WHO
South-East Asia
Journal of
Public Health

Accelerating access to essential medicines in the WHO South-East Asia Region: opportunities for greater engagement and better evidence
WHO South-East Asia Journal of Public Health

The WHO South-East Asia Journal of Public Health (WHO-SEAJPH) (ISSN 2224-3151, E-ISSN 2304-5272) is a peer-reviewed, indexed (PubMed, Index Medicus for the South-East Asia Region), biannual publication of the World Health Organization Regional Office for South-East Asia.

Information for authors
WHO-SEAJPH is a fully open-access journal and charges no author fees. Manuscripts should be submitted online at http://www.searo.who.int/publications/journals/seajph/en/.

Editorial process
All submitted manuscripts are initially screened for scope, relevance and scientific quality. Suitable manuscripts are sent for anonymized peer review. Recommendations of at least two reviewers are considered before making a decision on a manuscript; all papers reporting data are also reviewed by the journal’s statistical editor. Accepted manuscripts are edited for language, style, length, etc., before publication. Authors are responsible for obtaining permission to reproduce in their articles any material enjoying copyright protection.

© Copyright World Health Organization (WHO) 2018. Some rights reserved.

Rights and permissions
The articles in this publication are published by the World Health Organization and contain contributions by individuals. The articles are available under the Creative Commons Attribution 3.0 IGO licence (CC BY 3.0 IGO) http://creativecommons.org/licenses/by/3.0/igo/legalcode, which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited. In any use of these articles, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted.

In any use of these articles, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted.

Third party content: the World Health Organization does not necessarily own each component of the content contained within these articles and does not therefore warrant that the use of any third-party-owned individual component or part contained in the articles will not infringe on the rights of those third parties. The risk of claims resulting from such infringement rests solely with you. If you wish to re-use a component of the articles attributed to a third party, it is your responsibility to determine whether permission is needed for that re-use and to obtain permission from the copyright owner. Examples of components can include, but are not limited to, tables, figures or images.

Any mediation relating to disputes arising under this licence shall be conducted in accordance with the World Intellectual Property Organization Mediation Rules (http://www.wipo.int/amc/en/mediation/rules).

Disclaimer
The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city of area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. The published material is being distributed without warranty of any kind, either express or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

The named authors alone are responsible for the views expressed in this publication.

Editorial office
WHO South-East Asia Journal of Public Health, World Health Organization, Regional Office for South-East Asia, Indraprastha Estate, Mahatma Gandhi Marg, New Delhi 110 002, India
Tel. 91-11-23309309, Fax. 91-11-23370197
Email: seajph@who.int
Website: www.searo.who.int/publications/journals/seajph

Volume 7, Issue 2, September 2018, 59–128

Advisory board
Poonam Khetrapal Singh (Chair)
Nirmal K Ganguly
Somsak Chunharas
Rohan Jayasekera
Akmal Taher

Editorial board
Phyllida Travis (Chair)
Tjandra Y Aditama
Tasnim Azim
Angela De Silva
Michel D Landry
Rajesh Mehta
Gopinath Nair
Razia Pendse
Paras K Pokharel
Manisha Shridhar
Sirenda Vong

Editorial team
Sarah Ramsay (Editor)
Penny Howes (Copyeditor)
Deepti Munjal (Editorial assistant)

Production
Evolution Design & Digital Ltd (Kent)
United Kingdom of Great Britain and Northern Ireland
## Contents

**WHO South-East Asia Journal of Public Health**  
*September 2018 | Volume 7 | Issue 2*

**ISSN 2224-3151**  
**E-ISSN 2304-5272**

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Editorial</strong></td>
<td>Accelerating access to essential medicines in the WHO South-East Asia Region: opportunities for greater engagement and better evidence</td>
<td>Poonam Khetrapal Singh, Phyllida Travis</td>
</tr>
<tr>
<td><strong>Perspective</strong></td>
<td>Approaches to improving access to essential cancer medicines in the WHO South-East Asia Region</td>
<td>Meenakshi V Chivukula, Klara Tisocki</td>
</tr>
<tr>
<td></td>
<td>Access to pain relief and essential opioids in the WHO South-East Asia Region: challenges in implementing drug reforms</td>
<td>Nandini Vallath, MR Rajagopal, Suraj Perera, Farzana Khan, Bishnu Dutta Paudel, Klara Tisocki</td>
</tr>
<tr>
<td></td>
<td>Addressing the threat of antibiotic resistance in Thailand: monitoring population knowledge and awareness</td>
<td>Viroj Tangcharoensathien, Angkana Sommanustweechai, Sunicha Chanvatik, Hatairat Kosiypom, Klara Tisocki</td>
</tr>
<tr>
<td></td>
<td>National introduction of fractional-dose inactivated polio vaccine in Sri Lanka following the global “switch”</td>
<td>Deepa Gamage, Samitha Ginige, Paba Palihawadana</td>
</tr>
<tr>
<td></td>
<td>Improving access to assistive technologies: challenges and solutions in low- and middle-income countries</td>
<td>Viroj Tangcharoensathien, Woranan Witthayapipopsakul, Shaheda Viriyathorn, Walaiporn Patcharanarumol</td>
</tr>
<tr>
<td><strong>Original research</strong></td>
<td>Essential cancer medicines in the national lists of countries of the WHO South-East Asia Region: a descriptive assessment</td>
<td>Meenakshi V Chivukula, Klara Tisocki</td>
</tr>
<tr>
<td></td>
<td>Pricing policies for generic medicines in Australia, New Zealand, the Republic of Korea and Singapore: patent expiry and influence on atorvastatin price</td>
<td>Elizabeth E Roughead, Dong-Sook Kim, Benjamin Ong, Anna Kemp-Casey</td>
</tr>
<tr>
<td></td>
<td>Geographical disparities and determinants of anaemia among women of reproductive age in Myanmar: analysis of the 2015–2016 Myanmar Demographic and Health Survey</td>
<td>Hla Hla Win, Min Ko Ko</td>
</tr>
<tr>
<td></td>
<td>Factors associated with stillbirths in Haryana, India: a qualitative study</td>
<td>Preeti H Negandhi, Sutapa B Neogi, Ankan M Das, Sapna Chopra, Amit Phogat, Rupinder Sahota, Ravi Kant Gupta, Sanjay Zodpey, Rakesh Gupta</td>
</tr>
<tr>
<td><strong>Policy and practice</strong></td>
<td>Successes and challenges of expansion of environmental poliovirus surveillance in the WHO South-East Asia Region</td>
<td>Aarti Garg, Sirima Pattamadilok, Sunil Bahl</td>
</tr>
</tbody>
</table>
Accelerating access to essential medicines in the WHO South-East Asia Region: opportunities for greater engagement and better evidence

This issue of the WHO South-East Asia Journal of Public Health focuses on access to medicines. Progress on universal health coverage and the Sustainable Development Goal (SDG) for health, “Ensure healthy lives and promote well-being for all at all ages”, 1 will be achieved only if there is significant improvement in access to quality essential medicines. This is explicitly recognized in the declaration of the 2030 Agenda for Sustainable Development; 2 and for the first time there is an indicator for tracking progress: the “Proportion of the population with access to affordable medicines and vaccines on a sustainable basis” (SDG indicator 3.B.1). 1

There is an urgent need to improve access to medicines. The situation in the World Health Organization (WHO) South-East Asia Region was summarized in 2017.3 Despite limited data, which is a worldwide problem, a reasonably consistent picture emerged for the region, that, while the overall availability of medicines has improved, availability still tends to be lower in the public sector compared with the private sector; lower in health centres than in hospitals; and more of a problem for medicines for noncommunicable diseases than for those for communicable diseases. There are sometimes concerns about how to decide on additions to national lists of essential medicines; the quality of medicines being procured; and the prices paid. Looked at through a lens of universal health coverage, paying out of pocket for medicines is the main driver of impoverishment due to health-care spending in this region, affecting at least 65 million people, and affecting people most when they are sick. Access to medicines has rightly become increasingly prominent on both global and regional public health agendas.

“Proportion of the population with access to affordable medicines and vaccines on a sustainable basis”
Sustainable Development Goal indicator 3.B.1

There is much that can be done to increase access to quality essential medicines. Production can be expanded; improved drug formulations can be developed to more easily reach “those being left behind”; procurement and pricing policies and practices can be improved; creative ways to improve distribution to hard-to-reach areas, along with more appropriate use, can be developed; and effective strategies to increase protection from financial hardship can be introduced. Multiple parties need to be involved – national and subnational government bodies – including national regulatory authorities; pharmaceutical manufacturers; health professional bodies; civil society organizations; development partners; and academia. The medicines market in the WHO South-East Asia Region is unique in many ways. Several countries are major manufacturers of generic medicines, and are global not just regional suppliers. There are also some very small countries in the region that will always lack sufficient purchasing power for “economies of scale” when procuring medicines – in terms of both negotiating price and assuring quality.

Five priority areas for greater engagement and better evidence

There are five clear areas in which action, especially intercountry cooperation, will help to accelerate progress, and these have become priorities for this region. They are also areas in which more knowledge and evidence is needed.

Procurement, pricing and greater use of TRIPs flexibilities

Broadly, there are two categories of essential medicines. The first is common, off-patent essential medicines such as first-line antibiotics and medicines for blood pressure and diabetes, where the main issue is negotiating a fair price, especially for smaller countries with limited prospects for economies of scale. Two forms of cooperation are now under way in the region that should help: greater transparency of information on procurement price, and the first steps towards pooled procurement, starting with antidotes.4,5 There may also be relevant experience for medicines procurement from the experience with pooled procurement of vaccines by countries of the Association of South-East Asian Nations (ASEAN).6 Second, some innovative medicines that are still under patent and often high cost, have been accepted onto the WHO model list of essential medicines and address important health issues in the region – for example, drugs for hepatitis C and certain cancer drugs. Here, greater capacity to work within intellectual property and competition rules, and use the full provision and flexibilities of the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) is needed.6,9 A recent review found that TRIPS flexibilities were mainly used for HIV/AIDS or related conditions, but used far less frequently for cancer.10 In 2015, 16 cancer drugs, including three high-cost medicines, were added to the WHO model list of essential medicines.11 However, an analysis reported in this issue of the journal shows that, in many countries, this expansion has not yet been translated into inclusion in their national lists of essential medicines.12 In an accompanying perspective paper, the authors explore potential approaches to
improving the affordability and availability of essential cancer medicines in the region.13

Regulation
Effective regulation ensures the quality and safety of both generic and patented medicines. There are significant differences in regulatory capacity between countries, and existing expertise could be used more efficiently. The South-East Asia Regulatory Network (SEARN) was created in 2016, to improve access to safe, high-quality medical products in the region, by facilitating greater information-sharing, collaboration and convergence of regulatory practices across the region.14 Regulatory authorities from all 11 Member States of the region are members.14 Working groups have been created in five priority areas, as shown in Box 1.

Box 1. The South-East Asia Regulatory Network
The South-East Asia Regulatory Network (SEARN) was launched in 2016, to improve access to safe, high-quality medical products in the WHO South-East Asia Region.14 It has established working groups to encourage collaboration in five areas:

- quality assurance and standards of medical products, including laboratory networks;
- good regulatory practices;
- vigilance for medical products;
- an information-sharing platform, to provide easy access to information on regulatory policies, guidelines, standards, procedures and products;
- medical devices and diagnostics.

Rational use of medicines, with a focus on antimicrobials
Improvement in rational use of medicines is part of efforts to improve health service quality and is essential to achieving better health outcomes. The need for optimization of the use of medicines is as great as ever, and is increasingly urgent in the case of antimicrobials. A reappraisal of approaches may be merited in situations where little progress on appropriate use has been made. Innovative approaches that tackle the problem on the supply side, for example reducing incentives for inappropriate prescribing, are needed. Equally important, but often forgotten, is the need to reduce inappropriate demand for medicines. A perspective paper in this issue describes how Thailand successfully incorporated a module into the country’s 2017 national health and welfare survey, to assess public awareness of antibiotics. The findings will be used to design targeted public communications strategies.15

Data on access to medicines
There is an urgent need to improve data on access to medicines. A simple hand-held application to monitor the availability and price of medicines has been piloted in 19 countries in Europe, the Americas and Africa. A number of countries in the WHO South-East Asia Region also plan to pilot it in the next year.

Protection from financial hardship
The fifth area in which more knowledge is needed is how to reduce financial hardship caused by out-of-pocket payment for medicines. Countries in the region are using a range of policies.16 There is an urgent need to analyse their effectiveness, especially in terms of expanding financial protection for the most vulnerable groups.

Conclusion
There are some clear priorities for action and generating evidence on the agenda for access to medicines in the WHO South-East Asia Region. There are also areas where existing knowledge needs to be translated into action. For example, access to opioids, needed for severe pain, remains very low in the region. As described in this issue, though some progress has been made in recent years, well-formulated policies to increase access to opioid medications are urgently needed.17 National medicines policies and lists of essential medicines may need revision, to reflect today’s health needs. The WHO model list of essential medicines remains the benchmark for many countries,6 and judicious use of health technology assessment can also help national decisions.18,19 Better data are needed to monitor progress. More operational research is required to identify which types of policies and strategies help improve equitable access to quality medicines at scale, and can be sustained. Fundamental research and development work is also needed. There is much to do for the range of parties involved in improving access to essential medicines. The research community will play a pivotal role in evaluating and documenting what works in the WHO South-East Asia Region.

Poonam Khetrapal Singh
World Health Organization
Regional Director for South-East Asia
New Delhi, India

Phyllida Travis
Director, Department of Health System Development
World Health Organization Regional Office for South-East Asia
New Delhi, India

Correspondence to: Dr Phyllida Travis (travisp@who.int)

How to cite this paper: Khetrapal Singh P, Travis P. Accelerating access to essential medicines in the WHO South-East Asia Region: opportunities for greater engagement and better evidence. WHO South-East Asia J Public Health. 2018;7(2):59–61. doi:10.4103/2224-3151.239414.

References


4. Informal expert consultation to develop a price information sharing platform in the South-East Asia Region. Summary report. 14–15


Approaches to improving access to essential cancer medicines in the WHO South-East Asia Region

Meenakshi V Chivukula¹, Klara Tisocki²

¹Independent consultant, New Delhi, India, ²World Health Organization Regional Office for South-East Asia, New Delhi, India

Correspondence to: Dr Klara Tisocki (tisockik@who.int)

Abstract

The high cancer burden in the World Health Organization (WHO) South-East Asia Region represents not only a significant cause of death, disability and suffering but also a major threat to development. In 2015, the need for equitable access to cancer treatments was underscored by the addition of 16 cancer drugs to the 19th WHO model list of essential medicines, including three high-cost medicines. This paper explores strategies to improve access, including – but not limited to – managing costs through regional cooperation; coordinated procurement mechanisms; price controls; differential pricing; and licensing agreements. The composition of the region, with small and large pharmaceutical markets with a range of manufacturing capacities and supply-chain issues, offers a unique frame of comparison and consideration for access issues. Different approaches are needed that are tailored to specific country situations. However, in the absence of global collaborative funding mechanisms, the region can advocate now, with one voice, for regional action to improve the affordability and availability of essential cancer medicines and align national cancer-control strategies to leverage regional strengths. Delays will lead to more premature cancer deaths and more households in the WHO South-East Asia Region being impoverished through out-of-pocket payments for cancer medicines.

Keywords: access to health care, antineoplastic drugs, national health policy, South-East Asia, World Health Organization

Background

The cancer burden in the World Health Organization (WHO) South-East Asia Region is high, with 1.1 million cancer-related deaths and 1.7 million new cancer cases in 2012.¹ The annual number of new cancer cases globally is projected to increase from 14.1 million in 2012 to 21.6 million by 2030, yet barriers in access to safe, quality, effective and affordable options for prevention, detection and treatment continue to exist, especially in low- and middle-income countries, where patients often present with advanced disease, further limiting treatment options and benefits.² Management of cancer is complex and can be expensive. In high-income settings, cancer is a major economic burden and political inability to ensure fair access to affordable cancer treatment is criticized.³ In lower-income settings, such as the countries of the WHO South-East Asia Region, the challenge is therefore multiplied, since access to cancer medicines and other aspects of cancer care is severely limited.

In 2014, one initiative to improve access to cancer medicines in lower-resource settings was undertaken by the Union for International Cancer Control (UICC).⁴ At the invitation of WHO, UICC undertook the first comprehensive review in 15 years of the cancer medicines included in the WHO model list of essential medicines (WHO EML). A new, disease-based methodology was used that started by identifying the cancer types that would most benefit from systemic treatment and/or that cause the largest burden on the population.⁴ The UICC review resulted in significant changes to the 19th revision of the WHO EML in 2015,⁵ with 16 cancer drugs – including three high-cost medicines – being added.

This issue of the WHO South-East Asia Journal of Public Health reports the results of an investigation to quantify the extent to which the expanded WHO EML influenced inclusion of cancer medicines in the most recent national lists of essential medicines of the countries of the WHO South-East Asia Region, and an assessment of the availability and affordability of selected cancer medicines in countries in the region.⁶ The results indicated that there has been no significant shift in recent years in increasing the inclusion of essential cancer medicines in national lists of essential medicines, despite some lists in the study being dated post 2015.⁶ With respect to the availability and affordability of cancer medicines in the region, the picture is mixed but concerning, with a significant proportion of countries requiring patients and their families to bear full out-of-pocket costs.⁶ Clearly, there is an urgent need for different approaches to improve access to essential cancer medicines for countries in the region.
Reviewing cancer medicines on lists of essential medicines

The WHO EML aims to identify the medicines necessary for a basic health system to function. Time will tell whether the 19th WHO EML of 2015 marks a tipping point for access to essential cancer medicines in low- and middle-income countries, and propels a dramatic shift in strategy and global commitment analogous to strides in improving access to essential antiretroviral medicines for HIV/AIDS. In practice, countries of the WHO South-East Asia Region may use the 19th WHO EML as a tool to guide the rational selection of medicines and identify ways to improve public procurement and supply through targeted policies and programmes.

Prioritizing actions to improve access to cancer medicines in low- and middle-income countries

In individual countries, updated national lists of essential medicines can help shape the market and increase generic production of selected medicines, especially when linked to policies for universal health coverage targeting populations and diseases. However, inclusion of essential cancer medicines in national lists is only indicative of the government’s commitment to ensuring access. Policies and initiatives are needed to promote action.

Table 1 details initiatives in the four areas of access to care, pay, new payment methods, cooperation among stakeholders, and research for improving access to cancer medicines in low- and middle-income countries, with examples from the WHO South-East Asia Region. This table expands upon the work of Lopes Jr. et al. in 2013, and identifies quality-assured generic and biosimilar drugs; pricing policies; tiered pricing; health technology assessments; and value-based insurance as priority actions for countries of the region.

Governments have the greatest responsibility in ensuring access to essential cancer medicines, and need policy strategies to improve access. For example, to ensure access to new, patented and expensive medicines for noncommunicable diseases, governments should make full use of the flexibilities of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), and explore the use of compulsory licences for essential cancer medicines. Well-known cases are documented from India and Thailand, of decreasing prices of cancer drugs through compulsory licensing. Ways to counter intimidation from pharmaceutical companies and threats of trade barriers by importing countries should also be documented and shared by countries using TRIPS flexibilities. Importantly, in the WHO South-East Asia Region, there are five countries that meet the United Nations criteria of being a “least developed country”: Bangladesh, Bhutan, Myanmar, Nepal and Timor-Leste. Under the Doha Declaration, these countries can import lower-cost generic medicines produced with compulsory licences. There is an opportunity for these countries to come together to develop pathways to improve procurement under the Doha Declaration, with support from within the region.

Pharmaceutical companies also have a role to play in improving access to essential cancer medicines. In 2017, the Access to Medicine Foundation studied the inclusion of essential cancer medicines in access initiatives by major pharmaceutical companies in low- and middle-income countries, and found that there were access strategies for only 11 of the 56 products that matched the list of essential cancer medicines on the WHO EML. Also, despite the visibility of many such access programmes, they remain poorly evaluated, with limited evidence of meaningful impact.

Adapting health policies to improve access and ensure quality standards

To meet the increasing burden of noncommunicable diseases like cancers, countries need to create an enabling policy environment that engages stakeholders to work together to strengthen medicines management systems for cancer. Priority attention is needed for pricing of cancer medicines; reducing out-of-pocket payments for cancer care; strengthening local pharmaceutical companies that are capable of producing low-cost quality cancer medicines; and rational selection of products for use in public health systems. Special attention should be given to identifying candidates for compulsory licences based on health needs.

Countries can learn from the policies and programmes that contributed to improved access to antiretroviral medicines for HIV/AIDS globally. These include improving price transparency; stimulating production of low-cost generic medicines; and ensuring sustainable differential pricing, with specific licensed-originator, branded-generic and generic products for low- and middle-income countries. Countries in the WHO South-East Asia Region are already taking steps to share price information for medicines and improve price transparency. Additionally, it is also important to keep in mind ground realities, among other barriers to overcome, that reveal the need, for example, for strengthened regulatory capacity and timely support from federal regulatory authorities and WHO. One such case is biosimilar medicines. As with generic medicines, lower-cost biosimilar medicines could help to increase access to treatment in lower-resourced countries, once the patents of innovator biotherapeutic products have expired. WHO launched a pilot of prequalification of rituximab and trastuzumab in 2017 and will also review its 2009 guidelines on the evaluation of similar biotherapeutic products, to ensure that guidance to national regulatory authorities reflects recent evidence and experience. While complex to implement, these innovations are important to making systems work. Ideally, health authorities can take practical actions to review national cancer policy and standard treatment guidelines, strengthen supply chains with quality-assured WHO prequalified products, and advocate for collaborative funding mechanisms. Suggested actions are detailed next.

