countries, less than \$1.50 in lower-middle-income countries, and \$2.50 in upper-middle-income countries for individual best-buys of counselling and drug treatment for people at high risk of cardiovascular disease plus measures to prevent cervical cancer, in a scale-up period from 2011 to 2025. A previous report in 2009,<sup>56</sup> estimated the resources needed to achieve MDGs (including MDG 8e: access to essential medicines) in 49 low-income countries through strengthening of health systems and scaling up of service provision. Increased access to medicines for diabetes, chronic obstructive pulmonary disease, cardiovascular disease, and some cancers from their low levels in 2009, to at least 50% by 2015, will need an incremental cost of \$6.93 per head (compared with countries reaching the MGD for HIV/AIDS, which would need an estimated investment of \$10.24 per head).<sup>56</sup>

These additional costs should be considered in view of the present health expenditure per head of many countries. In the past few years, total per-head pharmaceutical expenditure on medicines has been \$20.3 for low-income countries, \$71.9 for lower-middle-income countries, and \$152.0 for upper-middle-income countries, with high variation between income groups.<sup>57</sup> Because many low-income and middle-income countries have moderate to strong economic growth, there is an especially clear case for increasing of domestic public funding, with at least \$1–2.5 per head for the provision of essential medicines for NCDs to reach the 25 by 25 goal. Although the full amount of nearly \$7<sup>56</sup> might not be possible immediately, most middle-income countries could make a modest investment first.

Some of the poorest countries with low levels of health expenditure and little potential to increase their health budget in absolute terms might need to rely on external support to fund long-term NCD treatments; therefore, an additional international financing mechanism is needed to safeguard the right to health of the poorest communities. Unfortunately, an explicit financial commitment, such as that made by the global community for the AIDS epidemic in 2001,<sup>58</sup> was not forthcoming in the 2011 UN high-level meeting on NCDs.

### **Integrate pharmaceutical management of NCDs with existing initiatives**

An especially important aspect for NCDs is the need to ensure patient adherence to long-term treatment. Patients cannot afford to travel far, especially when such travel expends 1 or more working days every month.<sup>59</sup> Long waiting times and frequent stock-outs do not support adherence. Public health systems need holistic patient-centred care with appointment systems, evening opening hours, and task-shifting and down-referral of chronic treatment to rural facilities close to home. The same issues apply to HIV/AIDS, and there is a strong rationale to extend existing efforts to ensure quality of care for HIV to patients with NCDs.<sup>60</sup> Simplified monitoring and treatment regimens,<sup>61</sup> point-of-care tests,<sup>62</sup> decentralisation of care to the periphery, shifting of tasks from doctors to nurses,<sup>63</sup> and use of adherence counsellors instead of provider-controlled directly observed treatment<sup>64</sup> have all supported improved adherence.<sup>65</sup>

The best-buy options for countries to reduce preventable deaths from NCDs include management of cardiometabolic risk in high-risk individuals at the primary health-care level. The new polypill—a fixed-dose combination of aspirin, a cholesterol-lowering drug, a  $\beta$  blocker, and an angiotensin-converting-enzyme inhibitor<sup>66,67</sup>—might have the many noted advantages of fixed-dose combinations for HIV, tuberculosis, and malaria, which have minimised prescribing errors and missed doses by patients while reducing costs by as much as 50% in some cases.<sup>68</sup> Furthermore, fixed-dose combinations greatly simplify supply-chain management and patient education and counselling.<sup>69,70</sup> More studies of health and economic effects are needed to establish clearly whether the polypill for secondary prevention or high-risk primary prevention for cardiovascular diseases has advantages compared with use of multidrug regimens. If a consensus formulation is reached, the polypill regimen will emerge as a health priority by 2015.

