Essential medicines are still essential

On Oct 21, WHO published the full report of the 20th Expert Committee on the Selection and Use of Essential Medicines,[1] with its new WHO Model List of Essential Medicines (EML).[2] The new list includes recently developed medicines for drug-resistant tuberculosis (bedaquiline and delamanid), a number of new cancer treatments (such as imatinib, rituximab, and trastuzumab), and, perhaps most controversially, new direct-acting antiviral drugs (DAA) for the treatment of hepatitis C (sofosbuvir, simeprevir, daclatasvir, ledipasvir, and ombitasvir). Several of these medicines are very expensive. For example, the new medicines to treat hepatitis C are priced up to US$95 000 per 12-week course of treatment, and their primary patents will only expire in 2024–30.[3] Despite the ability of some payers and intermediaries to negotiate large discounts, even high-income countries are struggling to pay for broad access to these treatments.[4]

It is not the first time that WHO has added expensive medicines to the Model List. In 2002, the agency included 12 antiretroviral medicines for HIV/AIDS that were patented in many countries, to focus global attention on a major global public health need and to stimulate interventions to expand access to these life-saving medicines.[5] These products were unaffordable for almost all countries at that time. The new Model List now expands further into other therapeutic areas.

The recent inclusion of new expensive medicines has raised many questions.[6] Has the original concept of essential medicines lost its original relevance as a list of basic medicines for resource-constrained settings? Should the list include medicines not yet authorised by stringent regulatory authorities or not easily available? Should the list include medicines for off-label indications? Should the list automatically include any medicine mentioned in a WHO treatment guideline?

Previous expert committees' reports have provided some answers to these questions. For instance, in 2013 bevacizumab was included for the treatment of macular degeneration, on the basis of available evidence but in the absence of regulatory approval for that specific indication.[7] In 2005, child-friendly formulations of zinc sulfate tablets were added, even though such dispersible dosage forms were not widely available at the time.[8]

For many years, the WHO Model List has been viewed by some as applicable only to resource-constrained settings, and was assumed to include only the most basic medicines. This is a profound misunderstanding. The same principle of a limited list of cost-effective services underpins the logic of managed care institutions, hospital formularies, and reimbursement lists. The idea of selecting a limited list of essential medicines applies in all countries and in a variety of settings.[9]

We therefore believe that the inclusion of the newly listed cancer treatments, as well as the much-needed options for drug-resistant tuberculosis, is consistent with the definition of essential medicines. In 2002, WHO decided that cost alone would not prevent a medicine from being listed, if other criteria of safety, efficacy, and comparative cost-effectiveness were fulfilled.[5] Yet the 2015 decision to include a range of DAAs for hepatitis C introduces a new approach of listing several very effective medicines, rather than selecting a single regimen. According to the Expert Committee, "Inclusion on the EML of all DAAs proposed in the applications aims at promoting competition among available alternatives and allowing for the selection of optimal combination treatment regimens, which may or may not be existing fixed-dose combinations". The Committee also noted that WHO is working to promote the rapid

Dieter Telemans

Pharmacy in Dar es Salaam, Tanzania

introduction of prequalified generic formulations as well as supporting countries or jurisdictions in negotiating lower medicine prices. This decision needs to be understood in the context of the ongoing uncertainty about the best regimen to be used in all settings.

The decision on adding DAAs for the treatment of hepatitis C also illustrates the more general difficulty of applying cost-effectiveness criteria at a global level.[10] What is defined as comparatively cost effective depends critically on the price of the medicine in a given situation. Historical experience has shown that most new medicines listed have decreased in price over time once generic versions became available, but often with large differences between countries. Recent calculations indicate that generic production costs of sofosbuvir can be as low as $101 per treatment.[11] Potential generic suppliers of trastuzumab have suggested that the medicine could be manufactured for $31 per g (or $242 per year) as compared with originator prices of $3000–9000 per g.[12]