- Update national cancer policy for the prevention, diagnosis, and treatment of cancer: there are examples of national cancer policy and national cancer-control plans in the WHO South-East Asia Region. Strengthening the implementation of these plans will play a role in improving access to essential cancer medicines. For example, strengthening partnerships can help facilitate resource mobilization; promote shared learning on specific areas like...
### Table 1. Approaches to improving access to cancer medicines in countries of the WHO South-East Asia Region

<table>
<thead>
<tr>
<th>Initiatives</th>
<th>Description</th>
<th>Benefits</th>
<th>Challenges</th>
<th>Example(s) from the WHO South-East Asia Region</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Access to care</strong></td>
<td>Government-initiated access programmes for selected high-cost medicines (through national health insurance)</td>
<td>- Free access to selected very high-cost medicines, including selected essential cancer medicines, to patients meeting strictly defined criteria</td>
<td>- Transparent and equitable health-care rationing, using the national list of essential medicines to define a special category of medicines for insurance coverage</td>
<td>- Challenge to implement, requires strong health systems (i.e. inventory management, national health insurance)</td>
</tr>
<tr>
<td>Universal health coverage</td>
<td>Government-provided health insurance coverage for the entire population</td>
<td>- Pooling of resources, financial protection</td>
<td>- Rising costs, financing challenges in low-resource setting, risk of lawsuits</td>
<td></td>
</tr>
<tr>
<td><strong>Quality-assured generic and biosimilar drugs</strong></td>
<td>Produced without a licence once patents or exclusive rights expire</td>
<td>- Lower costs to the payer, through increased competition</td>
<td>- Without regulatory oversight, there is a risk to safety and efficacy, perceived low quality</td>
<td></td>
</tr>
<tr>
<td><strong>Pricing policies – compulsory licensing:</strong></td>
<td>Using the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) for government to issue volunteer or compulsory licences, on grounds of public interest, to produce generic drugs while they are still within intellectual property rights; The Doha Declaration allows import of low-priced generic medicines produced with compulsory licences in least developed countries</td>
<td>- Early introduction of generic drug competition, lower costs to the payer</td>
<td>- Early introduction of generic drug competition, lower costs to the payer</td>
<td>Regional generic manufacturing in Bangladesh, India, Indonesia and Thailand; Notable examples of use of compulsory licensing from India and Thailand; There are five countries in the region that are designated as “least developed countries” and do not have manufacturing capacity; these five countries can leverage regional manufacturing of low-priced generic medicines produced with compulsory licences</td>
</tr>
<tr>
<td><strong>New payment methods</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tiered pricing (price discrimination)</strong></td>
<td>Different prices for the same product in different markets, based on ability to pay and elasticity of demand</td>
<td>- Increased affordability, companies expand their customer base, improved distribution channels</td>
<td>- Risk of parallel imports (illegal import of lower-priced drugs to higher-paying markets)</td>
<td>India: government-owned retail outlet with discounted cancer and cardiovascular medicines (Affordable Medicines and Reliable Implants for Treatment [AMRIT] shops)</td>
</tr>
<tr>
<td>Price ceiling</td>
<td>Government intervention on the maximum retail price</td>
<td>- Lower prices for selected products distributed</td>
<td>- Industry backlash</td>
<td></td>
</tr>
<tr>
<td><strong>Industry-led access programmes</strong></td>
<td>Industry-led tiered pricing in the form of rebates/discounts/extra products</td>
<td>- Companies expand their customer base</td>
<td>- Limited evidence of actual improvements to access, risk of parallel import</td>
<td></td>
</tr>
<tr>
<td><strong>Risk-sharing agreements</strong></td>
<td>The provider company gets paid only when conditions are met (i.e. clinical benefit)</td>
<td>- Decreases payer costs</td>
<td>- Lack of agreement on the definition of benefit</td>
<td></td>
</tr>
</tbody>
</table>
Advocate for collaborative funding mechanisms

- Establish WHO prequalification
- Review standard treatment guidelines


---

**Conclusion**

There is no single strategy to improve access to essential cancer medicines for countries in the WHO South-East Asia Region, especially unaffordable high-cost therapies. Different approaches are needed that are tailored to specific country situations and progress towards universal health coverage. Understanding what is included in national lists of essential medicines can be a first step to analysing a nation’s health priorities and capacities. Also, in the absence of global collaborative funding mechanisms, the region can advocate now, with one voice, for regional mechanisms to promote actions to improve the affordability and availability of essential cancer medicines and align national cancer-control strategies to leverage regional strengths. Regional strengths include experience in using compulsory licences to manufacture low-cost generic medicines and using health technology assessments to provide free cancer medicines via national health insurance.

To meet the global goals for the prevention and control of noncommunicable diseases in the context of universal health coverage, actions to improve access to essential cancer medicines are a priority. Time lost in rallying action will lead to more premature cancer deaths and more households in the WHO South-East Asia Region being pushed into poverty by out-of-pocket payments for cancer medicines.
Chivukula & Tisocki: Improving access to essential cancer medicines in the WHO South-East Asia Region

**Source of support:** The work contributing to this paper was supported by the World Health Organization Regional Office for South-East Asia, New Delhi, India.

**Conflict of interest:** None declared.

**Authorship:** MVC completed the data analysis and developed the manuscript. KT designed the study and reviewed the manuscript.

**How to cite this paper:** Chivukula MV, Tisocki K. Approaches to improving access to essential cancer medicines in the WHO South-East Asia Region. WHO South-East Asia J Public Health. 2018;7(2):62–66. doi:10.4103/2224-3151.239415.

**References**


Access to pain relief and essential opioids in the WHO South-East Asia Region: challenges in implementing drug reforms

Nandini Vallath¹, MR Rajagopal², Suraj Perera³, Farzana Khan⁴, Bishnu Dutta Paudel⁵, Klara Tisocki⁶

¹Tata Trusts, Maharashtra, India, ²Trivandrum Institute of Palliative Sciences, Thiruvananthapuram, India, ³National Cancer Control Programme, Ministry of Health, Colombo, Sri Lanka, ⁴Centre for Palliative Care, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, ⁵National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal, ⁶World Health Organization Regional Office for South-East Asia, New Delhi, India

Correspondence to: Dr Nandini Vallath (aanandini@gmail.com)

Abstract

It is a justifiable assumption that more than 15 million people in the World Health Organization South-East Asia Region are experiencing serious health-related suffering, much of it caused by persistent, severe pain. Despite this burden of suffering, overall access to pain relief and palliative care services is abysmal. The lack of access to controlled drugs for pain management is striking: the average morphine equivalence in the region in 2015 was just 1.7 mg per capita, while the global average was 61.5 mg per capita. Until recently, implementation of national legislation to facilitate medical and scientific use of opioids has proven to be very complex and difficult to achieve. The effects on the region of the exploitative British opium trade in previous centuries prompted countries to adopt draconian legislation on opioids, focused on restricting illicit use. In India, the Narcotic Drugs and Psychotropic Substances Act of 1985, for example, stipulated harsh custodial sentences for even minor clerical errors in hospitals stocking opioids. Decades of persistent efforts by civil society resulted in the landmark amendment of the Act in 2014 to improve medical access, but implementation remains highly protracted. Although some progress has been made in recent years in Bangladesh, India, Nepal, Sri Lanka and Thailand, pain is a symptom that is grossly undertreated in most parts of the region. On both human rights and public health grounds, there is an urgent need for well-formulated drug policies to increase access to opioid medications, coupled with capacity-building and comprehensive public health systems incorporating palliative care.

Keywords: essential opioids, legislation, opioid analgesics, pain, palliative care, South-East Asia

Background

The World Health Organization (WHO) South-East Asia Region is home to one quarter of the population of the world. Although the overall average lifespan in the region has increased, the last few decades have seen transitions in the patterns of morbidity.¹ While communicable diseases, including the chronic stages of HIV and tuberculosis, continue to challenge the region, there is an additional burden of noncommunicable diseases, with increasing prevalence of cancer, cardiovascular diseases, diabetes and stroke. This is attributed to factors such as changing lifestyles, increasing urbanization, changes in reproductive patterns and diet, obesity, and use of tobacco and alcohol. The escalation in the disease burden is projected to be highest in low- and middle-income countries, such as those of the WHO South-East Asia Region.² The cancer disease burden in the region is high, with 1.1 million cancer-related deaths and 1.7 million new cancer cases in 2012.³

Recognizing the global burden of chronic disease conditions, and, consequently, the role of pain relief and palliative care in alleviating suffering, WHO passed a landmark resolution during the 67th World Health Assembly in 2014.⁴ It recommended that all Member States should strengthen palliative care as a component of comprehensive care throughout the life-course, through integration within the public health-care system. Although the resolution suggested specific measures and strategies to implement the change, committed policies on, or investment in, developing palliative care in the WHO South-East Asia Region has been generally lacking.

In October 2017, The Lancet Commission on Global Access to Palliative Care and Pain Relief analysed the issue further and focused on “serious health-related suffering” as a real entity requiring global attention.⁵ The commission estimated that, in 2015, more than 61 million people experienced serious health-related suffering. Given that the population of the WHO South-East Asia Region is around one quarter of the global...
and Public Health, United States of America, has housed the
region are experiencing serious health-related suffering. Noting that “inequality of access to controlled drugs for pain management and other clinical uses is now a public health and human rights crisis”, the commission report also emphasized that much of this suffering can be alleviated at a low cost, and recommended affordable essential packages incorporating a palliative care approach and services that can be adopted even by low-income countries.5

Despite continued advocacy and evidence, palliative care is not yet a major focus in countries of the WHO South-East Asia Region. Even when policies have been declared, they are not in fully implementable form. For example, India announced a national programme for palliative care in November 2012, but without a specified budget, monitoring system or governance structure for rolling out the programme.6

Ensuring access to and availability of pain relief and palliative care services can effectively address serious health-related suffering. This article describes the status and challenges of, and ongoing efforts to improve, access to pain relief in the region, which is a critical component and accepted measure of the quality of palliative care. It aims to provide a perspective on the challenges of implementing drug reforms to ensure access to and availability of essential narcotic medications in the region, for relieving the persistent, severe pain such as that seen in cancer patients.

Access to and availability of essential opioids in the WHO South-East Asia Region

Persistent, severe pain is one of the major causes of serious health-related suffering. In low-income countries, most patients with long term illnesses, such as cancer, present at advanced stages, with a high burden of suffering and severe pain.7 Opioids are included in the WHO model list of essential medicines for both adults and children, as they are safe and effective medications for relieving persistent severe pain.8

Opioid analgesics are also controlled medicines. National governments report data on annual opioid consumption to the International Narcotics Control Board (INCB), an independent and quasi-judicial monitoring body for implementation of the United Nations international conventions on drug control.9 Consumption is not a measure of the amounts dispensed to or used by patients, but quantifies the amount of opioids distributed legally in a country for medical and scientific purposes, to those health-care institutions and programmes that are licensed to dispense to patients, such as hospitals, nursing homes, pharmacies, hospices and palliative care programmes. The annual opioid consumption per capita of a country has emerged as an indicator of the national capacity for/4 commitment to providing pain relief. As pain management is a critical component of quality care, the data on opioid consumption serve as a surrogate indicator of countries’ provision of palliative care. Since 1996, the University of Wisconsin School of Medicine and Public Health, United States of America, has housed the WHO Collaborating Centre, the Pain and Policy Studies Group (PPSG). Using the annual INCB data, and applying conversion

Contributors to poor access to and availability of opioids for medical use

Several factors have contributed to the poor availability of opioids for medical use in the WHO South-East Asia Region, not least the historical context. Historically, opium has been a trade crop in the region, and a drug of abuse. For over a century, the region was exploited by the British for the production, consumption or commercial passage of opium. India was a major producer under the British rule. Several other present-day countries of the region – Myanmar, Thailand and parts of Bangladesh – were part of the iniquitous golden triangle, an area implicated in the illicit historical trade. The region witnessed two opium wars in the 19th century, initiated by China against Britain, to put an end to the enforced trade by the British, when the proportion of young addicts in the country had risen to alarming levels.14

A civilized closure to the conflicts was achieved in the 20th century, through United Nations treaties and declarations.
The United Nations Single Convention on Narcotic Drugs in 1961 had the dual purpose of ensuring that the production, cultivation and trade of controlled substances including opioids was for medical and scientific use only, while their diversion and misuse were prevented. All countries that were signatories to the Single Convention were obliged to ensure balance within their own national narcotic policies. However, owing to the traumatic past, the countries from the WHO South-East Asia Region interpreted the mandates of the Single Convention more in terms of restricting illicit use, and developed intensely prohibitory national policies.

Despite the changing global perspectives and scientific evidence to support safe medical use of opioids, implementation of national legislation to facilitate medical and scientific use of opioids has proven to be very complex and difficult to achieve. The complexities of implementing regulatory reforms are illustrated next, using the example of India.

India’s National Drug and Psychotropic Substances (NDPS) Act of 1985

The National Drug and Psychotropic Substances (NDPS) Act of 1985 governs the access to and availability of opioid analgesics in India. It is heavily prohibitory in nature.

The important barriers came to light when a team that was commissioned by the WHO cancer unit in the mid-1990s conducted a study of the poor access to and availability of opioids in India – the country that produced most of the opium substrate for rest of the world. This team unearthed the restrictive clauses in the country’s drug policy, as well as its long-term consequences. They linked the issue of poor treatment of cancer pain in India with the multiple and complex licensing requirements stipulated under the NDPS Act and rules mandated for stocking and dispensing them in medical institutions.

The NDPS Act of 1985 had retained components of the 19th century British opium law, which was specially designed to ensure the Empire’s monopoly on opium trade in the region, by levying taxes and imposing licensing for every movement of opium across its administrative boundaries.

By retaining similar licensure procedures, the NDPS Act obliged medical institutions that needed to stock opioids to maintain import, export and transport licences, to be obtained from different government agencies – such as excise, revenue, health and others, for each of the states involved in transport and transit of the consignment.

The task of maintaining the validity of multiple licences, and the complexity of procedures stipulated by the law, discouraged most hospitals from stocking opioid medications. Further, the punishments were disproportionate, with rigorous imprisonment for even minor errors. The poor supply of opioid formulations in medical institutions affected the exposure and training of health-care professionals, who had no chance to experience the use of opioids for treating persistent pain. As such, generations of doctors qualified from medical school without having had any exposure to assessing chronic persistent pain, or in using opioids. The fear of causing addiction and respiratory depression overrode clinical judgement, when faced with severe pain requiring use of oral opioid formulations. The propagation of these drugs by the popular media as substances of abuse fostered the fears and misconceptions further. The overall lack of awareness about medical use of opioids led to opiophobia and resulted in very low demand for opioids as prescription medicines.

The lack of knowledge and experience to assess and treat pain gradually transformed into apathy towards evaluating and responding to persisting pain. Pain became a grossly under-assessed, undertreated symptom. A study in 2012–2013 on the predictors and prevalence of pain and its management in four major cancer hospitals of India found that the presence or severity of pain were not parameters that were routinely assessed, documented or managed, even in tertiary cancer-care settings. The study surveyed 1600 patients waiting to see oncology consultants and found that nearly 9 out of 10 patients (88%) reported pain. At the end of their consultation, two thirds (67%) of these patients received no analgesics or were given inadequate medications. Ironically, opioids have been included in India’s National list of essential medicines since 2003.

The policy has changed – but implementation lags behind

Significant changes in recent years, which sought to redress the dysfunctional demand–supply framework for essential opioids described, have influenced the drug policies of the region. PPSG has provided the model, resources and technical assistance to countries that sought support to analyse and amend their legislation to facilitate access to and availability of opioids.

Working with PPSG, several countries in the WHO South-East Asia Region have identified the negative influence of draconian regulations on the availability of essential opioids. Many are in the process of modifying or implementing new policies in line with the international mandates to ensure balance, for improving access to and availability of opioids for medical use, while preventing non-medical use.

In India, concerted efforts by civil society over two decades led to parliamentary amendment of the NDPS Act of 1985 in February 2014. The amended Act expanded the scope of the law and incorporated an additional mandate – that of improving access to and availability of opioids for medical and scientific use. This was a landmark achievement. As per the new law, procedural rules were made uniform and standardized across the country, as the federal government took control of the opioid medicines that it designated as “essential narcotic drugs”. The state drug controller became the single agency at the state level authorized to designate the status of recognized medical institution (RMI). The RMI status is for a period of 3 years and gives the designated institution the authority to stock and dispense essential narcotic drugs in alignment with the central government regulations, without need for any additional licences. In order to ensure development of capacity for safe and appropriate utilization of essential narcotic drugs, a RMI is required to have at least one doctor trained in the medical use of opioids.

However, in the 4 years that have elapsed since the amendment, the law is yet to be implemented in full in India’s 29 states and 6 union territories. Opioid availability in India remains abysmal, and awareness about chronic persistent pain, its presentations and management using opioids remains
very poor among medical professionals. The punitive clauses in the law, meant for illicit users, apply in equal measure to licit prescribers, users, dealers and recognized medical institutions. Punishment continues to be disproportionate in relation to error.

What can help improve the safe access to and availability of opioids in India?

This section considers possible strategies to ensure safe access to and availability of opioid medications in India, based on the barriers described.

Changes needed at governance level

In India, and in most countries of the WHO South-East Asia Region, the controls for illicit usage and the new regulations on medical use are under the single central government agency. For decades, the conventional mandates of these offices have been to prevent illicit use and are therefore strongly prohibitive in nature. It may be difficult for this machinery to internalize and incorporate a new purpose and translate the intentions of the amendment for improving availability for medical use. Hence, acknowledging the need for a “licit entity” for governing opioids for medical use is a primary strategy that is necessary to support the implementation of the expanded scope of the reformed law. Creation of a distinct governance system under this entity, with the specific mandate to govern and specific measures to facilitate safe medical and scientific use of opioids, is critical. This would not only streamline implementation, but could also tackle the apathy and barriers that are prevalent at the highest level.

Changes needed at the executive level

As per the current law, the state drug controller is responsible for execution of the mandate of the amended federal law. However, officers of most states are unfamiliar with the new mandate. Official orders, through proper channels and unambiguous information on standard operating procedures, with printed manuals for clarity, would help them fulfill their mandate. The officers may also fear that implementation of the new law allowing easier access could trigger an epidemic of diversion of medical opioids to non-medical and inappropriate use. This fear is justifiably high amongst officials in regions where there is an existing problem of drug abuse. This concern of officers is valid and needs to be acknowledged and addressed effectively and creatively. Facilitation of an interagency collaborative action would be essential at executive level, involving revenue intelligence, surveillance agencies and quality technologies. Such a collaborative venture could aim at developing strategies to monitor the supply chain, as well as to track the prescribers, dispensing units and users. If such a strategy were to become active, the total opioid consumption of each region, and the patterns of licit usage, could be accurately recorded, thus addressing the balancing measure, that of preventing misuse and diversion.

Changes needed at the institutional, practitioner and patient levels

The stakeholders in the context of opioid regulations at this level include: (i) medical institutions that have to stock and dispense the medicines according to the rules; (ii) professionals who would prescribe and administer opioids to patients for medical use; and (iii) the patients who need to use the drugs to relieve their pain.

Institutions

Medical institutions in the country that stock opioids are largely unaware of the changed procedures for procuring, stocking and dispensing opioids as per the amended regulations. Despite a declaration of new national rules for essential narcotic drugs in 2015, most institutions continue to procure opioid medications using procedures and licences as per the nullified, old state-level regulations. Worse still, state agencies such as excise departments continue to participate, despite no longer having the authority. Medical institutions need to be made aware of the change in procedures for stocking and dispensing opioids and the steps required to be authorized as RMs, as per the 2014 amendment. Also, the state departments, such as excise, that are no longer part of the RMI procedure, need to be made aware of the new authority as per the amended law, namely the office of the state drug controller.

Professionals and the public

Bridge training programmes for medical professionals on the evaluation and management of pain, and on best practices for using opioids, would counteract negative attitudes and the tendency for opiotherapy. Prescribers should also be updated on the requirements for record-keeping stipulated by the regulations, such that essential narcotic drugs are prescribed appropriately and patients are managed safely. In addition, public advocacy on their right to access pain relief and on the safety and effectiveness of opioids in managing severe pain is essential. The safety and efficacy of these drugs would become more clearly evident to the public, once medical prescriptions on opioids become mainstreamed into clinical practice.

Civil society, which successfully achieved the landmark policy change, continues to be active in raising awareness of this important topic in many parts of India. It has succeeded in sensitizing several state governments through workshops on the need for improved access to opioids. The scene of access to pain relief and palliative care is changing in India – very gradually, but definitely. Resources have been developed for prescribers and to help medical institutions follow the new regulations on opioids for medical use.14

Lessons learnt from other countries in the region

The country examples provided next stand testimony to the impact that concerted efforts at the national level can have on tackling poor access to pain relief.