### **Promote research and ensure access to new essential medicines for NCDs**

Unlike the first decade of AIDS treatment, most NCDs can be treated with inexpensive, off-patent medicines. Securing of global access to off-patent NCD medicines would already be an enormous achievement with profound effects on global health. However, access should also be ensured, when needed now and in the future, to newly developed, on-patent NCD medicines and vaccines, such as the HPV vaccine (panel 3). Important new NCD medicines are exceedingly expensive. For example, in the USA, the anticancer drugs erlotinib and rituximab cost \$2400 and \$13 000 per month, respectively.<sup>71</sup> Such expensive prices are largely because these treatments are under patent, which prevents generic competition. Most companies offer reduced prices to low-income and middle-income countries, but

### Panel 3: Access to a new vaccine for human papillomavirus (HPV)

The HPV vaccine protects against HPV types 16 and 18, which cause about 70% of cervical cancer cases. The vaccine is important in low-income and middle-income countries where cancer screening and treatment services are often unavailable. However, only very few of these countries have introduced HPV vaccines into national programmes because of their high price and challenges to start a separate vaccination programme for adolescents. Rwanda, Bhutan, and most recently, Uganda have included the vaccine, but only because of donations from the pharmaceutical industry.

The Global Alliance for Vaccines and Immunisation (GAVI) has played an important part in increasing procurement efficiency. It has worked with manufacturers on strategies to reduce vaccine prices. As a result, in 2011, one manufacturer announced an indicative price offer of US\$5 per dose for low-income countries, a 64% reduction in the lowest public price. To ensure that girls in the poorest countries have access to the vaccine, GAVI and its partners are working with manufacturers within the UNICEF tender process to ensure a sustainable price for low-income countries. This example shows that markets for newly developed essential products can be created by pooled and donor-funded procurement, leading to increased volume and, ultimately, reduced prices. To ensure sustainable prices for low-income and middle-income countries, further price decreases through competition from expected Indian vaccine versions are important.

such voluntary mechanisms are less effective than competition, as was shown for antiretroviral medicines for HIV.<sup>72</sup>

Since 2005, the World Trade Organization's (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement has required 20-year product and process patent protection in all but the poorest of its member countries.<sup>73</sup> Innovator companies use the sequential launch of branded reformulations to maintain market dominance even when patents of the original invention have expired.<sup>74</sup> Not surprisingly, the contested politics of intellectual property and debate about access to medicines surfaced in negotiation of the political declaration on NCDs. The Doha Declaration on the TRIPS Agreement and Public Health<sup>75</sup> was adopted by WTO's ministerial conference in 2001, in the context of widespread concern about the implications of TRIPS for affordability of medicines, particularly for HIV/AIDS. Without restriction to specific diseases or to epidemics, the Doha Declaration affirmed that TRIPS "can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all" and reaffirmed "the right of WTO members to use, to the full" TRIPS flexibilities, including the power to grant compulsory licences.<sup>75</sup>

In the negotiation of the political declaration on NCDs, there was disagreement between the USA and the European Union on the one side, and Brazil, India, Mexico, and other G77 members on the other about inclusion of references to the TRIPS agreement, the Doha Declaration, and the term epidemic.<sup>76</sup> This debate was yet another battle in long-running efforts by these countries and originator pharmaceutical companies to confine the application of TRIPS' flexibilities to medicines for infectious diseases.<sup>77</sup> Ultimately, although the political declaration affirmed the full use of TRIPS flexibilities for NCD medicines, the Doha Declaration was not specifically mentioned. The full use of TRIPS flexibilities was reaffirmed in the Rio+20 outcome document, which did mention the Doha Declaration.

Fierce debates about the association between intellectual property laws and access to medicines for NCDs are taking place in Indian courts in relation to medicines for the treatment of chronic leukaemia and renal and hepatocellular carcinoma (panel 4). These court cases are of global relevance because the Indian pharmaceutical industry supplies many medicines to low-income and middle-income countries,<sup>79</sup> and is referred to as the pharmacy of the developing world. The continuing efforts by the USA and European Union to include provisions stricter than those required by TRIPS<sup>80</sup> in trade negotiations, such as the Trans-Pacific Partnership Agreement<sup>81</sup> and the EU-India Free Trade Agreement, are a serious concern. This issue is an area in which the political declaration's recognition of the need for whole-of-government approaches across different sectors should be applied.