But part of the policy space that had allowed for the availability of low-price generic antiretroviral medicines in the early 2000s has closed. Key generic-producing countries have implemented the 1995 World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), and now have to provide 20-year patent terms for pharmaceutical products.[13] Some recent bilateral and regional trade agreements even add further barriers to generic competition. These changes in trade regulations represent serious challenges to implementation of the moral imperative that universal access to life-saving medicines should be assured. This principle was stressed by WHO Director-General Margaret Chan, when the new list was released: "When new effective medicines emerge to safely treat serious and widespread diseases, it is vital to ensure that everyone who needs them can obtain them…Placing them on the WHO Essential Medicines List is a first step in that direction."[14]

The new essential medicines reflect treatment advances of such high public health relevance that WHO decided that these products should be available to all people who need them in all countries. Governments around the world should now consider whether to include these expensive medicines in their national lists of essential medicines. National selection remains a responsibility for individual countries, and should be based on the priorities and possibilities of the national health system, including diagnostic, treatment, and implementation capacities.

However, placing medicines on a list alone does not guarantee patient access. The EML is only a first step in the policy process towards assuring access to these medicines, as part of broader global health and sustainable development goals. Comprehensive essential medicine policies are still needed, covering many different aspects, such as appropriate research and development, financing mechanisms, generic policies including various measures to overcome patent barriers, quality assurance, supply systems, and safe and cost-effective use. The 2016 report of the *Lancet* Commission on Essential Medicines Policies[15] will show how such policies remain essential and will recommend ways of implementing them through concrete actions at the national and global levels.

*Andy L Gray, Veronika J Wirtz, Ellen F M 't Hoen, Michael R Reich, *Hans V Hogerzeil*

The Lancet Commission on Essential Medicines Policies (ALG, VJW, EFM'tH, MRR, HVH); School of Health Sciences, University of KwaZulu-Natal, Durban, South Africa (ALG); Boston University School of Public Health, Boston, MA, USA (VJW); Harvard T H Chan School of Public Health, Boston, MA, USA (MRR); and University Medical Centre Groningen, 9713 AV Groningen, Netherlands (EFM'tH, HVH)

h.v.hogerzeil@umcg.nl

ALG is a member of the WHO Expert Advisory Panel for Drug Evaluation. EFM'tH works as a consultant for WHO and UNITAID. HVH has been a WHO staff member and Secretary of the Expert Committee on the Selection and Use of Essential Medicines. VJW and MRR declare no competing interests.

1 WHO. The selection and use of essential medicines. Report of the WHO Expert Committee. Technical Report Series 994. Geneva: World Health Organization, 2015. http://apps.who.int/iris/bitstream/10665/189763/1/9789241209946_eng.pdf (accessed Oct 20, 2015) .

2 WHO. The 19th WHO model list of essential medicines. Geneva: World Health Organization, 2015. http://www.who.int/medicines/publications/essentialmedicines/EML2015_8-May-15.pdf (accessed Oct 9, 2015).

3 WHO. Patent situation of key products for treatment of hepatitis C: sofosbuvir. Geneva: World Health Organization, 2015. http://www.who.int/phi/implementation/ip_trade/sofosbuvir_report_updated.pdf?ua=1 (accessed Oct 9, 2015).

4 New York Times. Costly Hep C medicines for everyone? *New York Times* Sept 2, 2015. http://www.nytimes.com/2015/09/02/opinion/costly-hepatitis-c-drugs-for-everyone.html?emc=eta1&_r=0 (accessed Oct 9, 2015).

5 WHO. The selection and use of essential medicines. Report of the WHO Expert Committee, 2002. Technical Report Series 914**:** 14–17. Geneva: World Health Organization, 2002.

6 Manikandan S. Are we moving towards a new definition of essential medicines? *J Pharmacol Pharmacother* 2015; **6:** 123–25.