Thailand

Pain relief and palliative care in Thailand has improved in recent years. In 2006, palliative care was included in the hospital accreditation standard of the Healthcare Accreditation Institute. In the same year, the Ministry of Public Health issued notification that allowed for a notable increase in the maximum amount of opioids available for hospitals.22 Policies implemented by the Thai Food and Drug Administration (FDA)
further facilitated improved opioid availability and lowered prices. Since 2009, the National Health Security Office has supported networking among palliative care services within hospitals and the communities they serve. Since 2010, the Government Pharmaceutical Organization has been able to produce immediate-release oral morphine tablets and the liquid formulation, both of which have been endorsed by the Thai FDA. There was a clear impact on the annual ME consumption, which rose from 3.96 mg per capita in 2010 to 5.85 mg per capita in 2015, the highest in the region. Although impressive, there is still a long way to go towards equitable levels of usage. The regulation of opioids in government hospitals is mainly dependent on physician judgement, and pain remains under-assessed and undertreated in the majority of cancer patients, even in tertiary care services.23

Sri Lanka
Sri Lanka has demonstrated the impact of concerted programmes in activating the human welfare element of the opioid law.24 Morphine is available in all 25 districts, at teaching hospitals, provincial general hospitals, district general hospitals and base hospitals, but the drug is prescribed mainly by cancer units – at 9 provincial units and 11 district units. There is a policy for community-based hospices to access morphine from the adjacent cancer centres. The State Pharmaceutical Corporation, a parastatal organization accountable to government, runs pharmaceutical retail shops – Rajya Osu Sala – and the government allows these retail shops to stock morphine. There is additional provision for general practitioners to dispense morphine for their palliative care patients, through a special allocation from the Medical Supplies Division. From an annual ME consumption of zero in 1988, the gradual improvement to the modest but significant figure of 1.21 mg per capita in 2015 may be attributed to the efforts put in by the government of Sri Lanka in building capacity in the field of palliative care. Examples include a policy of mandatory proactive assessment of patients presenting at clinics or hospitals with moderate-to-severe pain; development and dissemination of pain management guidelines; and establishment of dedicated pain management clinics at the National Hospital of Sri Lanka and National Cancer Institute Maharagama.

Bangladesh
In Bangladesh, after much effort, opioid availability has improved in regions in and around the capital city. Eight medical institutions and four pharmacies in Dhaka currently have licences to dispense oral morphine. The Centre for Palliative Care, Bangabandhu Sheikh Mujib Medical University, in the capital city, is the largest prescriber of morphine for cancer patients in the country. Opiophobia among both medical professionals and the public is still a major barrier to access.25

Nepal
Combined efforts by the Nepalese Government and civil society have improved the situation in recent years. A significant barrier to reliable access to opioids in Nepal was overcome in 2009, when a licence was issued for a Nepalese company to manufacture morphine.26 There is a marginal but definite improvement in the ME consumption in Nepal, which in 2015 was 0.27 mg per capita. In 2017, Nepal adopted a National Strategy for Palliative Care, to guide the development of palliative care countrywide over the next decade, and its integration into the health system.27 Further work is needed, however, to educate physicians and improve attitudes and knowledge on opioids among health professionals, policy-makers and the public.28

Conclusion
Caring for patients with serious health-related suffering related to chronic conditions is not fully represented within the public health-care models prevalent in the WHO South-East Asia Region, and the majority of the professional community continues to be oblivious to the constituents, scope and benefits of palliative care. Pain, a significant component of serious health-related suffering, is grossly undertreated in most countries of the region. The presence and severity of pain continues to be a parameter that is not routinely assessed, documented or responded to in conventional health-care settings in the region. Patients and their families are affected physically, psychosocially and economically by this avoidable health-related suffering. The needs for pain relief and palliative care remain critically high.

In 2011, WHO noted that, despite 50 years of the United Nations Single Convention on Narcotic Drugs, the obligation to ensure adequate availability of these drugs for medical and scientific purposes has been neglected and countries have adopted laws and regulations that consistently and severely impede the accessibility of controlled medicines.29 A review of the evidence by the Johns Hopkins–Lancet Commission in 2016 highlighted the wide range of impediments to access to and use of controlled drugs as a result of drug-control policy and regulations.30 The commission recommends ensuring “access to controlled medicines, establishing inter-sectoral national authorities to determine levels of need and giving WHO the resources to assist the INCB in using the best science to determine the level of need for controlled medicines in all countries”.30 It has called for drug law reforms centred on health and human welfare.

A well-formulated drug policy can positively influence the access to and availability of opioid medications to treat severe persistent pain. This aspect is especially critical for the WHO South-East Asia Region, although the complexities of implementation in each country may differ. Once this is coupled with capacity-building and a comprehensive palliative care policy in line with the WHO recommendations, the region may look forward to a reduction in its current levels of serious health-related suffering, which at present are unacceptably high.

Source of support: None.

Conflict of interest: None declared.

Authorship: NV was responsible for the concept, background research, content and editing. MRR contributed to the concept and editing. SP, FK and BDP contributed to the sections on Sri Lanka, Bangladesh and Nepal. KT contributed to the concept.

References


Addressing the threat of antibiotic resistance in Thailand: monitoring population knowledge and awareness

Viroj Tangcharoensathien¹, Angkana Sommanustweechai¹, Sunicha Chanvatik¹, Hatairat Kosiyaporn¹, Klara Tisocki²

¹International Health Policy Program, Ministry of Public Health, Nonthaburi, Thailand, ²World Health Organization Regional Office for South-East Asia, New Delhi, India

Correspondence to: Dr Viroj Tangcharoensathien (viroj@ihpp.thaigov.net)

Abstract

The 2015 Global action plan on antimicrobial resistance (GAP-AMR) highlights the key importance of improving awareness and understanding of antimicrobial resistance among consumers. While low levels of awareness are not exclusive to consumers in low- and middle-income countries, the challenges to improving understanding are compounded in these settings, by factors such as higher rates of antibiotic self-medication and availability through informal suppliers. In 2016, Thailand set an ambitious target to increase, by 2021, public knowledge of antibiotic resistance and awareness of appropriate use of antibiotic by 20%. This involved first establishing baseline data by incorporating a module on antibiotic awareness into the 2017 national Health and Welfare Survey conducted by the National Statistical Office. The benefit of this approach is that the data from the antibiotic module are collected in parallel with data on socioeconomic, demographic and geospatial parameters that can inform targeted public communications. The module was developed by review of existing tools that have been used to measure public awareness of antibiotics, namely those of the Eurobarometer project of the European Union and a questionnaire developed by the World Health Organization. The Thai module was constructed in such a way that results could be benchmarked against those of the other survey tools, to allow international comparison. The Thai experience showed that close collaboration between the relevant national authorities allowed smooth integration of a module on antibiotic awareness into the national household survey. To date, evidence from the module has informed the content and strategy of public communications on antibiotic use and misuse. Work is under way to select the most robust indicators to use in monitoring progress. The other Member States of the World Health Organization South-East Asia Region can benefit from Thailand’s experiences in improvement of monitoring population knowledge and awareness.

Keywords: antibiotic resistance, dispensing competencies, health knowledge, health professionals, national action plan, prescribing competencies, public awareness, South-East Asia Region

Antibiotic resistance: a growing global threat

Antibiotic resistance is one of the greatest challenges to global public health today. The threat is increasing and is fuelled by a range of factors, including the excessive and inappropriate use of antibiotics. This, in addition to use of poor quality and substandard antibiotics, results in selective pressure, accelerating the emergence of antibiotic-resistant bacteria. Of all the reports to the WHO Global Surveillance and Monitoring System for Substandard and Falsified Medical Products during 2013–2017, antibiotics accounted for 16.9%, second only to anti-malarials at 19.6% of all reports. Substandard and falsified antibiotics are a significant problem, particularly in low- and lower-middle-income countries, such as those of the World Health Organization (WHO) South-East Asia Region, where nonexistent or inadequate post-marketing quality surveillance of human and veterinary antibiotics allows the market in these substandard medicines to flourish.

Inadequate prevention and control of infection in health facilities transmits pathogens such as meticillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus and multidrug-resistant Acinetobacter from patients with these resistant strains to other patients. Mass international travel facilitates global spread of antibiotic resistance pathogens. These include the lactam-resistant Enterobacteriaceae and Klebsiella pneumoniae strains isolated from travellers who have visited countries in South Asia. In addition, South-East Asia is a hub for production of animal-source foods and major use of pharmaceuticals; both can increase the threat of antibiotic resistance in the region, for example via excessive use of antibiotics as growth promoters or as prophylactic agents
for livestock. In addition, untreated wastewater containing antibiotics is sometimes released from hospitals, livestock, poultry and aquaculture farms, and human dwellings.

The prevalence of antibiotic resistance is higher in communities where there is high-level use of non-prescription antibiotics. In low- and middle-income countries, the prevalence of self-medication of antibiotics is high, ranging from 19% to 82% in countries of the Middle East, an average of 39% in 34 studies in low- and middle-income countries; and 7% to 86%, with an overall average of 43% in 19 studies in the WHO South-East Asia Region. Penicillins are the most common self-medication drug class, mostly sourced from leftover medicines, from pharmacies and drug shops. Self-medication has been reported mainly for upper respiratory tract problems, or for fever or respiratory or gastrointestinal conditions. Inappropriate use includes wrong indications, such as use for viral infections, inflammation, influenza or the common cold, and inappropriate duration of treatment.

Use of subtherapeutic doses not only results in treatment failure but also raises the serious threat of emergence of antibiotic-resistance pathogens. Sales of antibiotics in drug stores offered by non-qualified lay persons exacerbate the inappropriate use. In the WHO South-East Asia Region, the majority of self-medicated antibiotics are obtained from a range of sources, such as pharmacies, leftover drugs, hospitals, or friends and family.

In May 2015, in response to health security threats posed by antimicrobial resistance, the World Health Assembly adopted the Global action plan on antimicrobial resistance (GAP-AMR), and called on WHO Member States to develop national action plans. In September 2015, at the regional committee meeting of the WHO South-East Asia Region, Member States committed to implementing national action plans in accordance with the GAP-AMR and regional priorities. The GAP-AMR underscored the need for an effective “one health” approach involving coordination among numerous sectors and actors, including human and veterinary medicine, agriculture, finance, environment, and well-informed consumers. The GAP-AMR has five overarching objectives, the first of which is to “improve awareness and understanding of antimicrobial resistance through effective communication, education and training”.

Responses by Member States in the WHO South-East Asia Region

As of April 2018, all 11 Member States of the WHO South-East Asia Region had developed a national action plan on antimicrobial resistance. These national action plans were developed in response to country situation analysis, using a tool developed by the WHO Regional Office for South-East Asia. The indicator on awareness-raising in this tool covers two sub-indicators: education and training strategies for professionals; and awareness campaigns for the public.

With respect to professionals, all countries have proposed strategies to strengthen antibiotic-prescribing competencies among pharmacists, veterinarians and physicians, through pre-service training and in-service continued professional development. These professionals who prescribe and dispense antibiotics are key stakeholders; with improved prescribing and dispensing competencies, they can be the change agents for ensuring appropriate use of antibiotics in the population.

With respect to the public, the national action plans also propose mechanisms to increase levels of knowledge about proper use of antibiotics and awareness of antibiotic resistance. However, countries also need to document the baseline and gaps in awareness of antibiotic resistance, knowledge of antibiotics, and the level of inappropriate use in populations that often self-medicate, as well as among health professionals. These baseline data are needed to inform effective interventions and allow regular monitoring of progress, which in turn will inform any need to reformulate strategies. Other than Thailand, none of the Member States of the WHO South-East Asia Region have set a target for an improved level of awareness in the population. Thailand has set an ambitious 5-year target to increase, by 2021, public knowledge of antibiotic resistance and awareness of appropriate use of antibiotics by 20% against the 2017 baseline.

This perspective paper provides an overview of how Thailand successfully incorporated a standard tool for measuring and monitoring public knowledge and awareness of antibiotic resistance into its national household survey, and discusses the lessons learnt.

Monitoring in the population: analysis of the content of the tools

Tools that have been used to measure public awareness of antibiotics include the European Commission Special Eurobarometers 338 and 445; the Flash Eurobarometer 444; and the WHO Antibiotic resistance: multi-country public awareness survey tool (hereafter called “the WHO tool”) used in 12 countries globally. Box 1 summarizes the common content of these tools.

Box 1. Summary of common content used by the Eurobarometer and WHO tools

- Use of antibiotics: the prevalence of self-medicated antibiotics, source of antibiotics and indication
- Knowledge of antibiotics
- Information about the use of antibiotics: source of information, impact of information on self-medication behaviour
- Knowledge and awareness of antibiotic resistance
- Use of antibiotics in agriculture and the environment

The Eurobarometer tool

The general Eurobarometer surveys are used to monitor public opinion in all 28 European Union (EU) Member States. Special Eurobarometer surveys are used for in-depth thematic studies and are integrated into the standard Eurobarometer. For the Special Eurobarometer tool on antibiotics, a four-section questionnaire was added to the standard Eurobarometer tool.

1. use of antibiotics in the last 12 months: this includes questions on the source of antibiotics (with or without prescription) and symptoms or indications leading to antibiotic use;
1. **use of antibiotics**: the question asks when the last use of antibiotic was (last month, last 6 months, last year, or more than a year); and about sources of self-medicated antibiotics and counselling if they are delivered by doctors and nurses;

2. **knowledge of antibiotics**: this section covers two true/false statements, namely, “use of antibiotics that were given to a friend or family member for the same illness is acceptable” (FALSE); and “buying the same antibiotic or requesting it from a doctor for symptoms that are similar to a previous episode is acceptable” (FALSE); and asks about when to stop taking antibiotics, and knowledge about what conditions can be treated by antibiotics (e.g. HIV/AIDS, gonorrhoea, urinary tract infection, diarrhoea, cold and flu, fever, measles, malaria, skin and wound infection, sore throat, body aches, headaches).

3. **knowledge and awareness of antibiotic resistance, sources of information and the use of antibiotics in the agriculture sector**: this section is quite lengthy and covers the following subsections:
   a. having heard of key terms (such as antibiotic resistance, drug resistance, antibiotic-resistant bacteria, superbugs, antimicrobial resistance);
   b. where did people get this information (health-care workers versus other sources);
   c. level of understanding of the issues of antibiotic resistance, using a few true/false statements, such as “antibiotic resistance occurs when the body becomes resistant to antibiotics and they no longer work as well” (FALSE); “many infections become resistant to treatment by antibiotics” (TRUE); “if bacteria are resistant to antibiotics, it can be very difficult or impossible to treat the infections they cause” (TRUE); “antibiotic resistance is an issue that could affect me or my family” (TRUE); “antibiotic resistance is an issue in other countries but not here” (FALSE); “antibiotic resistance is only a problem for people who take antibiotics regularly” (FALSE); “bacteria that are resistant to antibiotics can be spread from person to person” (TRUE);

4. **information about the use of antibiotics**: participants are asked whether they have received information about the correct use of antibiotics in the last 12 months; this section includes questions on the sources of information; the impact of information on future use of antibiotics; what additional information respondents require; and what respondents believe are trustworthy sources of information;

5. **use of antibiotics in agriculture and the environment**: in this section, respondents are asked whether sick animals should have the right to be treated with antibiotics, and also asked whether they know about the EU ban on the use of antibiotics to stimulate growth in farm animals.

### The WHO tool

The questionnaire developed by WHO, which has been used in 12 countries, contains three sections:23

1. **use of antibiotics**: the question asks when the last use of antibiotic was (last month, last 6 months, last year, or more than a year); and about sources of self-medicated antibiotics and counselling if they are delivered by doctors and nurses;

2. **knowledge of antibiotics**: this section covers two true/false statements, namely, “use of antibiotics that were given to a friend or family member for the same illness is acceptable” (FALSE); and “buying the same antibiotic or requesting it from a doctor for symptoms that are similar to a previous episode is acceptable” (FALSE); and asks about when to stop taking antibiotics, and knowledge about what conditions can be treated by antibiotics (e.g. HIV/AIDS, gonorrhoea, urinary tract infection, diarrhoea, cold and flu, fever, measles, malaria, skin and wound infection, sore throat, body aches, headaches).

3. **knowledge and awareness of antibiotic resistance, sources of information and the use of antibiotics in the agriculture sector**: this section is quite lengthy and covers the following subsections:
   a. having heard of key terms (such as antibiotic resistance, drug resistance, antibiotic-resistant bacteria, superbugs, antimicrobial resistance);
   b. where did people get this information (health-care workers versus other sources);
   c. level of understanding of the issues of antibiotic resistance, using a few true/false statements, such as “antibiotic resistance occurs when the body becomes resistant to antibiotics and they no longer work as well” (FALSE); “many infections become resistant to treatment by antibiotics” (TRUE); “if bacteria are resistant to antibiotics, it can be very difficult or impossible to treat the infections they cause” (TRUE); “antibiotic resistance is an issue that could affect me or my family” (TRUE); “antibiotic resistance is an issue in other countries but not here” (FALSE); “antibiotic resistance is only a problem for people who take antibiotics regularly” (FALSE); “bacteria that are resistant to antibiotics can be spread from person to person” (TRUE);

4. **level of awareness and knowledge of how to address the challenges of antibiotic resistance, such as knowing that people should use antibiotics only when they are prescribed by a doctor or nurse; farmers should give fewer antibiotics to food-producing animals; people should not keep antibiotics and use them later for other illnesses; parents should make sure all of their children’s vaccinations are up to date; and people should wash their hands regularly;**

5. **respondents’ opinion on the scale of antibiotic-resistance challenges and whether they are local or global, individual or a common problem for everyone that requires collective effort;**

6. **level of awareness of antibiotic use in the agriculture sector.**

### Monitoring in the population: lessons learnt from Thailand’s application of the tools

In 2016, Thailand established a working group on health policy and systems research on antimicrobial resistance (HPSR-AMR),24 to develop a monitoring tool to assess knowledge and awareness of antibiotic use and antibiotic resistance in the population, as well as other monitoring infrastructures such as establishment of surveillance of antimicrobial consumption.25 A scoping review of the existing tools available was done to inform the construction of a module for application in the Thai population. This module was then integrated into the 2017 Health and Welfare Survey conducted biannually by the National Statistical Office (NSO). The benefit of this approach is that the data from the antibiotic module are collected in parallel with data on socioeconomic, demographic and geospatial parameters that can inform targeted public communications. Three main areas of focus were identified in the key lessons learnt: tools, methods and policy utilities.

### Tools

The finding of the scoping review was that the Eurobarometer and WHO tools provide detail on knowledge of antibiotics and the level of awareness of antibiotic resistance. The WHO tool is very useful, as it probes true/false statements on the level of understanding of the challenges of antibiotic resistance, and the findings can support the design of effective public communication. The module for use in Thailand was constructed in such a way that the findings could be benchmarked against the results of surveys using the Eurobarometer tool. Review of and learning from international experiences contributed to the design of the module.

There are four sections in the Thai questionnaire, which include (i) antibiotic use and use profiles during the last month; (ii) antibiotic literacy; (iii) public information on proper use of antibiotics and on antibiotic resistance, and the source and impact of this information on future use of antibiotics; and (iv) awareness of the use of antibiotics in farm animals.
The challenge of household surveys in this area is that respondents frequently cannot distinguish antibiotics from other medicines. Thus, the prevalence of antibiotic use they report will be invalid if not all medicines are antibiotics. In small-scale research, investigators can conduct on-site verification of whether medicines are antibiotics; however, for the national household surveys, time does not allow interviewers to conduct such verification, owing to the large number of questions in other sections, such as those on health-care utilization, payment for health, and other risk behaviour. Also, medicines provided by stalls, hawkers or groceries do not provide proper package labelling. In this regard, we suggest that in the next household survey in 2019, the interviewers should be provided with a set of photos of common antibiotics and a guide on how to present these to participants with explanations.

It is important to estimate the prevalence of antibiotic use, such as the percentage of the population that uses antibiotics over a certain time period, which could be the last 12 months, 6 months or 1 month. For the 2017 survey, the HPSR-AMR decided to apply a 1-month period for valid recall. Literature reviews suggest that a 15-day recall is appropriate for acute health problems in linking use of medicines, including self-medication of antibiotics. For chronic health conditions, a longer recall period ranging from the previous month to the past 12 months is more appropriate.

The true/false statements used to assess participants’ knowledge of antibiotics should be developed from prior small-scale qualitative studies, which can be country and context specific. Each country has specific gaps of knowledge of antibiotics; it is advisable to identify these gaps in a small-scale qualitative study and to use the findings to inform the design of national survey questionnaires. However, the true/false statements can be standardized in the same way as those used by the Eurobarometer and WHO tools, in order to facilitate cross-country comparisons. The HPSR-AMR did not conduct such a small-scale qualitative study, but decided for the 2017 survey to apply the standard questions used by the Eurobarometer tool, in order to enable future cross-country comparisons. This may be seen as similar to the approach taken in the 1990s, when the AIDS Indicator Survey was applied via the Demographic and Health Survey Programme questionnaire to provide countries with a standardized set of questions. These questions probed, for example, knowledge on HIV/AIDS and on HIV prevention; misconceptions; attitudes; stigma; and higher-risk sexual behaviour, for effective monitoring of national HIV/AIDS programmes. The data collected contributed to comparable cross-country monitoring of the improvement of population knowledge and was regularly reported by the Joint United Nations Programme on HIV/AIDS (UNAIDS).

Methods
The module was introduced into the biannual Health and Welfare Survey conducted by the NSO, and the survey was conducted in 2017. With strong institutional relationships, mutual recognition and mutual respect between the NSO and the International Health Policy Program of the Ministry of Public Health, integration of this special module into the survey went smoothly. The NSO has committed to integrating the module on antibiotic resistance into future Health and Welfare Surveys for biannual national monitoring.