Research needed to address NCDs includes development of health technologies that are adapted to low-resource settings. Identified research and development needs include, for example, vaccines and safe and affordable medicines to address neglected cardiovascular diseases, such as rheumatic heart disease and Chagas disease (a cause of cardiovascular disease), and fixed-dose combination pills to manage diabetes and other risk factors for cardiovascular and renal disease.<sup>82</sup> Such research and development is typically neglected by industry because of low profit. A proposal by WHO experts for a research and development treaty aims to address the research and development needs specific for developing countries, and will only be considered by the World Health Assembly in 2016.<sup>83</sup>

### Address conflicts of interest for all aspects of access to essential NCD medicines

One overarching and crucial challenge to promotion of access to NCD medicines is how to address conflicts of interest—ie, when commercial concerns might take precedence over public health interests. This Series in *The Lancet* examines the steps that governments can take to address conflicts of interest in policy making for the tobacco, alcohol, and ultra-processed food industries.<sup>84</sup>

Challenges for governments dealing with the pharmaceutical industry—which manufactures products that are essential for health—are very different and in many ways more difficult than are those encountered with other industries. This difference is shown in key international documents—eg, MDG 8e was devised in terms of “in cooperation with pharmaceutical companies”. The Political Declaration calls on the private sector to “contribute to efforts to improve access and affordability for medicines and technologies”.<sup>14</sup> However, as noted in the HIV/AIDS crisis, this cooperation will not be easily attained.

Selling of long-term treatment to expanding markets is undoubtedly a specifically important commercial interest for the pharmaceutical industry, and such interests can conflict with those of public health. Previously, some individuals have criticised promotion of global treatment or screening targets that would bankrupt health systems even in high-income countries, and raised concerns that the definition of these targets was affected by the economic interests of some global corporations.<sup>85</sup> Conflicts of interest are also commonplace when specialists and patient organisations with close ties to pharmaceutical companies sit on the many NCD guideline committees. Formulary committee members, prescribers, and patient groups are faced with strong promotional pressures to recommend non-essential and high-cost medicines when lower-priced options are equally effective. There are suspicions that observational studies of nearly 360 000 patients with diabetes supported by one company are mostly serving a marketing purpose.<sup>86</sup>

Governments and global health organisations are increasingly turning to industries, including the pharmaceutical industry, for financial support. This reliance raises concerns about conflicts of interest that could threaten the legitimacy and effectiveness of decision making in global health. For communicable diseases, there are positive examples of public–private partnerships for contraceptives and other technologies.<sup>87</sup> Additionally, health-policy researchers have proposed a model for NCDs that capitalises on such partnerships,<sup>88</sup> particularly as a suggested function of a partnership as emphasised in the political declaration on NCDs. Non-governmental organisations have noted that government and public health institutions should avoid conflicts of interest in all aspects of governance.<sup>89</sup> To ensure the legitimacy of policy making, governments will need to ensure transparent and accountable processes in which stakeholders are equitably represented and all potential and actual conflicts of interest are explicitly identified and systematically addressed.

Legitimacy will also be improved by ensuring that people with NCDs are present to identify priority needs. Unfortunately, the NCD civil society movement is underdeveloped, and some patient groups have already compromised their independence and credibility by accepting pharmaceutical funding.<sup>90</sup> The availability of public and other non-commercial funding has often been

#### Panel 4: Disputes about intellectual property and access to medicines for non-communicable diseases in India<sup>78</sup>

##### The Glivec case

Novartis was refused a patent in India for the crystalline salt form of imatinib (imatinib mesylate, brand-name Glivec) for chronic myeloid leukaemia, on the basis of section 3(d) of the 2005 Indian Patent Act, which allows for new forms of a known medicine to be patented only if the change shows significantly improved therapeutic efficacy compared with existing medicines. The Indian Patent Office ruled that Glivec showed no significant advantage compared with the old form. As a result, Indian generic companies can supply imatinib at US\$124–174 per month, compared with the branded price of \$2478 per month. An appeal by Novartis is being presented to the Supreme Court of India and could lead to easier patenting of modifications. If Novartis is successful, there could be far-reaching negative consequences for generic drug production for different diseases.