7 WHO. The selection and use of essential medicines. Report of the WHO Expert Committee. Technical Report Series 985. Geneva: World Health Organization, 2013.

8 WHO. Report of the WHO Expert Committee, 2005. Technical Report Series 933. Geneva: World Health Organization, 2005.

9 Hogerzeil H. The concept of essential medicines: lessons for rich countries. *BMJ* 2004; **329:** 1169.

10 Moucheraud C, Wirtz VJ, Reich MR. Evaluating the quality and use of economic data in decisions about essential medicines. *Bull World Health Organ* 2015; **93:** 693–99.

11 van de Ven N, Fortunak J, Simmons B, et al. Minimum target prices for production of direct-acting antivirals and associated diagnostics to combat hepatitis-C virus. *Hepatology* 2015; **61:** 1174–82.

12 WHO. Proposal for the inclusion of trastuzumab in the WHO Model List of Essential Medicines for the treatment of HER2-Positive breast cancer. Geneva: World Health Organization, 2012. http://www.who.int/selection_medicines/committees/expert/19/applications/Trastuzumab2_8_2_A_Ad.pdf (accessed Oct 9, 2015).

13 World Trade Organization. Pharmaceutical patents and the TRIPS Agreement. World Trade Organization, 2006. https://www.wto.org/english/tratop_e/trips_e/pharma_ato186_e.htm (accessed Oct 9, 2015).

14 WHO. WHO moves to improve access to lifesaving medicines for hepatitis C, drug-resistant TB and cancers. Geneva: World Health Organization, 2015. http://www.who.int/mediacentre/news/releases/2015/new-essential-medicines-list/en/ (accessed Oct 9, 2015).

15 The Lancet. A new *Lancet* Commission on essential medicines. *Lancet* 2014; **384:** 1642.

Handwashing and community management of infections

Published **Online**
August 7, 2015
http://dx.doi.org/10.1016/S0140-6736(15)60460-3

See **Articles** page 1631

Influenza has a strong potential to transfer from individual to individual, and encounters in everyday life play an important part in its diffusion in the population. Wherever people meet—at work, in shops, on public transport—there is the risk of transmission, suggesting that the community is the context in which protection against further spread has to be orchestrated. Vaccination, personal hygiene (including handwashing), and measures against crowding are recommended measures.[1] Primary care is important in influenza vaccination because it can reach large numbers of people at high risk of influenza complications and provide them with effective protection against the virus.[2,3] At the same time, general practitioners and other professionals in primary care will be the point of contact for those who have contracted influenza. In this community context, the home environment has a special place, because people are together there for lengthy periods, often in limited space, and with intimate physical contact.

The study by Paul Little and colleagues[4] reported in *The Lancet* provides important information. The investigators studied the effects of handwashing in a trial in more than 16 000 households randomised from 344 UK general practices. Their findings showed a small but tangible protective effect of handwashing on the contraction and transfer of infections: after 16 weeks, 4242 (51%) individuals reported one or more episodes of respiratory-tract infections in the intervention group compared with 5135 (59%) individuals in the control group (multivariate risk ratio 0·86, 95% CI 0·83–0·89). This reduction was accompanied by lower demand for professional care (1021 (11%) *vs* 951 (10%); 0·90 (0·82–0·98) and fewer antibiotic prescriptions (617 [6%] *vs* 535 (6%); 0·83 (0·74–0·94).

Little and colleagues deserve praise for their ability to preserve the real-life environment of busy primary care in the research setting of their trial, which facilitates the translation of the study into routine practice. Their use of the internet to reach households, inform and instruct individuals about handwashing, and maintain its application is innovative. This approach was founded on important values of general practice and primary care: its relation to a defined community population, with the family and household setting as a key focus, and empowerment of people to care for their own health as a core objective.[5] Furthermore, the success of the web-based intervention will have been at least partly determined by the fact that it was delivered from a trusted source; innovative approaches

Ruth Jenkinson/Getty Images