As part of the Health and Welfare Survey, the module on antibiotic resistance involves a face-to-face interview conducted by NSO field staff, which does not allow proxy respondents in cases where the eligible respondents are absent. The respondents are adult members of the sample household who are more than 15 years old. A total 27 960 households and 27 762 adults were enumerated in the 2017 Health and Welfare Survey. The sample households were selected using a two-stage stratified sampling method. In the first stage, urban and rural enumeration areas were selected using probability proportional to size in all 77 provinces. In the second stage, samples of 10 and 15 households in each of the rural and urban enumeration areas were selected using a systematic random sampling method. In comparison, the WHO tool applies either face-to-face street interviews or online electronic surveys, while the Eurobarometer tool uses face-to-face interviews in the respondent’s house, and the Flash Eurobarometer tool applies telephone interviews.

Policy utilities
Evidence generated from the module on antibiotic resistance has contributed to the design of public communications in both content and strategies. For example, the survey indicated that the public communication in Thailand for proper use of antibiotics should include the following messages: (i) antibiotics should not be used for symptoms such as headache, backache, diarrhoea, cough, cold, flu and fever; (ii) people with conditions such as pneumonia, bronchitis, rhino-pharyngitis and urinary tract infection should seek medical attention instead of self-medicating with antibiotics; and (iii) completing a full course of antibiotics and adhering to treatment regimens are essential for successful outcomes and to prevent antibiotic resistance. Public communication can be prioritized, based on the knowledge gaps identified from the survey and transmitted through the trustworthy sources identified by the respondents. Baseline knowledge of antibiotics can be measured by various indicators; for example, the percentage of participants who responded correctly to three out of five statements, or four out of five statements, or all five statements. By 2021, Thailand should achieve a 20% increase in each of these three possible knowledge indicators, as well as the percentage of the population who are aware of antibiotic resistance. On the other hand, negative indicators can be measured; for example, the percentage of the adult population who respond incorrectly to all five statements should be significantly reduced. A series of consultations with stakeholders to finalize these indicators is planned in 2018. Evidence from monitoring knowledge and awareness will be communicated to the National Steering Committee on Antimicrobial Resistance chaired by the deputy prime minister, for further policy actions.

Remaining challenges
This section identifies a few remaining monitoring gaps that warrant policy attention.

Monitoring gaps in the animal and food safety sector
There are limited surveys with special focus on the farmers and veterinarians who use antibiotics in animals reared for food. In 2016, The European Food Safety Authority (EFSA) conducted
a survey among the consumers who use animal products and the veterinarians who prescribe antibiotics on farms. The EFSA questionnaire covered four sections: (i) understanding the relationship between antibiotic use and antibiotic resistance in animals and human health; (ii) risk perceptions of developing antibiotic resistance in animal farming; (iii) reasons and rationales underpinning risk perceptions; and (iv) channels that influence respondents’ perceptions and practices.31

The EFSA suggested that, for farmers, the level of knowledge about, and practice of, the antibiotic-withdrawal period (the minimum duration from administration until harvesting of food from an animal) should guide specific messages for practice modifications.31 We suggest that countries that have more resources and capacity should introduce surveys in the animal and food safety sector to generate evidence for precise and effective messages. In the area of food safety, there is an urgent need to monitor knowledge and awareness of antibiotic resistance and hygienic practice among food-handling personnel – from farms to tables, as unsafe food handling is one of the major transmission pathways, which is often overlooked and an unknown area.

**Monitoring gaps in health professionals’ practice**

There are no global standardized survey tools to assess the prescribing and dispensing practices and competencies among health professionals who are the change agents: the physicians, veterinarians and pharmacists, particularly in low- and middle-income countries that often legally dispense antibiotics without prescription.32 Monitoring knowledge and practice, awareness and incentives for prescribing antibiotics among physicians and veterinarians is more sporadic; most information is acquired from research projects and, less frequently, small-scale surveys.33,34 Yet, there is an urgent need to monitor professional prescribing competency, practice and knowledge, as well as awareness of local antibiotic-resistance profiles. Gaps in prescribing and dispensing competency will guide the design of in-service continued professional education.

**Conclusion**

Increasing societal literacy on antibiotics and awareness of antibiotic resistance can be an efficient strategy to improve proper use of antibiotics and address antibiotic resistance. Setting national targets creates demand for evidence; it is an entry point to establish a baseline, through the review of existing tools, and to develop a national monitoring tool. Application of the Eurobarometer and WHO tools is useful, as the findings can be benchmarked with international peers. Integration of the survey module into the existing national household survey can be benchmarked with international peers. The EFSA suggested that, for farmers, the level of knowledge about, and practice of, the antibiotic-withdrawal period (the minimum duration from administration until harvesting of food from an animal) should guide specific messages for practice modifications.31

Monitoring gaps in health professionals’ practice

There are no global standardized survey tools to assess the prescribing and dispensing practices and competencies among health professionals who are the change agents: the physicians, veterinarians and pharmacists, particularly in low- and middle-income countries that often legally dispense antibiotics without prescription.32 Monitoring knowledge and practice, awareness and incentives for prescribing antibiotics among physicians and veterinarians is more sporadic; most information is acquired from research projects and, less frequently, small-scale surveys.33,34 Yet, there is an urgent need to monitor professional prescribing competency, practice and knowledge, as well as awareness of local antibiotic-resistance profiles. Gaps in prescribing and dispensing competency will guide the design of in-service continued professional education.

**References**

7. Arcilla MS, van Hattem JM, Tmaid.2016.11.018.

**Acknowledgements**

We thank the Thai National Statistical Office for integrating the antibiotic module in the National Health Welfare Survey 2017, and their field staff for conducting the survey. We thank our colleagues from the Drug System Monitoring and Development Centre and the Thai Food and Drug Administration, who provided insight and expertise that greatly assisted the design of the survey module.

**Source of support**: None.

**Conflict of interest**: None declared.

**Authorship**: VT and AS conceptualized and drafted the manuscript. All authors contributed to the development of all sections of the manuscript. VT and AS further revised the manuscript. All authors reviewed and approved the final revised version.

Tangcharoensathien et al.: Monitoring population awareness of antibiotic resistance in Thailand


National introduction of fractional-dose inactivated polio vaccine in Sri Lanka following the global “switch”

Deepa Gamage, Samitha Ginige, Paba Palihawadana
Epidemiology Unit, Ministry of Health, Colombo, Sri Lanka
Correspondence to: Dr Deepa Gamage (deepagamage@gmail.com)

Abstract
As part of the Polio eradication and endgame strategic plan 2013–2018 to achieve and sustain a polio-free world, the use of oral polio vaccine (OPV) must eventually be stopped. This process started in April 2016, with the worldwide, planned synchronized “switch”, whereby use of OPV containing poliovirus type 2 ceased. Prior to the switch, in line with international guidance on risk mitigation, Sri Lanka had introduced a single full dose (0.5 mL intramuscularly) of inactivated polio vaccine (IPV) into routine immunization. However, the two global suppliers of World Health Organization (WHO)-prequalified IPV had significant challenges in scaling up production to meet the new demand, resulting in a global shortage in April 2016. The WHO Strategic Advisory Group of Experts on Immunization recommended that countries should consider a two-dose schedule of intradermal fractional IPV (fIPV). After rapid consideration of the programmatic cost and logistic implications, Sri Lanka was the first country to roll out this dose-sparing schedule nationwide. The country ensured smooth implementation of fIPV use, reaching out to all eligible infants, maintaining equity and sustaining the IPV vaccination. With expedited refresher training in intradermal vaccination, confident, well-trained and dedicated health-care staff, from the field up to provincial levels, worked together as a dedicated team. Health authorities at all levels reported that public acceptance of the additional injections of the new schedule was high. A post-introduction evaluation and an assessment of population-level immunity are under way.

Keywords fractional-dose inactivated poliovirus, national immunization programme, oral polio vaccine, poliovirus, poliovirus type 2

Background
In May 2012, the 65th World Health Assembly declared the completion of poliovirus eradication to be “a programmatic emergency of global proportions for public health”. The goal of the subsequent Polio eradication and endgame strategic plan 2013–2018 was to end poliomyelitis (polio) disease resulting from both wild poliovirus and circulating vaccine-derived poliovirus (cVDPV), to achieve and sustain a polio-free world. Part of the plan’s strategy called for strengthening of routine immunization and globally synchronized withdrawal of oral poliovirus vaccine (OPV), beginning with cessation of the use of OPV type 2 by mid-2016. Globally, the last wild poliovirus type 2 (WPV2) was reported in 1999 but cVDPV has been reported, owing to suboptimal population-level immunization coverage of trivalent OPV (tOPV: containing polio vaccine viruses types 1, 2 and 3). In September 2015, the Global Commission for the Certification of Poliomyelitis Eradication declared the worldwide eradication of WPV2, and recommended that the synchronized global “switch” from the use of tOPV to bivalent OPV (bOPV: containing polio vaccine viruses types 1 and 3) should occur during April 2016. Prior to the “switch”, the 155 countries and territories using tOPV in their routine immunization programmes were recommended to introduce injectable inactivated polio vaccine (IPV) before the end of 2015. This strategy was intended to mitigate the potential consequences should any re-emergence of poliovirus type 2 occur following the switch in April 2016. In line with the global recommendations, the World Health Organization (WHO) Regional Office for South-East Asia worked with its 11 Member States to monitor country situations and ensure introduction of IPV and continuation through the switch from tOPV to bOPV by April 2016.

Sri Lanka is an island in the Indian Ocean, with a total land area of 65,610 km² and a population of 20,277,597 at the last census in 2012. For 2016, the estimated population was 21,203,000 and the number of annual live births was 331,073. Sri Lanka is administratively divided into nine provinces and 25 districts. For health service provision, 342 divisions function as basic operational units under the provincial and regional directors of health services. Each health administrative division is named as a medical officer of health (MOH) area. The MOH of the area, together with other categories of public health staff, is responsible for the provision of integrated primary public
health services to the community. In addition to the provision at community clinics, immunization services are provided in curative health-care institutions/hospitals and are under the supervision of the regional epidemiologist and MOH. The vaccine storage facilities at district-level stores or MOH offices receiving vaccine stocks for divisional vaccine stores are responsible for providing stocks of vaccines to curative health-care institutions/hospitals and also responsible for cold-chain management at the institution and data handling in providing information on vaccinations. The regional epidemiologist at the district level is responsible for overall immunization and vaccine-preventable disease programmes in the districts, and accountable for all immunization service provisions at MOH areas and at curative health-care institutions/hospitals.

Sri Lanka has been a Gavi (The Vaccine Alliance)-graduate country since 2015 and thus is not eligible for financial support for vaccination programmes. However, special support was extended by Gavi for IPV introduction, through a commitment to support the supply of IPV vaccine from 2015 to 2018, through the United Nations Children’s Fund (UNICEF), under the Global Polio Eradication Initiative. In compliance with the regional guidance, by July 2015 Sri Lanka had successfully introduced a full-dose 0.5 mL IPV single intramuscular vaccination to all infants at 4 months of age. This was the first time the IPV vaccine was introduced through the national immunization programme and all infants had been receiving only tOPV up to July 2015. Since the country planned to change over from tOPV to bOPV on 30 April 2016 as the “switch” date, it introduced trivalent IPV for all infants aged 4 months into the national schedule from the preceding July, in order to maintain immunity to poliovirus type 2.

A subsequent IPV consignment was expected in mid-2016. However, in April 2016, the country received a verbal communication from WHO informing them of a worldwide supply shortage of IPV. The two global suppliers of WHO-prequalified IPV had significant challenges in scaling up production to meet the new demand. Categorized as a low-risk country for polio (a tier-4 country in the risk-categorization scale of high to low from 1 to 4), Sri Lanka was at the lowest priority to receive scarce IPV supplies. A joint deputation from UNICEF and WHO formally informed the Ministry of Health of the short supply of IPV in May 2016 and that the subsequent consignment of IPV to Sri Lanka would be delayed to beyond September 2017, owing to the global scarcity.

The Central Epidemiology Unit, the implementing authority of the national immunization programme for the Ministry of Health, Sri Lanka, was stunned by this unexpected information and the deferment of the subsequent IPV consignment. Discussions were held with relevant global and regional authorities, to comprehend the reasons for the IPV scarcity and explore the options for forward planning to receive the required supplies of IPV in the country. However, efforts to receive vaccines ahead of the postponed rescheduled timeline were not successful.

Devising a country strategy in the face of the global shortage of inactivated polio vaccine

In the context of the IPV shortage, WHO advised countries to consider using fractional doses (one fifth of the full IPV dose) via the intradermal route, as an alternative to the intramuscular injection of a full dose of IPV, depending on the programmatic cost and logistic implications. Countries were advised to consider instituting a two-dose schedule of intradermal fractional IPV (fIPV) of 0.1 mL per dose administered to infants at 6 and 14 weeks, separated by a minimum interval of 4 weeks.

To devise a strategy to maintain population immunity for poliovirus type 2 in the face of the IPV stock-out, in early June 2016, the National Advisory Committee on Communicable Diseases (ACCD) in Sri Lanka, which is equivalent to the national immunization technical advisory group, deliberated on the evidence compiled by national officers, with assistance from the WHO Regional Office for South-East Asia. In addition, the experience in India, as the first country to introduce fIPV into their immunization schedule at subnational levels, was sought via personal communication. The key points listed next were considered by ACCD in their decision-making.

- Study findings considered in the decision-making by the WHO Strategic Advisory Group of Experts on Immunization, and in the WHO position paper on polio vaccines, were reviewed. The evidence for non-inferior seroconversion rates for the fIPV two-dose schedule compared with the single full-dose IPV schedule was an important factor in decision-making.
- The reduction in required stocks associated with changing over to a fractional dose (estimated 70,000 2.5 mL vials per year, reduced to 28,000 2.5 mL vials), which was a 60% reduction of the initial stock requirement, would permit the country to use existing vaccine stocks for an extended period, to sustain IPV vaccination until mid-2017.
- There would also be a reduction of the vaccine cost per child, from US$ 1.90 per dose per child for a single 0.5 mL IPV dose, to US$ 0.76 per child for two fIPV doses. This is a 60% cost reduction for an “IPV fully immunized child” to develop the expected immunity to poliovirus type 2.
- The fIPV schedule could be continued even if an adequate supply of IPV were to become available in the future, until the global recommendations for the schedule change for full withdrawal of OPV are put in place.
- Implementation feasibility was also considered:
  - Rapid refresher training could be provided for midwives, as they would all have already received hands-on skill training in intradermal vaccination during their basic training;
  - Refresher training in intradermal vaccination could be easily provided for nursing officers alongside BCG nursing officers;
  - 0.1 mL auto-disable syringes could be used until Gavi supplies become available;
  - It would be feasible to co-administer the first fIPV dose with pentavalent (diphtheria–tetanus–whole cell pertussis, hepatitis B and Haemophilus influenzae type b) vaccine and bOPV at 2 months, and the second dose at 4 months, within the existing vaccination schedule;
  - Full-dose IPV at 4 months of age could be continued for a further 2 months, in parallel with the fIPV schedule starting at 2 months of age, until infants who received the fractional dose at 2 months reach the age of 4 months.
- Manufacturer positions considered were:
  - Manufacturer licensing was only for intramuscular use and not for intradermal use at the time of the decision;
thus, the ACCD committee decision was based on the recommendations of the WHO position paper;11
  - the manufacturer recommendation that a higher number of punctures should not be made on the vaccine vial stopper of 10-dose vials was not relevant, since Sri Lanka only had 5-dose vials;
  - the manufacturer had neither opposed nor specifically endorsed fIPV implementation by countries.

Based on this information, the ACCD recommendation to introduce fIPV into the national immunization schedule on an “off-label” basis was endorsed by the National Medicinal Drug Evaluation Committee of the National Medicinal Drug Regulatory Authority. All experts in ACCD acknowledged that the decision taken by ACCD was crucial, as Sri Lanka was the first country to take the decision to change over to fIPV nationwide, to mitigate imminent stock-out of IPV in a rational manner and sustain the immunization programme.

Planning and implementation of the strategy

Planning of the schedule change for IPV into a fractional two-dose schedule implemented within the routine immunization programmes was examined systematically, in order to provide the best available services in an appropriate, affordable and cost-effective manner.17 Regional epidemiologists were advised to organize immediate district-level refresher training on intradermal administration of the vaccine, for public health midwives and immunization nurses in curative health-care institutions/hospitals. National-level training-of-trainer programmes were conducted for the regional epidemiologists on how to administer fIPV, using the 5-dose vials of IPV that were available. The doses, route and site of administration were explained for the two doses to be given at the age of 2 months and 4 months, together with the other two recommended vaccines (OPV and pentavalent vaccine), and to be administered intradermally to the left upper arm. The WHO multidose vial policy continued to be used for IPV, whereby vials opened in a fixed clinic could be used at more than one immunization session, provided that: (i) the expiry date had not passed; and (ii) the vaccine was stored under appropriate cold-chain conditions. Guidelines on the changes to the vaccination schedule and stock balancing were circulated.

Immediate training of public health-care workers was started at district level as refresher training (as all public health midwives have had initial hands-on skill training during the basic midwifery training), with one full day of training providing relevant information on the importance of IPV vaccination, the schedule change and video clips on the technique. The hands-on skill training included a half-day training of vaccination of volunteers drawn from adult health staff colleagues during the training, with a subsequent 1–2 days spent undertaking intradermal vaccination of BCG vaccine to neonates alongside BCG vaccination nursing officers at health-care institutions. Nursing officers involved in vaccination, at immunization clinics in curative care institutions/hospitals were also given the refresher training on intradermal vaccination, together with BCG nurses.

Given the urgency of the training schedule, the initial expenditure required for training (US$750–1000) was mobilized from the existing central-level Ministry of Health budget for the national-level training. Subsequently, considering the country priority, it was decided to implement the programme with minimum additional expenditure, by integrating it into existing programmes for training health-care staff. Provincial and district health authorities took responsibility for providing training from provincial health budgets, bearing the minimum cost of around US$ 250–500 for refreshments and travel for each programme at district and divisional levels. Health-care staff volunteered as resource persons for training, without expecting additional fees.

An intensive mass-media campaign was not conducted; as it had already been done during the introduction of IPV vaccine, this was deemed to be only a schedule change. However, print media were used to ensure general public awareness. Awareness among parents was raised by public health midwives during their home visits for routine services, and at health educational sessions in maternal and child health-care clinics. The public health midwives were assisted to be confident in answering questions from the public by the use of role-plays during their training sessions.

Other essentials for programmatic readiness to change the schedule for the IPV vaccination, such as stock management, were conducted with close monitoring of existing IPV stocks at each level. A decision was taken to move extra vaccine stocks from divisional levels (which is the lowest level of vaccine stores) to district-level walk-in cold rooms (as a result of IPV-dose sparing in the schedule change), to optimize cold-chain monitoring as a precautionary measure to minimize vaccine wastage.

Discussion

Sri Lanka is the first country to have implemented the use of fIPV in their national immunization programme. The Central Epidemiology Unit of the Ministry of Health, Sri Lanka, as the centrally accountable authority for both the national immunization programme and the vaccine-preventable disease surveillance programme, took the leadership for fIPV implementation in the country, as part of an incorporated, coordinated system of communicable disease surveillance. The Central Epidemiology Unit has the capacity to make policy decisions on immunization, and to coordinate the planning and implementation of such decisions throughout the country. The stock management of vaccines and other supplies, cold-chain monitoring, and implementation of the immunization programme is centrally coordinated, monitored and supervised by the Central Epidemiology Unit.

Sri Lanka rapidly evaluated the required elements of the schedule change from a full intramuscular dose to the alternative intradermal fIPV, considering the programmatic cost and logistic implications of this option in the context of an IPV shortage. The country also ensured smooth implementation of fIPV immunization for all eligible infants, sustaining the sequential IPV vaccination programme as recommended by the Global Polio Eradication Initiative,2 to maintain population-level immunity to poliovirus type 2.
The recommendation of early and appropriately timed protection, provided by scheduling fractional intradermal doses, administered at 6 and 14 weeks (separated by a minimum interval of 4 weeks),7 was met by providing fIPV within the regular immunization programme schedule at 8 and 16 weeks. The country opted to take the initiative of off-label use of the vaccine at the time of decision-making, and relevant strategic decisions were successfully implemented.

Confident, well-trained and dedicated health-care staff working at grassroots level in the field; medical officers of health, including medical officers, public health nursing sisters, public health midwives and public health inspectors and staff of the hospital-level immunization clinics; district health authorities; and provincial health authorities worked as a dedicated team. Their monumental efforts ensured smooth and successful implementation of fIPV immunization as a national programme. Each immunization clinic is conducted by a qualified medical officer and this has facilitated the provision of quality immunization services for intradermal fIPV administration at immunization clinics. All relevant health professionals receive high-quality, comprehensive basic public health training at their initial recruitment, which gave national authorities the confidence that refresher training on administration of intradermal vaccine was sufficient to make implementation a success. Health authorities at all levels reported high levels of public acceptance of the additional injections resulting from the change in schedule.

Health authorities identified the challenge of accurate documentation of the vaccinations and vaccine stock balance over the initial period of implementation while the two schedules (full dose and fractional dose) overlapped for a period of 2 months, until all those receiving the fractional dose at 2 months had reached the age of 4 months. Further, the authorities identified the challenge of stock management at divisional level, which is the lowest level of vaccine storage and is expected to store only 1 month of buffer stock in addition to stock for the current month. This challenge has been addressed through arrangements to re-collect additional vaccine stocks resulting from the change from 5-dose vials to 25-dose vials. Relevant changes in the dose schedule for IPV were incorporated into the web-based immunization information system, and related training of health-care professionals was successfully carried out to implement the flow of information to the central level.