##### The Nexavar case

Bayer was granted a patent in India on sorafenib tosylate (brand-name Nexavar) for renal and hepatocellular carcinoma. In March, 2012, the Indian Government issued a compulsory licence allowing an Indian company to produce a copy of the drug on the grounds that: (1) Bayer had not priced the drug at a level affordable to all Indian patients; and (2) Bayer had not ensured availability of sufficient quantities in India. The decision to grant a patent resulted in a price drop from more than US\$5500 to \$175 per month, and then to \$125 per month. Reportedly, the US Government has expressed concern about India's use of compulsory licensing. Bayer has appealed.

key in allowing most HIV civil society groups to act only in the interests of people with HIV/AIDS. Therefore, public support for civil society groups for NCDs should be increased, which would reduce their dependence on commercial sources.

#### Monitor progress towards access to medicines for NCDs

Development of indicators, benchmarks, and targets is an important component of the rights-based approach and allows communities to hold their governments accountable.<sup>91</sup> Setting of targets and monitoring of progress for HIV has been an important way to track financial investments, treatment outputs, and health outcomes for this disease.<sup>92</sup> In November, 2012, WHO member states agreed on a set of indicators for medicines and technologies for NCDs: (1) drug treatment to prevent heart attacks and strokes (including for glycaemic control); (2) the availability of generic essential NCD medicines and basic technologies in public and private facilities; (3) access to palliative care; and (4) vaccination against human papillomavirus and hepatitis B virus as infectious causes of cancer.<sup>93</sup> A voluntary target for drug treatment to prevent heart attacks and stroke is that 50% of eligible people receive drug

|   | For national agencies  | For international agencies and donors   |
|---|--|---|
| Increase efficiency in selection, procurement, supply, and use to promote access to medicines within the existing health budget | Develop evidence-based national clinical guidelines and a national list of essential NCD medicines for training, supply, and reimbursement<br>Promote use of generic NCD medicines through legislation, quality assurance, advocacy, and financial incentives<br>Create a dedicated national body that is responsible for promotion of safe and efficient use of medicines<br>Review laws and practices and remove unnecessary constraints on use of opioid analgesics | WHO should regularly update their model list of essential medicines and evidence-based model clinical guidelines for prevention and treatment of NCDs<br>WHO should include selected NCD medicines (eg, insulin) in the WHO/UN Prequalification of Medicines Programme<br>WHO should increase their support to a few effective regulatory agencies in low-income and middle-income countries to collaborate with countries with less capacity<br>WHO, the UNODC, and the INCB should support countries to adopt and implement laws and policies that ensure the adequate availability and rational medical use of opioid analgesics |
| Finance NCD medicines through domestic funding, as part of universal access   | Finance universal access to essential medicines for NCD through tax-based or obligatory health insurance schemes   | High-income countries should establish an international financing mechanism to support access to essential NCD medicines for the poorest communities in low-income countries with supportive public health policies   |
| Integrate pharmaceutical management for NCDs with existing initiatives  | Establish patient-centred primary care delivery to enhance patient adherence to treatment<br>Use new communication technologies to monitor rural stocks of essential medical products  | WHO and donors should promote and support research of cost estimations, operational research, and regulatory hurdles in the use of a multidrug regimen versus the polypill for high-risk prevention of cardiovascular disease in low-income and middle-income countries<br>Donors should facilitate integration of NCD medicines into other medicines initiatives   |
| Ensure access to new essential medicines for NCDs   | Use flexibilities of the TRIPS agreement and resist pressure to adopt higher intellectual property standards than required by the TRIPS agreement  | Member states and WHO should support the development of international agreement to finance research and development for diseases that mostly affect people in low-income and middle-income countries  |
| Address conflicts of interest for all aspects of promotion of access to essential NCD medicines                                 | Ensure transparent and accountable processes in which potential and actual conflicts of interest are explicitly identified and addressed<br>Increase public support for civil society groups, reducing their dependence on commercial sources  | International agencies and donors should identify and manage all potential conflicts of interest for NCDs, and ensure consultation and participation of publicly funded independent patient and consumer representatives in all relevant policy fora  |
| Monitor progress  | Establish or empower an existing national body to monitor appropriate use of medicines and patient adherence to NCD treatment and prevention<br>Monitor the proportion of the population unable to access essential NCD medicines  | The UN should increase reporting in the MDG reports of access to essential medicines for NCDs<br>Member states should agree and work consistently toward a target for access to NCD medicines in the NCD global monitoring framework<br>Member states and the UN should adequately monitor access to medicines for NCDs as part of the post-2015 development agenda   |