The country has shown that the additional funding required for training and implementation was not a constraint on implementation of the emergency decision taken by the national immunization programme, since the government considered it a priority and health-care staff and existing integrated maternal and child health-care services committed to the programme without expecting any additional expenses.

The national immunization programme is currently conducting a post-introduction evaluation of the fIPV programme, to identify any implementation challenges. In addition, the country plans to assess the population-level immunity for poliovirus type 2, comparing children who have received full-dose IPV with those receiving fIPV, to ensure adequate development of immunity from the fractional dose. during the decision-making procedure. The authors also wish to acknowledge all members of the National Advisory Committee on Communicable Diseases.

**Source of support:** None.

**Conflict of interest:** None declared.

**Authorship:** DG was responsible for conception, design and drafting of the manuscript; SG and PP reviewed and approved the final manuscript.

**How to cite this paper:** Gamage D, Ginige S, Palihawadana P. National introduction of fractional-dose inactivated poliovirus vaccine in Sri Lanka following the global “switch”. WHO South-East Asia J Public Health. 2018;7(2):79–83. doi:10.4103/2224-3151.239418.

**References**


13. Resik S, Tejeda A, Lago PM, Diaz M, Carmenate A, Sarmiento L et al. Randomized controlled clinical trial of fractional doses of


Improving access to assistive technologies: challenges and solutions in low- and middle-income countries

Viroj Tangcharoensathien, Woranan Witthayapipopsakul, Shaheda Viriyathorn, Walaiporn Patcharanarumol
International Health Policy Program, Ministry of Public Health, Nonthaburi, Thailand
Correspondence to: Dr Viroj Tangcharoensathien (viroj@ihpp.thaigov.net)

Abstract
Assistive technologies can benefit a wide range of people, including those with disabilities; those with age-related frailties; those affected by noncommunicable diseases; and those requiring rehabilitation. Access to these technologies is limited in low- and middle-income countries but the already-high need will inevitably rise further because of demographic and epidemiological transitions. Four key gaps contribute to limited access. First, although need is high, demand is low, not least because of widespread lack of awareness among potential beneficiaries, their caregivers, and their health-care providers. Second, product designs are insufficiently informed by users’ and caregivers’ preferences and environments, and transfer of technologies to low-resource settings is limited. Third, barriers to supply include low production quality, financial constraints and a scarcity of trained personnel. Fourth, there is a dearth of high-quality evidence on the effectiveness of different types of technology. Adoption of the World Health Assembly Resolution WHA71.8 in 2018 marked convergence of, commitment to and strengthening of efforts to close these gaps and improve access to assistive devices. The Global Cooperation on Assistive Technology workplan identifies four overarching, interlinked solutions for countries to improve access. First, a national policy framework for assistive technology is needed. Second, product development should be encouraged through incentive schemes that support and promote affordable assistive products. Third, capacity-building of personnel is needed, through undergraduate and in-service training. Fourth, provision needs to be enhanced, especially through integration of services with the health system. These actions need to be underpinned by government leadership, a multisectoral approach and adequate funding.

Keywords: assistive devices, frail older adults, health services for people with disabilities, health services needs and demand, people with disabilities

Background: the global context
Assistive technologies include any item, piece of equipment or product used to increase, maintain or improve the functional capabilities of people with disabilities. Assistive technologies include low-vision devices, hearing aids, augmentative and alternative communication systems, walking frames, wheelchairs and prostheses such as artificial legs.

In addition to low-cost, simple products, more advanced solutions exist, such as screen-reading software, customized telephones and computer-assisted devices. Assistive technologies can benefit a wide range of people, including those with disabilities; those with age-related frailties; those affected by noncommunicable diseases, such as stroke and diabetes; and those requiring rehabilitation. These technologies therefore have the potential to play a significant role in enabling large sectors of society to function and live independently or, at least, less dependently. These technologies also have socioeconomic benefits, by reducing direct health and welfare costs, enabling a more productive labour force, and stimulating economic growth. They can enable older people to continue to live at home and can delay or prevent the need for long-term care; they also enable people with difficulties in functioning to live independent, productive, healthy, dignified lives, and to participate in education, the labour market and social life.

The World report on disability estimated that, based on population data from 2010, more than one billion adults and children worldwide – 15% of the global population – were living with some form of disability – a substantial increase from the previous estimate of about 10% in the 1970s. Of those aged 15 years and older living with a disability, an estimated 2.2–3.8% had significant difficulties in functioning.

In the same report, analysis of the Global Burden of Disease (GBD) data from 2004 allowed estimates of the prevalence of disability by World Health Organization (WHO) region. Although
there is substantial uncertainty about the GBD estimates for regions and conditions where the data are scarce or of poor quality, the WHO South-East Asia Region was reported to have the second highest prevalence of moderate disability (16%) and the third highest prevalence of severe disability (2.9%). Since potential beneficiaries of assistive technologies include not only people with disabilities but also the increasing numbers of those living longer, those with noncommunicable diseases and those requiring rehabilitation, it is clear that they comprise a significant proportion of the world’s population.

International frameworks and instruments have reiterated the commitments of governments and other stakeholders to support implementation and monitor progress that is relevant to assistive technologies. Chief among these is the United Nations Convention on the Rights of Persons with Disabilities (CRPD), which was adopted in 2006 and, at the time of writing in 2018, has been ratified by 177 States Parties. Although the CRPD mandates access to good quality and affordable assistive technologies for people with disabilities, progress in implementation in low- and middle-income countries has been slow, not least because of a lack of funding support. 

With respect to the Sustainable Development Goals (SDGs), disability is referenced specifically in the goals related to poverty (SDG 1); education (SDG 4); growth and employment (SDG 8); inequality (SDG 10); accessibility of human settlements (SDG 11); and peace and inclusivity (SDG 16); disability is also directly referenced in 12 SDG indicators. However, assistive technologies are relevant to the SDGs even where disability is not specifically mentioned, and analysis indicates that achievement of all 17 SDGs can be achieved only by improved access to these products.

The need to improve the accessibility of assistive devices has been underscored by WHO in recent years. The WHO global disability action plan 2014–2021 supports the implementation of measures designed to meet the rights of people with disabilities as enshrined in the CRPD. There are three objectives: (i) to remove barriers and improve access to health services and programmes; (ii) to strengthen and extend rehabilitation, habilitation, assistive technology, assistance and support services, and community-based rehabilitation; and (iii) to strengthen collection of relevant and internationally comparable data on disability, and support research on disability and related services. Among the indicators of success of the second objective is the proportion of people with disabilities that receive the assistive technologies that they need.

In 2014, WHO established the Global Cooperation on Assistive Technology (GATE), an initiative in partnership with international organizations, donor agencies, professional organizations, academia, and user groups, to improve access to high-quality affordable assistive products worldwide. In 2016, GATE launched the Priority assistive products list. The priority products are defined as “Those products that are highly needed, an absolute necessity to maintain or improve an individual’s functioning and which need to be available at a price the community/state can afford.” Three additional tools are under development to assist countries to develop national assistive technology policies and programmes, as an integral component of universal health coverage. These are a policy framework, a training package and a products service-delivery model.

The WHO Global strategy and action plan on ageing and health in 2016 noted that harnessing innovations such as assistive technologies may also help low- and middle-income countries to develop service models that “leapfrog” models delivered in other settings. One of the 10 mid-term progress indicators of the 2016–2020 action plan is the number of countries with legislation or regulations that support older adults to obtain access to assistive devices on the WHO Priority assistive products list.

In May this year, the World Health Assembly adopted Resolution WHA71.8, which drew together the aims of the CRPD and SDGs, urging Member States to develop, implement and strengthen policies and programmes to improve access to assistive technologies within universal health and/or social services coverage. As a consequence, WHO will, by 2021, report on effective access to assistive technology based on the best available scientific evidence and international experience, and will subsequently report back to the World Health Assembly every 4 years until the end of the SDGs in 2030. This reporting requirement holds all actors accountable for improving access to assistive technologies.

This perspective paper reviews the needs and demands for assistive technologies, identifies various gaps and suggests potential solutions to improve access, in particular in low- and middle-income countries.

Challenges in accessing assistive technologies in low- and middle-income countries

Gaps in the need and demand for assistive technologies

It is well recognized that the need for assistive technologies is high but demand is low, and supply is even lower, especially in low- and middle-income countries. This mismatch between need and demand itself presents a challenge to improving access, and is the result of many factors, not least a widespread lack of awareness among potential beneficiaries, their caregivers, and their health-care providers. Only 10% of potential beneficiaries have access to assistive products, owing to factors such as high costs and lack of financing, availability, awareness and trained personnel. For example, 70 million people need a wheelchair but only 5–15% have access to one, and production of hearing aids meets only 10% of global need and 3% of the need in low- and middle-income countries. Moreover, 200 million people with low vision do not have access to spectacles or other low-vision devices.

A survey of the needs of older people living with disabilities in six countries in the WHO Western Pacific Region found they gave higher priority to functional daily living than to social activities. The top four functional activities that could be facilitated by assistive technologies were: eating and drinking as independently as possible; transferring to or from a bed or a chair; being able to be clean and hygienic; and being able to hear and communicate with others.

There is also a significant unmet need for assistive technologies in the prevention and management of ill health and injury – again, this high level of need does not translate into a high demand. For example, falls are an important external cause of unintentional injury and disability that increase in frequency with age and frailty, yet they remain a neglected public health problem in low- and middle-income countries. In a Canadian study, approximately 30% of people older than 65 years and...
50% of people older than 85 years living in the community had experienced a fall at least once a year. In the United States of America (USA), an estimated 40% of those aged 65 years or older living at home will fall at least once each year, and about one in 40 of them will be hospitalized. Of those admitted to hospital after a fall, only about half will be alive a year later. Most falls are associated with identifiable risk factors, such as weakness, unsteady gait, confusion and use of psychoactive medications, and research indicates that prevention of these risk factors through the application of assistive technology can significantly reduce rates of falling. Where the predominant risk factors are gait and balance disturbances, use of assistive technologies such as walkers, canes and modified shoes should be an integral part of prevention, together with gait training and appropriate management of other underlying causes.

Smartphone applications that facilitate the detection and prevention of falls also have a major role to play, and significant progress has been made in development. Fall-detection systems trigger notification alarms, send messages and call for help as soon as a fall occurs. Fall-prevention applications usually use data on the medical and behavioural histories of users, in order to predict the possible risk of falls.

There are other examples of the role of assistive technologies in prevention. For instance, housing modifications and provision of appropriate assistive technologies can reduce the need for long-term care for people with physical disabilities. Access to appropriate and affordable assistive devices can enhance the autonomy of people with disabilities. Self-care technologies contribute to a reduction in care hours and enhanced autonomy.

Despite these benefits, the use of assistive technologies for prevention is low. For example, in six low- and middle-income countries where the most rapid growth in the population aged 65 years and older is expected – Brazil, Cambodia, Egypt, India, Turkey and Zimbabwe – all had some assistive technologies designed for older adults with existing disabilities, but had limited technologies designed to prevent impairment and disability among older adults.

Gaps in research, product design and technology transfer

As noted earlier, despite high levels of need in low- and middle-income countries, lack of awareness of assistive technologies results in a lack of demand, which in turn impedes their development and adoption. For those who are aware of these technologies, as is more common in high-income settings, use is further hindered by concerns about their effectiveness and suitability; social stigma and privacy; usability and computer literacy; and affordability. Research, development and design processes have yet to include consultations with users and caregivers to develop products to best suit their physical and social environments and preferences. Although computer and information technologies hold promise in applications to boost the functions of existing assistive technologies, product designers have yet to consult and accommodate the different preferences and needs of older people with disabilities. Challenges associated with usability often relate to screen design, input device design, complex commands and operating procedures.

With respect to low- and middle-income countries, international cooperation and global health actors championing assistive technologies have yet to lead to increased support for technology innovation or transfer of technologies and expertise. Thus, in these settings, where imported products are unaffordable, there may be limited capacities to produce assistive technologies locally. In addition, lack of affordability means that many of the high-technology devices created for low-resource settings are actually only affordable in more affluent emerging economies. There is also concern that these technologies are developed without taking into consideration the true environmental, social and resource factors that impede the adoption of technology in low-resource settings.

Gaps in access to assistive technologies

Challenges to improving access to assistive technologies in low- and middle-income countries stem from low production and limited quality; financial barriers; and lack of government funding, provisions and human resources. There is a scarcity of personnel trained to provide these technologies, especially at provincial and district levels. In many settings where access might be possible, the costs are prohibitive.

Even in high-income settings, such as the USA, access to these technologies and qualified providers is frequently limited and varies considerably across states and districts, as well as urban and rural areas. Factors such as culture and language, expectations, legal constraints, stereotyping, autonomy and dignity also hamper access to assistive technologies. A systematic review of barriers to adoption of assistive technologies by older people found that privacy was their top concern, followed by worries about trust, functionality and added value. Other key barriers were cost and affordability; ease of use and suitability for daily use; perception of “no need”; stigma; fear of dependence; and lack of training.

The 2011 World report on disability notes that these accessibility challenges also apply in low- and middle-income countries and are reinforced by inadequate policies and standards; negative societal attitudes towards people with disabilities; and lack of provision of medical rehabilitation, vocational training and welfare services. In nationally representative surveys of the living conditions of people with disabilities in Namibia, Malawi and Zambia, shortcomings were found in assistive device services, in addition to lack of vocational training, welfare services and counselling. The unmet need was high; only 17%, 18% and 26% of people with disabilities who were surveyed had access to assistive devices in Malawi, Namibia and Zimbabwe, respectively.

As discussed earlier, demand-side barriers contribute significantly to the gaps in access to and use of these technologies. At all levels – policy-makers, care providers and potential beneficiaries – there is a lack of understanding about the benefits of assistive technologies and a lack of information about what devices are available. It is critically important to understand and address the mismatches between high need and low demand, to devise policies to improve access to and use of assistive technologies.

Gaps in the evidence

There is a significant lack of data overall on the size of unmet need in this area. For example, accessibility in individual countries can be difficult to estimate, since the CRPD States Parties’ reports provide only the number of people with disabilities who have access to these technologies but not the total number of people with disabilities who need them,
so the proportions whose needs are being met and unmet are unknown.\textsuperscript{31}

Furthermore, although it is acknowledged that there is a large and growing need for assistive technologies within low- and middle-income countries, there is a lack of research in these settings, which hinders the development of evidence-informed policy and practice. A scoping review of research on assistive technologies from low- and middle-income countries and other research-limited settings from 2000 to 2016 aimed to characterize the evidence available.\textsuperscript{32} The review found that, of the 252 studies included, over 80% focused on types of assistive technology addressing mobility (45.2%) and vision (35.5%) needs, with spectacles and prosthetics accounting for over 50% of all publications. The review found that evidence was most lacking on assistive technologies to address hearing, communication and cognition needs.\textsuperscript{32}

Unsurprisingly, most research assessing the effectiveness of various types of assistive technologies is from high-income settings. Several reviews summarizing findings to date have highlighted the lack of high-quality, well-designed research in this area. For example, while much has been published on the potential role of electronic assistive technology for memory support to people with dementia, assessments of effectiveness have been of low quality.\textsuperscript{33} Likewise, although assistive technology is one of the most frequent interventions used by people with rheumatoid arthritis, a systematic review found only one small randomized trial of low quality assessing a device that is not commonly used.\textsuperscript{34} The absence of reliable information on effectiveness is a gap that urgently needs to be addressed. This is critical not only for informing more rational use of resources in the high-income settings where such technologies are available, but also to allow evidence-informed decisions in lower-income settings. In assessing the impact of assistive technologies, the outcome measurement should be relevant not only to the target populations, but also, importantly, to families and caregivers.\textsuperscript{35} In addition, there are limited numbers of rigorous cost analyses of assistive technologies for people with dementia and their caregivers.\textsuperscript{36}

Solutions to improving access to assistive technologies in low- and middle-income countries

Based on the GATE workplan,\textsuperscript{10,12} there are four overarching, interlinked solutions for countries to improve access to assistive technologies. First, a national policy framework for assistive technology is needed, with adequate funding support and a focal unit to promote intersectoral actions. Second, product development by research and development partners should be encouraged through incentive schemes that support and promote affordable assistive products. Third, capacity-building of personnel is needed, through undergraduate and in-service training, as well as training of formal and informal caregivers. Fourth, provision needs to be enhanced, especially through integration of services with the health system. Several key focus areas are described next.

Increasing awareness and demand
In the World Health Assembly Resolution WHA71.8, Member States are urged to develop a national list of priority assistive products that are affordable, cost effective and meet quality and safety standards, based on the Priority assistive products list.\textsuperscript{2,10} It is anticipated that national lists will trigger awareness among health-care providers, especially if governments also commit to allocating adequate funding to improve delivery systems and training of health workforces. In turn, health awareness among professionals, and improved availability of these priority assistive devices, should gradually increase public awareness and demand.

Product development and adoption
WHO initiated GATE as a platform for international collaboration across governments, United Nations agencies and civil society groups, to incentivize the development of products that are affordable for adoption in developing countries.\textsuperscript{8,9} The Priority assistive products list should stimulate interest in improved product designs that take into account user-defined needs to facilitate wider adoption and use.\textsuperscript{10} Promoting low-cost locally produced items, raising awareness and fostering targeted research will improve access. Six criteria for assessment of the merits of assistive devices are described in Box 1.

Box 1. Six domains of assessment of the merits of assistive technologies
- Availability: assistive technologies are available in sufficient quantity for those in need and are provided close to their communities
- Accessibility: those who need assistive technology services know about them and are able to get them
- Acceptability: the assistive technology and related services are appropriate, useful and helpful in the lives of those who need them
- Adaptability: assistive technologies are adaptable and sufficiently adjustable to meet each individual’s needs
- Affordability: assistive technologies are available at a cost the user and their family can afford
- Quality: assistive technology and services are of sufficient quality for their intended purposes

Source: modified from the 2014 WHO survey questionnaire.\textsuperscript{13}

Financing and delivery
In the context of the SDGs and universal health coverage and the adoption of World Health Assembly Resolution WHA71.8,\textsuperscript{2} governments need to embed assistive technologies and associated services in health and community services, and subsidize the provision of assistive devices and services such that they are free of charge. Government subsidies for assistive technologies are required, as household out-of-pocket payment for these services can be a major barrier to access. In-service training of existing cadres of health personnel can be rapidly scaled up to support the initiation or strengthening of service provision. This should run in parallel with a long-term plan for undergraduate curriculum development and training.

Focus should be on improving the economies of scale in manufacturing and assembling products locally, and reducing or exempting import duties, especially where importing countries do not have local production capacities.\textsuperscript{3} Appropriate products should be made available and properly prescribed and fitted; users should receive proper training with appropriate
follow-up; and societal and environmental barriers should be removed.25

**Multisectoral action**

Effective multisectoral collaborations contribute to a holistic approach to fostering functional capability and autonomy among all potential beneficiaries of assistive devices. This requires a whole-of-government approach. Universal designs for assistive technologies, buildings, transport, and information and communication technologies require multisectoral actions across government and business sectors. Multisectoral involvement, especially of governments, manufacturers, users and consumers, can be embedded in the national assistive technology policy framework. For example, in a project in Thailand, architects and engineers supported design and housing modifications to enable independent living by people with disabilities, with community involvement and funding support from local government.19 Government agencies, industries and research groups demonstrated successful innovation in assistive technology through coordinated knowledge transfer, partnerships and focused funding that support training, local research and development, and manufacture of high-quality solutions, with involvement and active participation by people with disabilities.19 Effective governance of multisectoral action requires leadership capacity across sectors and levels of government and cultivation of champions in different sectors who can agree on common objectives.37

**Closing the evidence gap**

Regular surveys of needs and unmet needs for assistive technologies are critical for public monitoring of progress and holding governments accountable. This evidence should be made public and used to ensure accountability, especially regarding commitments to the CRPD and SDGs. Data on unmet needs have been collected in high-income settings38–40 and also in low- and middle-income countries, as shown by reports from Namibia,28 Malawi,29 and Zambia.30 Culturally relevant assistive technologies for specific subpopulation groups also help to minimize unmet needs.41

The World Health Assembly Resolution WHA71.8 urges WHO Member States to promote investment in research and development, innovation and product design, in order to make existing assistive products affordable and to develop a new generation of products, including high-end or advanced assistive technology.2 This can be done by taking advantage of universal design and new evidence-based technologies, in partnership with academia; civil society organizations, in particular with people with disabilities and older persons and their representative organizations; and the private sector.

**Conclusion**

The potential beneficiaries of assistive technologies include not only people with disabilities but also the increasing numbers of those living longer, those with noncommunicable diseases, and those requiring rehabilitation. Despite this large and increasing need, assistive technologies can have low rates of adoption and use, resulting from low levels of awareness and, consequently, demand. There are also gaps between product designs and user preferences and needs, including those of caregivers and health-care providers. Affordability is a major barrier in low- and middle-income countries where governments do not invest adequately in service provision and training of human resources. There is limited evidence to show that assistive technologies improve the functioning of users. This requires action by the scientific community, research and development agencies, and the manufacturing sector, to fill these gaps through consultation with potential beneficiaries and, as appropriate, their caregivers.

Various global frameworks such as the CRPD and SDGs support governments in improving access to these technologies, although progress is often impeded by a low level of country capacity, and inadequate fiscal space and financial commitment to embed assistive technologies into service provision. Global collaboration, in parallel with national- and local-level multisectoral actions, is essential to enhance access to these technologies, to mitigate the effects of impairment and empower users through greater autonomy.