NCD=non-communicable disease. TRIPS=Trade-Related Aspects of Intellectual Property Rights. UNODC=UN Office on Drugs and Crime. INCB=International Narcotics Control Board. MDG=Millennium Development Goal.

**Table: Recommendations for national and international agencies**

therapy and counselling; for availability of generic essential NCD medicines, the member states agreed on 80% availability in public and private facilities.<sup>93</sup>

Many countries have already collected ad-hoc facility-based information about price and availability of NCD medicines.<sup>94</sup> Routine monitoring systems should now be established, which would not only provide such facility-based information regularly, but would also provide information about the quality and efficiency of use of medicines. Furthermore, the proportion of the population who cannot access NCD medicines when needed, and the amount of out-of-pocket expenditure for NCD medicines, should be monitored. Countries should add these questions to their routine household surveys to monitor the effect of their investments in NCDs. Such specific indicators and targets for access to NCD medicines will fill the gap of quantitative data that has made meaningful reporting of MDG 8e so difficult until now.<sup>10</sup>

## Conclusions

In the UN political declaration, states have committed to enhancing access to safe, affordable, effective, and quality medicines for NCDs. 30 years of experience with essential medicines policies and scaling up of treatment for HIV/

AIDS have provided the knowledge to address barriers to long-term quality treatment. But what does success look like for 2025? Millions of patients still do not have access to life-saving vaccines, treatments, and basic palliation, so what will change? We envision a helical strategy in which commitments built on existing initiatives and those specific to NCDs are strongly supported by countries and international agencies to ensure access to essential treatments (table). At a minimum, such support will enable achievement of the target of 80% national availability of quality essential medicines for NCDs in public and private health facilities worldwide, and the target of 50% of eligible people receiving drug treatment and counselling to prevent heart attacks and stroke, with progress towards WHO's global 25 by 25 mortality target.

Success is dependent on the crucial pathways outlined in this report: leveraging of efficiencies in selection, procurement, and use of off-patent medicines; and increased funding for medicines, including those from domestic sources. Pharmaceutical management should be integrated with existing initiatives for other diseases, including HIV and AIDS, and inequities in access to controlled opioids for palliation should be redressed. Countries should guarantee access to on-patent medical



products by full use of flexibilities in the TRIPS agreement, and conflicts of interest should be identified and managed carefully. After 2015, access to medicines for NCDs should move from a neglected part of the development agenda to a genuine priority, supported by action, resources, and systematic monitoring. If these steps are taken, the right to health will be affirmed across borders, generations, and populations to enable access to essential treatments by millions of current and future patients with NCDs. Such a new approach to NCDs requires that each individual counts; no-one should be left behind.

#### Contributors

JL and SPK developed the first draft outline and core messages. VJW, HVH, TvS-A, SS, FNM-P, and RK-M made further suggestions, and all authors contributed sections. HVH wrote the first draft, for which all authors provided several rounds of comments. HVH finalised the report for submission. Two rounds of reviewers' comments and feedback at two lead authors meetings attended by HVH, SPK, SS, JL, and VJW were discussed with all authors. HVH, JL, and VJW edited the report at its final stages.

#### Conflicts of interest

We declare that we have no conflicts of interest.

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