**Acknowledgements:** We recognize and acknowledge the contributions of researchers and civil society organizations who consistently bring the challenges faced by people with disabilities to the policy agendas and monitor government implementation of the United Nations Convention on the Rights of Persons with Disabilities.

**Source of support:** None.

**Conflict of interest:** None declared.

**Authorship:** VT designed the work. All authors contributed equally in writing. WP commented on the first draft. VT finished and finalized the work. All authors approved the final draft.

**How to cite this paper:** Tangcharoensathien V, Witthayapipopsakul W, Shaheda Viriyathorn S, Patcharanarumol W. Improving access to assistive technologies: challenges and solutions in low- and middle-income countries. WHO South-East Asia J Public Health. 2018;7(2):84–89. doi:10.4103/2224-3151.239419.

**References**


Original research

Essential cancer medicines in the national lists of countries of the WHO South-East Asia Region: a descriptive assessment

Meenakshi V Chivukula¹, Klara Tisocki²
¹Independent consultant, New Delhi, India ²World Health Organization Regional Office for South-East Asia, New Delhi, India

Correspondence to: Dr Klara Tisocki (tisockik@who.int)

ABSTRACT

Background In 2015, the need for equitable access to cancer treatments in low- and middle income countries was underscored by the addition of 16 essential cancer medicines to the 19th World Health Organization (WHO) model list of essential medicines (WHO EML). This study assessed the degree to which this expanded WHO EML from 2015 has influenced inclusion of cancer medicines in the most recent national essential medicines lists of the countries of the WHO South-East Asia Region.

Methods The inclusion of a selected list of 38 essential cancer medicines in the 2015 WHO EML was assessed in the most recent national lists of essential medicines from the 11 countries of the WHO South-East Asia Region. Additionally, the availability of six essential cancer medicines common to the national lists of essential medicines from six countries of the WHO South-East Asia Region was explored.

Results Of the 38 selected essential cancer medicines included in the 19th WHO EML, a mean of 18.0 (range 2–33) were included in the national lists of countries of the WHO South-East Asia Region. Of the 25 essential cancer medicines included in the WHO EML prior to the 19th revision, a mean of 14.6 (range 2–21) were included in national lists; notably fewer of the 13 cancer medicines added in the 2015 revision were included: mean 3.4 (range 0–12).

Conclusion Compared with the WHO EML, there is a lag in the inclusion of essential cancer medicines in national lists of essential medicines in the WHO South-East Asia Region. Alignment of essential cancer medicines in national lists of essential medicines among the 11 countries in the region varies significantly. These differences may hinder regional strategies to improve access to essential cancer medicines, such as pooled procurement of selected high-cost medicines. The link between the availability and affordability of essential cancer medicines warrants further investigation, in the context of access to medicines for universal health coverage.

Keywords: access to health care, antineoplastic drugs, national health policy, South-East Asia, World Health Organization

Background

The burden of cancer in the WHO South-East Asia Region

The four major noncommunicable diseases – cardiovascular diseases, cancers, chronic respiratory diseases and diabetes – are the leading causes of death both globally and in the World Health Organization (WHO) South-East Asia Region.¹ The burden of noncommunicable diseases among individuals in the most economically productive age span is rapidly increasing because of population ageing and epidemiological transition. Compared with the global average and other WHO regions, the impact on the WHO South-East Asia Region is especially concerning, with the highest proportion of 30 year olds in 2015 projected to die before their 70th birthday from cardiovascular disease, cancer, chronic respiratory disease or diabetes (23.2%, global proportion = 18.8%).² Moreover, loss of productive life-years more profoundly and disproportionately affects the poor, who lack access to affordable medicines and health care.

The cancer burden in the WHO South-East Asia Region is high, with 1.1 million cancer-related deaths and 1.7 million new cancer cases in 2012.³ The annual number of new cancer cases globally is projected to increase from 14.1 million in 2012 to 21.6 million by 2030, yet barriers in access to safe, quality, effective and affordable options for prevention, detection and treatment continue, especially in low- and middle-income
countries, where patients often present with advanced disease, further limiting treatment options and benefits. After a long absence from the global health agenda, the substantial and increasing burden of noncommunicable diseases was recognized by the United Nations in 2011, at the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. The political declaration of the meeting acknowledged that “the global burden and threat of non-communicable diseases constitutes one of the major challenges for development in the twenty-first century, which undermines social and economic development throughout the world and threatens the achievement of internationally agreed development goals.” The resulting commitment by countries, including the Member States of the WHO South-East Asia Region, to raise awareness of and combat noncommunicable diseases, included promoting access to comprehensive and cost-effective prevention, treatment and care for the integrated management of noncommunicable diseases, with increased access to affordable, safe, effective and quality medicines. Following the political declaration, WHO Member States agreed the voluntary global targets of the Global action plan for the prevention and control of noncommunicable diseases 2013–2020, including a 25% relative reduction in the overall mortality from cardiovascular diseases, cancers, chronic respiratory diseases and diabetes.

**Availability and affordability of essential medicines for noncommunicable diseases in low- and middle-income countries**

The availability of essential medicines for noncommunicable diseases in low- and middle-income countries is lower than that for communicable diseases. Furthermore, these medicines are less available in public facilities than in private facilities. Unaffordable medicines disproportionately impact poor and disadvantaged populations and impede a country’s social and economic development. In India alone, as many as 63 million people are forced into poverty every year, owing to catastrophic health expenses, the majority of which are out-of-pocket payments for medicines. The impoverishing impact of unaffordable out-of-pocket costs is a major barrier to the availability of essential medicines for noncommunicable diseases in low- and middle-income countries.

**Challenges to accessing comprehensive cancer care**

Access to medicines is just one component of equitable access to comprehensive cancer care, especially in low- and middle-income countries. Detection and treatment programmes require coordination of multiple disciplines, from pathology to radiation and surgery, at various levels of care. Molecular confirmation through immunohistochemistry may be required to select the appropriate, targeted treatment. Access to cancer care must therefore be strengthened across the care continuum. In addition, policies are needed to promote prevention through expanded vaccination coverage (i.e. human papillomavirus [HPV] vaccine to prevent cervical cancer and head and neck cancer); increase early detection through screening at primary care; and improve access to palliative care to ease suffering and pain.

**Universal health coverage and the Sustainable Development Goal for health** can only be achieved in the WHO South-East Asia Region by 2030 if there is significant improvement in access to medicines and health care. The challenges to access are amplified in cancer care, spanning intensive engagement with prevention and detection at the primary care level, to specialized treatment, all of which require investment in health infrastructure and a qualified workforce. Improving access to cancer care must also link affordability and accessibility, by improvements such as strengthening public procurement and supply systems for essential cancer medicines.

**Inclusion of cancer medicines in national lists of essential medicines**

Essential medicines are intended to be available within the context of functioning health systems, at all times in adequate amounts, in the appropriate dosage forms, with assured quality and at a price the individual and the community can afford. Essential medicines satisfy the priority health-care needs of the population and are selected with due regard to cost effectiveness, although cost alone does not preclude selection.

A list of essential medicines serves as a cost-effective planning tool for health systems, by including a limited set of products that best serve the population’s health needs and provide safe and effective treatments for the majority of communicable and noncommunicable diseases. The WHO model list of essential medicines (WHO EML) is not prescriptive. It is designed to guide governments in developing national lists of essential medicines. In practice, countries use the WHO EML as a starting point to evaluate the relevance of a medicine to their unique epidemiological situation (i.e. disease prevalence) and health system costs. Periodic review is required to add or remove items and ensure relevance according to the best available evidence for therapeutic options. The WHO model list of essential medicines is revised every 2 years, following the review of an expert committee, and, likewise, countries are recommended to regularly update their national list of essential medicines.

In practice, a country’s national list of essential medicines may guide the procurement and supply of medicines in the public sector; medicine reimbursement schemes (such as health insurance); medicine donations; and local medicine production. Indeed, identification of a medicine as essential, by WHO and individual countries, has stimulated the entry of new manufacturers where there were shortages, underscored a medicine’s importance, and rallied stakeholder support to improve affordability and access, as was seen with antiretroviral medicines for HIV/AIDS.

**Cancer medicines and the 2015 revision of the WHO model list of essential medicines**

In 2014, at the invitation of WHO, the Union for International Cancer Control (UICC) convened experts to review Section 8.2 of the WHO EML, which recommends chemotherapeutic and hormonal agents for cancer treatment. This was the first full review of Section 8.2 in 15 years. The original WHO EML in 1977 included six cancer medicines, and new medicines...
were added after reviews in 1984, 1995 and 1999. Rather than augmenting the most recent list of 30 cytotoxic and adjuvant medicines for cancer already listed in the WHO EML, the experts convened by UICC developed a new approach, beginning with identification of cancer types that would most benefit from systemic treatment and/or cause the largest burden on the population. Thus, diseases were chosen that (i) are highly responsive to treatment but rare (chronic myeloid leukaemia); (ii) are highly responsive to treatment and common (breast cancer); and (iii) have a lower response to treatment but are highly burdensome (non-small-cell lung cancer).21

The 19th revision of the WHO EML in 201522 was therefore highly significant because it added 16 essential cancer drugs, including three high-cost medicines, imatinib, rituximab and trastuzumab, and therefore underscored the importance of improving equitable access to innovative treatments for cancer that are widely unavailable in low-resource settings.23 The long-term aspiration, likened to the 20-year progression of access to HIV/AIDS treatment, is to shape market forces and reduce the prices of essential cancer medicines so they are affordable and accessible, thereby expanding coverage. While there are obvious differences between the disease dynamics and options for prevention and treatment of cancer and HIV/AIDS, the point here is to focus on unifying shared strategies,24 like national lists of essential medicines, to improve equitable access to medicines.

Access to cancer medicines in the WHO South-East Asia Region
A recent analysis by Cuomo and Mackey found that the degree of concordance between national formularies of low- and middle-income countries and the 19th WHO EML regarding cancer medicines was less than 50%.25 In 2014, a study by Bazargani et al. included 8 of the 11 countries of the WHO South-East Asia Region and found a median of 23.5 (interquartile range [IQR] 26) essential oncology medicines included in the national lists of essential medicines at that time.26 In 2016, for counties of the WHO South-East Asia Region, Robertson et al. reported a median of 21 (range 2–24) of 25 cancer medicines from the 2013 WHO list and 1 (range 0–13) of 16 cancer medicines added in the 2015 WHO list revision.27 All countries in the region have revised their national formularies since these previous studies. Therefore, the present study aimed to report current country-level alignment of essential cancer medicines in the WHO South-East Asia Region with the 19th WHO EML. Of note, there is no standard methodology to compare alignment between national lists of essential medicines and WHO model lists. The level of alignment, in terms of cancer medicines, has rarely been studied, and the few prior studies focus on global comparisons, with subgroup analysis of WHO regions. To the authors’ knowledge, this is the first study to survey the selection of essential medicines for cancer in a group of countries within a WHO region.

The composition of the WHO South-East Asia Region, with small and large pharmaceutical markets with a range of manufacturing capacities and supply-chain issues, offers a unique frame of comparison and consideration for access issues. The aim of presenting this country-level comparison of the WHO South-East Asia Region is to stimulate discussion on improving access to cancer medicines at country and subregional levels. As expressed by key coordinators of the 2015 WHO EML, “the challenge is to provide access to effective medicines without creating ad hoc vertical programmes and, at the same time, to avoid diverting funds from other important health-care services”.20 As such, as a first objective, this paper presents the inclusion of cancer medicines in national lists of essential medicines from the WHO South-East Asia Region. The second objective was to further explore the availability and affordability of selected cancer medicines in countries in the region, based on a recent survey by the European Society for Medical Oncology (ESMO) of the availability, out-of-pocket costs and accessibility of antineoplastic medicines outside of Europe.26 In an accompanying paper in this issue of the WHO South-East Asia Journal of Public Health, these findings are linked to a discussion on how to improve access, including – but not limited to – managing costs through regional cooperation; coordinated procurement mechanisms; price controls; differential pricing; and licensing agreements.29

Methods

Data collection

Comparing national lists of essential medicines to the 2015 WHO list
All national lists had been updated in the past 5 years, the majority following publication of the 19th WHO EML in 2015; therefore, the 2015 WHO EML was selected as a single reference of comparison across the 11 countries. In the 2015 WHO EML, Section 8 lists essential “Antineoplastics and immunosupressives”, and is divided into three sections: 8.1 Immunosuppressive medicines; 8.2 Cytotoxic and adjuvant medicines; and 8.3 Hormones and antihormones. Because the definition of medicines used in cancer treatment can vary, and this study aimed to restrict analysis to a manageable set of essential cancer medicines that could be easily identified by a non-expert reviewing the WHO EML, it was decided, for this analysis, to operationally define “essential cancer medicines” as only those included in subsection 8.2. As a result, all essential cytotoxic and adjuvant cancer medicines from subsection 8.2 of the 19th WHO EML were selected – a total of 38 medicines. Of these, 13 of the 16 cancer medicines added in the 2015 revision were included; anastrazol, bicalutamid and leuprolrelin were listed in Section 8.3, and thus excluded. Additionally, other examples of medicines in Section 8.3 included prior to 2015, such as tamoxifen for early-stage and metastatic breast cancer, and bicalutamide for metastatic prostate cancer, were excluded.

Exploring the availability and affordability of selected cancer medicines
The ESMO survey used an online survey tool adapted from prior collaborative studies, which was completed by at least
two field reporters in each country, usually an oncologist or oncology pharmacist. Data were collected during 2015 and externally validated and corrected, as necessary, in the first half of 2016. The results on “actual availability with a valid prescription” were categorized as available “always”, “usually”, “half”, “occasionally”, or “never”, and those on “out-of-pocket cost” were categorized as “free”, “partial cost” or “full cost” (based on reimbursement for indication). Although an estimate of relative affordability was not detailed (i.e. comparison to per capita income, or number of days’ wages needed to purchase a course of treatment by the lowest-paid unskilled government worker), it may be assumed that a full-cost cancer medicine is not affordable to the majority of the population in a low- or middle-income country.

The ESMO study included data from six countries from the WHO South-East Asia Region: Bangladesh, India, Indonesia, Myanmar, Nepal and Thailand. Of the cancer medicines surveyed by ESMO from national reimbursement lists, the six cancer medicines that were common to all six countries’ national lists of essential medicines were selected, to compare their availability and affordability. These were bleomycin, cyclophosphamide, doxorubicin, vinblastine and vincristine, which had been included in the WHO EML before 19th revision in 2015, and cisplatin. Cisplatin is an illustrative example of the dynamic nature of selected medicines based on available evidence, as it was first added to the WHO EML in 2000, removed and replaced by carboplatin in 2009, and then reintroduced in the 19th WHO EML in 2015, after both agents were recognized as required.

Results

Alignment of essential cancer medicines in national lists of essential medicines in the WHO South-East Asia Region

Of the 38 selected essential cancer medicines included in the 19th WHO EML, a mean of 18.0 (range 2–33) were included in the national lists of countries in the WHO South-East Asia Region. Thus, the mean percentage alignment of national lists of essential medicines for the region to the 19th WHO EML was 47% (range 5–87%) (see Fig. 1). Overall, most countries of the region included more than half of the selected essential cancer medicines. However, the alignment of the national lists of essential medicines in four countries was lower than half, with Bangladesh closer to one third, and the smallest countries by population, Bhutan, Maldives and Timor-Leste, even lower (see Fig. 1).

Fig. 1 illustrates the inclusion of essential cancer medicines, by separating those included before 2015 from those added in the 2015 revision. However, countries may have already included specific medicines from those added in the 2015 revision in national lists of essential medicines revised prior to 2015.
Of the 38 selected essential cancer medicines from the WHO EML, 13 were added in the 19th revision in 2015. National lists of essential medicines of countries of the WHO South-East Asia Region included a mean of 3.4 of these medicines (range 0–12) (dark shaded area in Fig. 1). Of note, no medicines from this newer group were included in the three countries with the lowest alignment: Bhutan, Maldives and Timor-Leste. The four countries with the highest number of newer medicines were Myanmar, India, Thailand and Sri Lanka.

Twenty-five of the 38 essential cancer medicines listed in the 2015 WHO EML were included prior to the 2015 revision (light shaded area in Fig. 1). National lists of essential medicines of countries of the WHO South-East Asia Region included a mean of 14.6 of these medicines (range 2–21). The mean alignment for this group included prior to 2015 across the region was 59% (range 8–84%), markedly greater than the mean for the group of newer medicines added in the 2015 revision, of 26% (range 0–92%). No country had 100% alignment with this subgroup of 25 medicines.

Table 1 summarizes the 38 cancer medicines in ascending order, based on the number of countries of the WHO South-East Asia Region including the medicine in their most recent national lists of essential medicines. This table details the uptake of newer agents and high-cost medicines, including imatinib for chronic myeloid leukaemia in India, Myanmar and Thailand and trastuzumab for early-stage and metastatic breast cancer in India, Sri Lanka and Thailand. Overall, the newer agents cluster towards lower inclusion.

Enablers and barriers to access
The six selected cancer medicines – bleomycin, cyclophosphamide, doxorubicin, vinblastine and vincristine, plus cisplatin – were among those most often occurring in the national lists of the region’s countries; all were included in at least 8 of the 11 national lists of essential medicines.

In the six countries assessed in the ESMO survey, overall, the six essential cancer medicines surveyed were always or usually accessible with a valid prescription (see Table 2). By contrast, the out-of-pocket costs ranged from free to full cost, suggesting unaffordability and financial risk for many patients.

Of the six countries surveyed, Thailand and Indonesia enable access to affordable essential medicines through social health insurance programmes promoting universal health coverage. Not surprisingly, the pattern of always available and free (versus full cost), both enablers of access, was found in countries with social health insurance. Bangladesh, India, Myanmar and Nepal do not yet provide universal medicines coverage as a national policy. The study results suggest that in these countries the cancer drugs surveyed are only available at full cost. While there are limited free drug programmes (the scope of which was beyond this study), cancer medicines may not be included in these countries. There were no examples of limited availability (half, occasionally or never). However, in reality, shortages of free or price-controlled medicines is a known issue, especially in public sector pharmacies. Dominant barriers to access were also included in the ESMO survey and revealed the issues of no supplier or unreliable supply as those most frequently identified.26

Discussion

Inclusion of essential cancer medicines in national lists of essential medicines
In this study, a mean of 18 of 38 (range 2–33) of the selected essential cancer medicines from the 19th WHO EML were included across the most recent national lists of essential medicines from the 11 countries of the WHO South-East Asia Region. Of the 25 medicines listed in the WHO EML prior to 2015, a mean of 14.6 (range 2–21) were included in national lists; and notably fewer of the 13 medicines were added in the 2015 revision (mean 3.4; range 0–12). Similar to Robertson et al.,27 the results of the present study suggest a gap in alignment for cancer medicines added in 2015 to the 19th WHO EML.

Further exploration is needed to understand why many of these cancer medicines included in older WHO model lists, prior to 2015, are still not included in many of the updated national lists of essential medicines in the region. Investigation into in-country challenges to accessing these cancer medicines from older WHO model lists should also be considered.

Given the wide range of alignment across countries, comparisons should be interpreted with caution. The purpose of this study is to provide a crude regional overview of the inclusion of essential cancer medicines for the 11 countries of the WHO South-East Asia Region. The reasons for the relatively lower uptake of the newer essential cancer medicines warrant further exploration.

The countries in the lowest quintile of alignment – Bhutan (13%), Maldives (5%) and Timor-Leste (5%) – are small countries with challenging geographies that lack the capacity for local pharmaceutical production. They may also use alternative strategies, such as sending patients with cancer for treatment abroad.

Overall, the results of this study show a similar pattern to the limited previous research suggesting no significant shift in recent years in increasing the inclusion of essential cancer medicines for both older and newer targeted therapies in national lists of essential medicines. This is despite some national lists in this study being dated post 2015.

In this descriptive analysis, comparing the alignment of cancer medicines included in the national lists of essential medicines to the 19th WHO EML rests on certain assumptions. First, it is assumed that the selection of essential cancer medicines in national lists of essential medicines is indicative of the respective governments’ commitment to ensuring equitable access to treatment and reducing the burden of disease. However, it is possible that some prioritized cancer medicines are available, despite not being included in national lists, because they are provided in other ways, such as through donations; specialized hospital lists; or other reimbursement models.

Second, it is assumed that the 19th WHO EML is a meaningful standard of comparison, based on the noteworthy addition of cancer medicines. The year of revision should therefore be noted when interpreting the relative alignment of individual country lists. Clearly, not all countries from the WHO South-East Asia Region, have, to date, revised their national lists of essential medicine since April 2015, when the 19th WHO EML was published. Notably, the lists for Nepal and Sri Lanka are from 2014. Also, for the lists revised in 2015 from
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bendamustineb</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Fludarabineb</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Irinotecanc</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Vinorelbineb</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Rituximabb</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Tioguanine</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>ATRAb</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Allopurinol</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Capecitabineb</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Filgrastimb</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Imatinibb</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Procarbazine</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Trastuzumabb</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Carboplatin</td>
<td></td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Gemcitabineb</td>
<td></td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Oxaliplatinb</td>
<td></td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Docetaxel</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Hydroxycarbamide</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Mesnae</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Cytarabine</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Caclitaxel</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Calcium folinate</td>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Dacarbazine</td>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Etoposide</td>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Ifosfamidec</td>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Asparaginase</td>
<td></td>
<td></td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Bleomycinf</td>
<td></td>
<td></td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Cisplatinf</td>
<td></td>
<td></td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td></td>
<td></td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Vinblastinef</td>
<td></td>
<td></td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Doxorubicinf</td>
<td></td>
<td></td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Methotrexate</td>
<td></td>
<td></td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Vincristinef</td>
<td></td>
<td></td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Cyclophosphamidef</td>
<td></td>
<td></td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10</td>
</tr>
</tbody>
</table>

* Essential cancer medicine included in national essential medicine list; not included.

* Democratic People’s Republic of Korea.

** All-trans retinoic acid. Introduced in the 2015 revision of the WHO model list.22

† Fixed-dose combination of ifosfamide + mesna (Nepal, Sri Lanka).

‡ Additional information on availability and affordability is provided in Table 2.

* Reintroduced in the 2015 revision of the WHO model list after 2009 removal; first added in 2000.
the Democratic People's Republic of Korea, India and Timor-Leste, it is difficult to know whether there was enough time for national committees to incorporate the 19th WHO EML revisions of April 2015. We assume countries need time to assemble experts and evaluate the magnitude of clinical benefit and the risk–benefit profile of medicines – the main criteria for inclusion of cancer medicines, especially considering the financial implications to health systems of including these high-cost medicines.

Interestingly, Sri Lanka’s national list of essential medicines was revised for 2013–2014, showing that the five newer medicines were included prior to the 19th WHO EML in 2015. In a review in 2013 of national lists of selected low- and middle-income countries, inclusion of new-generation cancer medicines not yet included in the WHO EML was also observed for India and Indonesia. This lag may reflect in part that the WHO model list had not been updated to keep up with changes in treatment protocols over time.

Previous studies have focused on global comparisons between regions, whereas this analysis focuses on comparing selected essential cancer medicines within a WHO region. In order to ease the comparison of selected medicines across the 11 countries of the WHO South-East Asia Region, the 2015 WHO EML was used as a single reference of comparison, and the analysis was restricted to the 38 essential medicines from Section 8.2 Cytotoxic and adjuvant medicines. As a result, comparisons for certain widely used essential cancer medicines, such as tamoxifen for breast cancer, are not presented here.

### Strengthening the link between availability and affordability to improve access

Strategies and policies to promote universal health coverage are central to improving the affordability of essential cancer medicines. From the ESMO survey study by Cherny et al. 2017, it is observed that cancer medicines may be available in the countries of the WHO South-East Asia Region, but not affordable. Full out-of-pocket costs appear to be borne by patients in Bangladesh, India and Nepal, putting these patients and their families at risk of catastrophic expenses that push households into poverty. In Indonesia and Thailand, countries with policies for universal health coverage, the studied medicines are available free of cost, offering financial protection to cancer patients in these countries. Myanmar offers an intermediate example of where some cancer medicines are free, while others are available at full cost.

### Table 2. Availability and out-of-pocket costs of selected essential cancer medicines in Bangladesh, India, Indonesia, Myanmar, Nepal and Thailand

<table>
<thead>
<tr>
<th>Policy implementation and medicine availability* and affordabilityb</th>
<th>Upper-middle income</th>
<th>Lower-middle income</th>
<th>Low income</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>Bangladesh</td>
<td>India</td>
<td>Indonesia</td>
</tr>
<tr>
<td>UHC policy implemented</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Bleomycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Availability</td>
<td>Always</td>
<td>Always</td>
<td>Usually</td>
</tr>
<tr>
<td>Affordability</td>
<td>Free</td>
<td>Full cost</td>
<td>Free</td>
</tr>
<tr>
<td>Cisplatin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Availability</td>
<td>Always</td>
<td>Always</td>
<td>Always</td>
</tr>
<tr>
<td>Affordability</td>
<td>Free</td>
<td>Full cost</td>
<td>Full cost</td>
</tr>
<tr>
<td>Cyclophosphamidec</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Availability</td>
<td>Always</td>
<td>Always</td>
<td>Always</td>
</tr>
<tr>
<td>Affordability</td>
<td>Free</td>
<td>Full cost</td>
<td>Full cost</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Availability</td>
<td>Always</td>
<td>Always</td>
<td>Always</td>
</tr>
<tr>
<td>Affordability</td>
<td>Free</td>
<td>Full cost</td>
<td>Full cost</td>
</tr>
<tr>
<td>Vinblastine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Availability</td>
<td>Always</td>
<td>Always</td>
<td>Usually</td>
</tr>
<tr>
<td>Affordability</td>
<td>Free</td>
<td>Full cost</td>
<td>Full cost</td>
</tr>
<tr>
<td>Vincristine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Availability</td>
<td>Always</td>
<td>Always</td>
<td>Always</td>
</tr>
<tr>
<td>Affordability</td>
<td>Free</td>
<td>Full cost</td>
<td>Full cost</td>
</tr>
</tbody>
</table>

IV: intravenous; UHC: universal health coverage.

* Evaluated as available with a valid prescription (always, usually, half, occasionally, never).

b Evaluated as out-of-pocket cost (free, partial cost, full cost).

c Cyclophosphamide intravenous injection and tablet dosage forms surveyed; response applies to both forms, unless specified.

Conclusion
The 2015 revision of the 19th WHO EML to include essential hepatitis C, drug-resistant tuberculosis and cancer medicines was announced as an important, and perhaps overdue, recognition of the need “to improve access to innovative medicines that show clear clinical benefits and could have enormous public health impact globally.”44 However, there is an apparent lag between the 2015 revision of the WHO EML and the inclusion of essential cancer medicines in national lists of essential medicines in the WHO South-East Asia Region. Also, there is variance in the overall alignment of essential cancer medicines in national lists of essential medicines among the 11 countries in the region. These differences in alignment may hinder regional strategies to improve access to essential cancer medicines, such as pooled procurement of selected high-cost medicines. The link between availability and affordability of essential cancer medicines warrants further investigation, in the context of access to medicines for universal health coverage.

Source of support: The work contributing to this paper was supported by the World Health Organization Regional Office for South-East Asia, New Delhi, India.

Conflict of interest: None declared.

Authorship: MVC completed the data analysis and developed the manuscript. KT designed the study and reviewed the manuscript.


References


Pricing policies for generic medicines in Australia, New Zealand, the Republic of Korea and Singapore: patent expiry and influence on atorvastatin price

Elizabeth E Roughead¹, Dong-Sook Kim², Benjamin Ong³, Anna Kemp-Casey¹

¹Sansom Institute for Health Research, University of South Australia, Adelaide, Australia, ²Pharmaceutical Policy Research Team, Research Centre, Health Insurance Review and Assessment Service, Seoul, Republic of Korea, ³Health Products Regulation Group, Health Sciences Authority, Singapore

Correspondence to: Dr Anna Kemp-Casey (anna.casey@unisa.edu.au)

Abstract

Background Little is known about how the different policies available to promote use of generic medicines affect the price per unit supplied or sold. This study compares the influence of pricing policies for generic medicines on atorvastatin prices in Australia, New Zealand, the Republic of Korea and Singapore, after market entry of generic atorvastatin.

Methods The annual price of atorvastatin per defined daily dose supplied (price/DDD) was examined for each country from 2006 to 2015 (≥2 years before and ≥4 years after generic market entry). Prices were converted to international dollars and cumulative percentage price reductions were calculated for the first 4 years following generic entry.

Results Prior to market entry of generic atorvastatin, New Zealand had the lowest price ($0.10/DDD), and the Republic of Korea the highest ($2.89/DDD). The price/DDD fell immediately after generic entry in all countries except New Zealand, which already had low prices. The largest immediate decrease was observed in Singapore (46%, year 1). By the fourth year after generic entry, the price had fallen by 46–80% in all countries; however, large price differences between countries remained.

Conclusion New Zealand’s tendering system and use of preferred medicines resulted in very low atorvastatin prices well before patent expiry. Pricing policies in the other three countries were effective in reducing atorvastatin prices, with reductions of between 46% and 80% within 4 years of generic entry. Where tendering and use of preferred medicines were the mechanisms for atorvastatin procurement (New Zealand), prices were lowest before and after generic entry. Mandatory price cuts, combined with price-disclosure policies (Australia), produced similar relative price reductions to tendering systems (New Zealand, Singapore) at 4 years. By comparison, mandatory price cuts upon generic entry as the sole measure, while initially effective, were associated with the smallest relative reduction in price after 4 years (Republic of Korea).

Keywords: Asia, international comparison, medicines, policy, procurement mechanism, regulation
differentials exist. There is widespread variation in these elements across countries. Variations in the price of generic medicines have been observed to range between 3- and 36-fold across countries, and uptake of generic medicines across European countries ranges from 5% to 80%.

Different countries have employed a range of policies to influence the price and uptake of generic medicines in their health-care systems. Mandatory or optional generic substitution, where pharmacists may substitute a generic product that is equivalent to the branded product, is one mechanism used to promote uptake. Pricing strategies may include within-country (internal) reference pricing (i.e. the price is set relative to therapeutically similar medicines); external reference pricing, by taking an average of prices for the same pharmaceutical product in other countries; price caps (i.e. a maximum price that will be subsidized or reimbursed is set); and mandatory percentage price reductions compared with the innovator brand upon introduction of the generic medicine to the market. Where discounting to wholesalers or pharmacies occurs due to competition between multiple generic products, price-disclosure policies may be used to price products. Medicines can also be purchased via competitive tendering mechanisms, before or after patent expiry and entry of generic products to the market. Some countries do not regulate the price of generic medicines, allowing their price to be set by the manufacturer, with the expectation that market competition will achieve the best price. Several studies have examined the impact of a single policy on the price of generic medicines immediately after implementation; however, little is known about how different policies affect the price per unit supplied/sold (i.e. accounting for both price and uptake), or how this changes over time following policy implementation.

This study was set among four high-income countries in the World Health Organization (WHO) Western Pacific Region, namely Australia, New Zealand, the Republic of Korea and Singapore, all of which provide universal health care to their citizens. Across these countries, there is considerable variability in the pricing mechanisms for generic medicines. New Zealand uses a competitive tender approach, often limiting the market to one government-funded brand (with alternative brands available for out-of-pocket purchase on the open market). The tender may be won by the originator or generic supplier. New Zealand also uses similar, but not generic, products to negotiate commercial agreements with lower prices that reduce prices and costs overall (see case-study). Singapore has free pricing, allowing prices to be set by the manufacturer, but does tender for the medicines supplied in its public hospitals and government clinics. Australia and the Republic of Korea have regulated pricing policies for generic medicines, with mandatory percentage discounts referenced internally to the originator product at the time of entry of generic products to the market. Subsequently, the Republic of Korea has a second mandatory price reduction in the second year after generic entry, while Australia operates a price-disclosure policy of the ex-manufacturer price to the market. Under Australia’s price-disclosure policy, sales revenue, sales volume and the value of incentives or discounts provided to the supply chain are reported for medicines subsidized under the national Pharmaceutical Benefits Scheme, and a weighted average disclosed price (WADP) is calculated, based upon this information. If the current ex-manufacturer price is more than 10% above the WADP, it is reduced to the WADP. The pricing policies for generic medicines for each of the participating countries are summarized in Table 1.

Generic atorvastatin was introduced into the markets of Australia, New Zealand, the Republic of Korea and Singapore between 2008 and 2012, providing the opportunity to examine the influence of these countries’ different pricing policies for generic medicines on the overall prices of atorvastatin. Other statins were available in the countries at this time and were used in different proportions (see Fig. 1); however, the focus of the present study was on the change in price in atorvastatin pre and post the patent expiry of atorvastatin. The aim of the study was to compare the influence of the policies for generic medicines on the total prices of atorvastatin therapy (single-ingredient products only) within Australia, New Zealand, the Republic of Korea and Singapore, after the introduction of generic atorvastatin.

### Methods

#### Study period

The study was undertaken using data covering the period 2006–2015. Generic atorvastatin products entered the national markets in the Republic of Korea in March 2008; New Zealand in September 2010; Singapore in November 2011;
and Australia in May 2012. No adjustment was made for the month of generic entry, as data by month were not available. Data for each country covered the period for at least 2 years prior to entry of the first generic product, with follow-up data on prices undertaken for 4 years post entry of the first generic product to the market.

Data extraction and sources
All participating countries have national health insurance systems in place. Data for Australia were publicly available. Data for New Zealand, the Republic of Korea and Singapore were provided by government agencies.

Data extracted for each country were annual prices for single-product atorvastatin (Anatomical Therapeutic Chemical [ATC] code C10AA05), as well as the annual volume supplied or sold, standardized to WHO defined daily doses (DDDs). The DDD of atorvastatin is 20 mg. National prices were converted into international dollars, using purchasing power parities (PPPs) from the International Monetary Fund. PPPs are more stable than exchange rates and reflect the value of a set basket of goods and services in different countries. Fixed-dose combination products containing atorvastatin were excluded from the analysis, because the majority of the combination products also included an on-patent medicine, and different pricing policies for combination products may have been in place.

Australia
Data were sourced from Australian statistics on medicines, an annual publication of data tables that includes national estimates of the total volume of medicines dispensed under Australia’s Pharmaceutical Benefits Scheme. National government expenditure is also included. Data include community use of prescription medicine for the national population of approximately 23 million.

New Zealand
Data were sourced from the database of the pharmaceutical management agency, PHARMAC. Data were supplied as average published subsidy prices (cost to the health system) per 40 mg tablet, per quarter of year. No volume data were available, but the average subsidy prices account for volume. To compare with the other countries, the price per 20 mg tablet at January each year was calculated, based on the average subsidy price for 40 mg in the same month. The actual cost was lower, owing to the presence of confidential rebates. Data represent all medicine use for the national population of approximately 4 million individuals who were eligible for this treatment. Simvastatin, a therapeutically equivalent product suitable for most patients, was available at substantially lower pricing.

The Republic of Korea
Data were sourced from the Health Insurance Review and Assessment Service database. They were supplied as the volume and subsidy price. Data included all community and hospital dispensing of subsidized medicine for the national population of approximately 50 million.

Singapore
Data were sourced from IMS Plus (2007 to 2014), which is a database of all public and private pharmaceutical sales in Singapore, including medicines for community and hospital use. Data included the retail sales price and volume. The national population was approximately 5 million.

Outcome measures and analysis
The primary outcome assessed was annual price per DDD supplied or sold in each country. Cumulative percentage price reductions over the first 4 years following entry of the first generic product to the market were calculated, using the year prior to the introduction of the generic product to the market as the reference year. Time-series analysis was used to assess the annual price per DDD and annual cumulative percentage change in price per DDD over time. The proportion of all lipid-lowering medicines supplied or sold in each country represented by atorvastatin in 2014 (2013 data used for Korea) was calculated. As a secondary outcome, the total volume of atorvastatin supplied or sold in each country was also assessed.

Case-study of New Zealand
A post-hoc case-study of pricing for atorvastatin in New Zealand is reported because the prices in New Zealand were generic equivalents for the branded product well before patent expiry; thus, the influence of generic pricing policies was not the major determinant of price. Information for the case-study was sourced from the New Zealand agency responsible for pharmaceutical management, PHARMAC. The results are reported in narrative form.
Results

Prior to the introduction of generic atorvastatin in 2006, the price for atorvastatin ranged from $0.10 per DDD supplied in New Zealand, to $0.87 per DDD supplied in Australia, $2.72 per DDD sold in Singapore and $2.89 per DDD supplied in the Republic of Korea (see Fig. 2). In all of the countries examined, the price per DDD supplied was already decreasing prior to entry of the first generic product (except for New Zealand, where it was already low).

All countries except New Zealand had notable falls in the price per DDD at the time of atorvastatin patent expiry (see Fig. 2). The published price in New Zealand was very low for the branded product prior to atorvastatin patent expiry, and rose in the year after the expiry (although a confidential rebate meant that the cost did not actually increase). However, it was always lower than the prices in all other countries and while there was an initial increase, the price per DDD subsequently declined, reaching one third of the pre-generic introduction price within 3 years. In 2014, which was the last year of comparable data in all countries, prices varied from $0.03 per DDD supplied in New Zealand, to $0.14 per DDD in Australia, $0.47 per DDD in Singapore and $1.15 per DDD in the Republic of Korea.

The cumulative percentage price change after the introduction of the first generic product (see Table 2) shows that Singapore had the fastest initial decrease in price following introduction of the generic product. New Zealand was the only country to have an increase in price (although the cost did not increase) at any time following generic entry. By the fourth year after generic entry, the price had fallen by between 46% and 80% in all countries; however, there were still large differences in price between countries (e.g. $0.03 per DDD in New Zealand, $0.14 in Australia, $0.47 in Singapore and $1.43 in the Republic of Korea).

The volume of atorvastatin supplied or sold increased across the study period for the Republic of Korea and Singapore but was relatively stable in Australia (see Fig. 3). No consistent relationship was observed between the volume supplied or sold and the price per DDD.

The case-study of New Zealand’s competitive tendering system is presented on page 104.

Table 2. Cumulative percentage reduction in price per defined daily dose supplied or sold post introduction of generic atorvastatin, by country

<table>
<thead>
<tr>
<th>Time from introduction</th>
<th>Australia</th>
<th>New Zealand</th>
<th>Republic of Korea</th>
<th>Singapore</th>
</tr>
</thead>
<tbody>
<tr>
<td>First year post</td>
<td>2%</td>
<td>2%</td>
<td>25%</td>
<td>46%</td>
</tr>
<tr>
<td>Introduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second year post</td>
<td>39%</td>
<td>351%</td>
<td>40%</td>
<td>61%</td>
</tr>
<tr>
<td>Introduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Third year post</td>
<td>61%</td>
<td>86%</td>
<td>44%</td>
<td>71%</td>
</tr>
<tr>
<td>Introduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth year post</td>
<td>80%</td>
<td>69%</td>
<td>46%</td>
<td>80%</td>
</tr>
<tr>
<td>Introduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 2. Annual price of atorvastatin (international dollars) per defined daily dose supplied or sold in Australia, New Zealand, the Republic of Korea and Singapore
**Discussion**

This study has demonstrated widespread variation in the price per volume of use supplied for atorvastatin, both before and after the introduction of generic atorvastatin. All countries successfully reduced the price of atorvastatin with the market entry of the generic product, despite differing pricing policies and practices for generic medicines; however, the rate of decrease and the longevity of decreasing prices varied. The New Zealand tendering system and use of preferred medicines resulted in atorvastatin prices that were independent of the patent expiry, with very low prices established well before patent expiry, suggesting that generic policies have less influence on prices in markets where tendering systems operate and therapeutic alternatives are available. Singapore, which has free pricing coupled with tendering for medicines within the public sector, had the most rapid initial fall in price per volume of use after the introduction of the generic medicine, and maintained falling prices over the 4 years of follow-up. Australia, with its initial mandatory price cut, coupled with a mandatory price-disclosure policy, was observed to have the equal-greatest (with Singapore) cumulative fall in price. Australia’s Pharmaceutical Benefits Scheme does not restrict the number of generic products that can be listed on the scheme, and at the end of 2016 there were 15 different generic products listed for atorvastatin, possibly contributing to price competition. Prices in the Republic of Korea fell in a manner that was consistent with the mandatory price cuts of 30% in the first year and a further 10% in the second year. Based on the observable data, however, subsequent flow-on effects of reduced prices appear minimal, with only a 6% further cumulative drop in price per volume supplied in the subsequent 2 years. This was much
Roughead et al.: Pricing policies for generic medicines: patent expiry and atorvastatin price

Case-study: New Zealand’s competitive tender system

New Zealand uses competitive tender to determine which brand(s) of a medicine are to be publicly subsidized. The duration of tenders is up to approximately 3 years, allowing ongoing price negotiation between the government and manufacturers.

Rather than focusing on an individual product, New Zealand considered statins to be therapeutically interchangeable; the main two funded products have been simvastatin and atorvastatin. Simvastatin is the market leader, owing mainly to progressive opening of access as a result of negotiated price concessions between the funder and the suppliers of this drug. Prior to 2002, funding was restricted to people with the greatest clinical need, using levels of blood cholesterol as a marker. When a new commercial agreement was reached in 2002, New Zealand was able to open access to simvastatin to most people, while maintaining restrictions based on these clinical markers for atorvastatin. A smaller group of people with the greatest need could still access a full subsidy for the more expensive atorvastatin, while most people’s clinical needs were met through simvastatin, so costs to the funder were lowered overall.

With regard to atorvastatin, the originator was the sole subsidized brand prior to the study period. Between 2000 and the beginning of the study period in 2006, the New Zealand government had negotiated an 89% price reduction for the originator brand, i.e. from $0.95 to $0.10 per DDD (details on the negotiation were not available from PHARMAC, owing to commercial sensitivities). The originator brand continued to hold the tender for the sole-subsidized atorvastatin brand until 1 year after patent expiry. Consequently, New Zealand had experienced large reductions in price prior to patent expiry, and the expiry date could not act as a potential price-reduction point, as it did in the other countries.

In addition to the low published prices, New Zealand negotiated with suppliers across the study period; thus, the actual costs were lower – even while more patients received access to treatment in 2002 when restrictions were removed from simvastatin and usage grew rapidly. This growth was also seen in atorvastatin once its restrictions were removed, from 2010. The magnitude of these price reductions was not disclosed, to maintain trust between the government and suppliers.

This case-study demonstrates that patent expiry may not be a determinant of price in a tender system. New Zealand had negotiated a low price per DDD and a confidential rebate prior to atorvastatin going off-patent, and subsequently the expiry date itself was not associated with a decrease in price subsidy, but it was associated with a reduction in real cost. However, the price of atorvastatin did continue to fall in the years following patent expiry.

less than observed in the other participating countries, which continued to see falls of between 20% and 30% in prices in years three and four post generic introduction, and may be due to there being no further price-reduction policies in place after the second year post entry. The New Zealand tendering model, which tenders across a therapeutic class and results in a limited preferred medicines list within therapeutic classes, suggests that low prices can be achieved, even when patent protection exists, and that in these instances other generic pricing policies may be less relevant. This model may be of particular relevance to low- and middle-income countries when formulating their pricing policies for generic medicines.

New Zealand was the only country where an increase in published price was observed following entry of generic atorvastatin; however, at no time did the actual cost in New Zealand increase, owing to the presence of confidential rebates (Ms J Urlich, PHARMAC, personal communication, 16 October 2017). Additionally, at no time did the price of atorvastatin in New Zealand rise above the prices paid in any other country participating in this study, remaining at almost half the cost in any other country assessed. It should be noted that the cumulative percentage changes in price, which appear high for New Zealand in the year after generic entry, are relative to the baseline price and so need to be interpreted in keeping with the actual prices, which for New Zealand were lowest of all.

The study findings of variable prices for medicines across countries is consistent with previous research showing wide variability in the prices of medicines. The majority of previously published research provides descriptive comparisons of policy implementation across countries; reports average effects of specific policies on a group of medicines, such as evaluation of the effect of reference pricing; or provides estimated effects of price savings with full generic substitution. Less is known about other mechanisms for pricing of generic products. The present research found no other study that reports the results of the combined intervention of price regulation with mandatory price-disclosure policies, which was the Australian example.

This study used price per volume of medicine dispensed or sold as its outcome measure. These results not only give information regarding the price achieved for generic products but also encompass the extent of use of generic products in practice, thus reflecting the overall savings achieved. This measure has also been employed in other studies that have evaluated the consequences of a combination of pharmaceutical policy interventions. As policies for generic medicines are usually implemented nationally, the present study does demonstrate the value of international comparisons for policy evaluation.

A limitation of the study is that it was observational and descriptive in nature. The interventions that were compared all occurred in different years in each country, owing to different dates of patent approval and expiry. Other components of each country’s pharmaceutical policy, including the number of registered generic medicines, and the size of the market for
lipid-lowering drugs, may also have had some influence on the results.1 The amount of atorvastatin used as a proportion of all statin therapy varied between countries, as demonstrated in Fig. 2. While the proportion of the overall market accounted for by atorvastatin may have affected the initial price, the relative change in price after patent expiry should not necessarily be affected by market share.

The study used price per DDD in order to allow for potential differences in strengths and pack sizes between countries. Consequently, the method assumed that price reductions due to patent expiry would not be different across pack sizes or strengths within each country, but would fall similarly. The results do not take into account patient co-payments, which also differ across countries, ranging from $0.25 per month in the Republic of Korea (2015), to $2.08–10.40 per month in New Zealand (co-payments reduced for different age groups between 2004 and 2007),20 and $4.27 or $12.63 per month in Australia (low-income versus general patients). Co-payments in Singapore vary, based on the patient’s paying status and the scheme under which the medicine is covered. For this reason, pricing comparisons must be interpreted with care, as the prices reported in this study reflect government costs prior to confidential rebates. Differences in patient contributions may have affected some of the differences observed in price per DDD. The New Zealand price per DDD, when only the branded product was available, was much lower than for any other country. This highlights a limitation in the study design when only the impact of the patent expiry is assessed and when use of other products in the class is not considered.

Conclusion

The results of this study demonstrate the influence of four differing pricing policies for generic medicines in four countries from the WHO Western Pacific Region. In one jurisdiction (New Zealand), the price of atorvastatin was independent of the pricing policies for generic medicines, with very low prices achieved while the product was still on patent. In other countries, pricing policies for generic medicines were effective in reducing costs, with countries achieving reductions of between 46% and 80% in price 4 years post patent expiry. Differences were observed in the rate of change over time. Tendering systems (New Zealand, Singapore) resulted in particularly low prices. Where tendering and use of preferred medicines were the procurement mechanisms for atorvastatin (New Zealand), prices were lowest both before and after generic entry. Mandatory price cuts, combined with subsequent price-disclosure policies, produced similar relative percentage price reductions at 4 years (Australia). By comparison, mandatory price cuts upon generic entry as the sole measure were associated with the smallest relative reduction in price at 4 years’ follow-up (Republic of Korea). This study highlights the need to continually evaluate the effectiveness of implementation of policy for generic medicines and to consider the mix of strategies that maximizes value for money.

Acknowledgements: We are grateful to PHARMAC, New Zealand, and the Republic of Korea Health Insurance Review and Assessment Service, for providing data for this study.

Source of support: None.

Conflict of interest: None declared.

Authorship: EER conceived the study. EER and AK-C drafted the manuscript, performed the statistical analysis and interpreted the data. D-SK and BO aided with data interpretation, assisted with acquisition of data and critically reviewed the manuscript. All authors read and approved the final manuscript.


References


Geographical disparities and determinants of anaemia among women of reproductive age in Myanmar: analysis of the 2015–2016 Myanmar Demographic and Health Survey

Hla Hla Win¹, Min Ko Ko²
¹Department of Preventive and Social Medicine, University of Medicine (1), Yangon, Myanmar, ²Population and Family Health Department, University of Public Health, Yangon, Myanmar

Correspondence to: Dr Min Ko Ko (drminkoko.mph@gmail.com)

Abstract

Background Anaemia is a significant public health challenge in Myanmar. In 2015–2016, the first demographic and health survey was done in Myanmar, and showed that almost half of all pregnant women had anaemia. To inform policy decisions, this secondary analysis of the Myanmar Demographic and Health Survey 2015–16 was done to determine the geographical disparities in prevalence of anaemia and related factors among women of reproductive age.

Methods Analyses were based on weighted samples of 12 489 eligible women aged 15–49 years. Regions and states were clustered into four geographical zones: hilly, coastal, delta and central plain zones. Baseline characteristics were analysed by descriptive statistics. Odds ratios and 95% confidence intervals (CIs) were estimated using univariable and multivariate logistic regression.

Results The prevalence of anaemia varied by geographical zone. Compared with women in the hilly zone, women of the coastal zone had adjusted odds of having anaemia of 1.7 (95% CI 1.43–2.05), while for those in the delta and central plain zones, the adjusted odds were 1.6 (95% CI 1.41–1.92 and 1.38–1.88, respectively). Other factors that significantly raised the adjusted odds of having anaemia were being married, pregnant, underweight/thin or aged ≥40 years, and parity of more than six children. By contrast, urban residence, educational status, employment status and wealth status were not significantly associated with anaemia.

Conclusion Anaemia among women of reproductive age is a major public health problem in Myanmar, and those in the coastal region are the most vulnerable. Introducing provision of iron tablets for non-pregnant women, and improving the current low levels of provision to pregnant women, would be a simple and effective policy. As with other health outcomes, further analyses on disparities in anaemia among women of reproductive age at the state and regional level in Myanmar are warranted.

Keywords: anaemia, determinants, Myanmar, women of reproductive age

Background

Anaemia among women of reproductive age is a public health challenge for many low- and middle-income countries, with long-term negative consequences for health, social and economic development. In 2012, the World Health Assembly Resolution 65.6 endorsed the Comprehensive implementation plan on maternal, infant and young child nutrition. This specified six global nutrition targets for 2025, the second of which is a 50% reduction in anaemia in women of reproductive age.¹

Anaemia has significant health implications, especially for children and mothers, as well as an impact on development of human capital. Anaemia among women of reproductive age contributes to higher risk of having unfavourable pregnancy outcomes, such as premature births, or low-birth-weight babies.² Anaemia and iron deficiency reduce individuals’ well-being, cause fatigue and lethargy, and impair physical capacity. This affects their productivity at work and thus may have an impact on a country’s socioeconomic development.³,⁴ The burden of anaemia is not uniformly distributed across regions or countries in the world.⁴,⁵

The results of an analysis of population-representative data worldwide indicated that, in 2011, 29% of non-pregnant women and 38% of pregnant women aged 15–49 years had anaemia.⁴,⁵ In addition, mean haemoglobin concentrations and the prevalence of anaemia were highest in central and west
African and South Asia. Anaemia is a significant challenge in the World Health Organization (WHO) South-East Asia Region, where, in 2011, more than 200 million women of reproductive age had anaemia, including 191 million non-pregnant women and 11.5 million pregnant women. A regional expert consultation in 2016 noted that anaemia is a severe public health problem in Bangladesh, India, Myanmar and Nepal, where coverage of anaemia programmes is inadequate; safe water and sanitation status is moderate or poor; rates of open defecation are significant; the incidence of diarrhoeal diseases is high; and, in specific areas, there is a significant prevalence of malaria.

Myanmar is the largest country in mainland South-East Asia, and is classified by the World Bank as a “least developed country”. The latest census was in 2014 and reported a population of about 51.5 million, of which 70% are living in rural and 30% in urban settings. Despite the country’s abundant natural resources and local development plans, poverty and socioeconomic inequalities within and among the states and regions are challenging. Administratively, Myanmar comprises Nay Pyi Taw Council, seven states and seven regions. Geographical disparities in health outcomes are long established, and some states and regions are particularly affected. A health system review of the country in 2014 by the Asia Pacific Observatory on Health Systems and Policies noted that “Addressing health inequities is of paramount importance for Myanmar, needing a major reform that will ensure health care services reach the poor and the disadvantaged groups, minority groups in particular, and in conflict-affected and hard-to-reach areas”.

The Myanmar Demographic and Health Survey (MDHS) 2015–16 was the first survey of its kind to be implemented in the country as part of the worldwide programme of demographic and health surveys. This survey showed that the rate of malnutrition in Myanmar is among the highest in Asia, with one in three children stunted and 7% acutely malnourished. Nearly 60% of children aged 6–59 months and almost half of pregnant women had anaemia. As with other health outcomes, the prevalence of anaemia among women of reproductive age varied, with the highest, at 55%, in Rakhine State and Tanintharyi Region.

To date, there has been no research on anaemia among women of reproductive age in Myanmar using a nationally representative sample. The objective of this study was to determine the geographical disparities in prevalence of anaemia and related factors from the MDHS (2015–2016) data, to inform evidence-based policy and priority interventions.

Methods

This is a secondary data analysis of the MDHS (2015–2016), which was a cross-sectional nationally representative population-based survey conducted by the Ministry of Health and Sports. A two-stage sample of households was used (441 clusters; 30 households per cluster), stratified by urban and rural areas in the 15 states and regions. Because of the non-proportional sample allocation, data were weighted such that results were representative at the national and regional/state levels. Further details have been published elsewhere. The MDHS (2015–2016) collected data on social, behavioural and demographic indicators, including health status and reproductive health issues, from women aged 15–49 years and men aged 15–59 years.

This analysis was based on weighted samples of women of reproductive age (15–49 years), from all 15 administrative states and regions of Myanmar. Anaemia was defined in the MDHS (2015–2016) as a blood haemoglobin level below 12.0 g/dL in non-pregnant women and below 11.0 g/dL in pregnant women. Capillary blood from a finger prick, collected in a microcuvette, was used to test for anaemia. Haemoglobin analysis was carried out on site. Detailed information on the methods is provided in the MDHS (2015–2016) report.

For this analysis, the 15 states and regions were grouped into four geographical zones: hilly, coastal, delta and central plain. The hilly zone includes Chin State, Kayah State, Shan State, Kayin State and Shan State. The coastal zone includes Mon State, Rakhine State and Tanintharyi Region. The delta zone includes Ayeyarwady Region, Bago Region and Yangon Region. The central plain zone includes Magway Region, Mandalay Region, Nay Pyi Taw and Sagaing Region. Other variables assessed were the household characteristics (urban/rural residence, wealth-index quintile) and individual characteristics (age, educational status, marital status, employment status, body mass index [BMI; underweight/thin: <18.5 kg/m², normal: 18.5–24.9 kg/m², overweight: 25.0–29.9 kg/m², obese: ≥30.00 kg/m²], and pregnancy status). All independent variables were analysed as categorical variables.

Data analysis was done using STATA (StataCorp. Released 2017. Stata Statistical Software, Version 15, College Station, TX: StataCorp LLC). Missing values and weighted samples were checked. Baseline characteristics were analysed by descriptive statistics. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using univariable and multivariate logistic regression. All test statistics were two-sided and a P value of less than 0.05 was considered statistically significant.

Ethical consideration

The datasets of the MDHS (2015–2016) were accessed with permission from ICF International. The primary demographic and health survey data were collected in accordance with international and national ethical guidelines.

Results

A total of 12,885 women aged 15–49 years participated in the MDHS (2015–2016), corresponding to a response rate of 96%. After exclusion of women for whom data were missing, the final weighted sample of women of reproductive age in this analysis was 12,489. The background characteristics of these women by geographical zone are shown in Table 1. In all four zones, the majority were living in rural settings, were aged less than 40 years, were not employed, had a normal BMI, and were not pregnant. Other than in the delta zone, most women had an education level of primary or below. With respect to wealth quintile, the coastal zone had the highest proportion of women in the poorest quintile (35.6%), and the lowest proportion (13.6%) in the richest quintile.

The overall national prevalence of anaemia among women of reproductive age was 46.5%. Fig. 1 shows the prevalence
Table 1. Background characteristics of the study population by geographical zone (n = 12,489)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Geographical zone, n (%)</th>
<th>Residence</th>
<th>Age</th>
<th>Educational status</th>
<th>Marital status</th>
<th>Employment</th>
<th>Body mass index</th>
<th>Wealth quintile</th>
<th>Pregnancy status</th>
<th>Parity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hilly (n = 2097)</td>
<td>Coastal (n = 1469)</td>
<td>Delta (n = 4699)</td>
<td>Central plain (n = 4224)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>559 (26.7)</td>
<td>298 (20.3)</td>
<td>1802 (38.3)</td>
<td>893 (21.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1538 (73.3)</td>
<td>1171 (79.7)</td>
<td>2897 (61.7)</td>
<td>3331 (78.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40 years</td>
<td>1602 (76.4)</td>
<td>1092 (74.3)</td>
<td>3476 (74.0)</td>
<td>3066 (72.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥40 years</td>
<td>495 (23.6)</td>
<td>377 (25.7)</td>
<td>1223 (26.0)</td>
<td>1158 (27.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Educational status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary or below</td>
<td>1255 (59.8)</td>
<td>872 (59.4)</td>
<td>2247 (47.8)</td>
<td>2372 (56.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above primary</td>
<td>842 (40.2)</td>
<td>597 (40.6)</td>
<td>2452 (52.2)</td>
<td>1852 (43.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not married</td>
<td>1376 (65.6)</td>
<td>880 (59.9)</td>
<td>2840 (60.4)</td>
<td>2452 (58.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>721 (34.4)</td>
<td>589 (40.1)</td>
<td>1859 (39.6)</td>
<td>1772 (42.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not working</td>
<td>1454 (69.3)</td>
<td>781 (53.2)</td>
<td>2882 (61.3)</td>
<td>3186 (75.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working</td>
<td>643 (30.7)</td>
<td>688 (46.8)</td>
<td>1817 (38.7)</td>
<td>1038 (24.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight/thin</td>
<td>186 (8.9)</td>
<td>248 (16.9)</td>
<td>765 (16.3)</td>
<td>671 (15.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1379 (65.8)</td>
<td>916 (62.4)</td>
<td>2659 (56.6)</td>
<td>2561 (60.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>393 (18.7)</td>
<td>241 (16.4)</td>
<td>984 (20.9)</td>
<td>780 (18.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>139 (6.6)</td>
<td>64 (4.4)</td>
<td>291 (6.2)</td>
<td>212 (5.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wealth quintileab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (poorest)</td>
<td>354 (16.9)</td>
<td>523 (35.6)</td>
<td>910 (19.4)</td>
<td>435 (10.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>425 (20.3)</td>
<td>282 (19.2)</td>
<td>847 (18.0)</td>
<td>814 (19.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>388 (18.5)</td>
<td>236 (16.1)</td>
<td>839 (17.9)</td>
<td>1126 (26.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>467 (22.3)</td>
<td>228 (15.5)</td>
<td>917 (19.5)</td>
<td>987 (23.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 (richest)</td>
<td>463 (22.1)</td>
<td>200 (13.6)</td>
<td>1186 (25.2)</td>
<td>862 (20.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not pregnant</td>
<td>1996 (95.2)</td>
<td>1404 (95.6)</td>
<td>4533 (96.5)</td>
<td>4107 (97.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant</td>
<td>101 (4.8)</td>
<td>65 (4.4)</td>
<td>166 (3.5)</td>
<td>117 (2.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>692 (33.0)</td>
<td>586 (39.9)</td>
<td>2014 (42.9)</td>
<td>1807 (42.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>336 (16.0)</td>
<td>221 (15.0)</td>
<td>814 (17.3)</td>
<td>662 (15.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 or 3</td>
<td>651 (31.0)</td>
<td>368 (25.1)</td>
<td>1283 (27.3)</td>
<td>1131 (26.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 or 5</td>
<td>276 (13.2)</td>
<td>170 (11.6)</td>
<td>415 (8.8)</td>
<td>425 (10.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥6</td>
<td>142 (6.8)</td>
<td>124 (8.4)</td>
<td>173 (3.7)</td>
<td>199 (4.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Percentages may not add up to 100 because of rounding.

b Wealth index: in the Myanmar Demographic and Health Survey 2015–16, households were given scores based on the number and kinds of consumer goods they owned, ranging from a television to a bicycle or car, plus housing characteristics such as source of drinking water, toilet facilities and flooring materials. These scores are derived using principal component analysis. National wealth quintiles were compiled by assigning the household score to each usual household member, ranking each person in the household population by their score, and then dividing the distribution into five equal categories, each with 20% of the population.

by geographical zone. The lowest prevalence was found in the hilly zone (36.7%) and the highest prevalence was in the coastal zone (49.8%).

The results of the unadjusted and adjusted logistic regression analyses of the determinants of anaemia in women of reproductive age in Myanmar are shown in Table 2. In both unadjusted and adjusted analyses, the variables associated with anaemia were geographical zone, age, marital status, BMI, pregnancy status and parity of more than six children. By contrast, urban/rural residence, educational status, employment status and wealth status were not statistically associated with anaemia in women of reproductive age. After controlling for the other variables, compared with women in the hilly zone, women of the coastal zone had odds of 1.7 (95% CI 1.43–2.05) of having anaemia, while those in the delta and central plain zones had odds of 1.6 of having anaemia (95% CI 1.41–1.92 and 1.38–1.88, respectively). Women aged ≥40 years had an adjusted OR of 1.3 (95% CI 1.17–1.46) of having anaemia; women who were pregnant had an adjusted OR of 1.9 (95% CI 1.50–2.44) of having anaemia; and women who were married were 17% less likely to have anaemia than women who were not married. Women who were underweight/thin were more likely to have anaemia than women with normal or above-normal BMI. For example, women with a normal BMI
had a 15% lower risk of having anaemia than underweight/thin women (see Table 2).

Other factors that significantly raised the adjusted odds of having anaemia were being married, pregnant, underweight or aged ≥40 years, and parity of more than six children. By contrast, urban residence, educational status, employment status and wealth status were not significantly associated with anaemia.

### Discussion

The MDHS (2015–2016) was the first survey of its kind in Myanmar, and gives the opportunity to explore anaemia in women of reproductive age using a nationally representative sample. The overall prevalence of anaemia in women of reproductive age in Myanmar was 46.5%, which is higher than the WHO-estimated average in 2011 of 41.9% for the WHO South-East Asia Region.4

Analyses of demographic and health survey data from other countries have found an inverse relationship between wealth quintile and anaemia.12–15 One study conducted in the hilly zone of Myanmar during 2014 also found an inverse relationship between family per capita income and anaemia in lactating women.16 However, in this analysis of MDHS (2015–2016) data, there was no relationship between wealth quintile and the presence of anaemia in women of reproductive age. Similarly, no relation was found with other socioeconomic factors, such as urban/rural residence, education level or employment. These findings are consistent with two previous cross-sectional studies in Myanmar: one conducted in the hilly zone during 2014,17 and the second in a tertiary hospital of the central plain zone during 2012–2013.18

Nutritional deficiencies, mainly of iron, caused by inadequate diet are the predominant immediate cause of anaemia in women of reproductive age in the WHO South-East Asia Region.6 One possible reason for the lack of association of anaemia with socioeconomic factors in the overall sample of women in the MDHS (2015–2016) could be that low-cost, high-nutrient diets are made possible by the availability of fish, particularly in the coastal and delta zones of Myanmar.19 However, compared with the hilly zone, women in the other three zones were more likely to have anaemia, especially in the coastal zone. The coastal and delta zones are prone to natural disasters, including cyclones, flooding and landslides, which tend to lead to food insecurity through the destruction of productive assets, increases in food prices and loss of livelihoods, among many other serious consequences for affected populations. In Rakhine State, in the coastal zone, conflict has been a major contributory factor for poor maternal and child nutrition.20

Recent data on the prevalence of micronutrient deficiencies among women and children in Myanmar are lacking, and a new Myanmar micronutrient and food consumption survey (MMFCS) is under way. However, the most recent previous survey, in 2005, found that levels of intestinal worm infestation were especially high in the coastal zone: 92% of pregnant women and 70% of children had infestation with one or more of three common worm types (Ascaris, Trichuris and hookworm), compared with the national estimates of 45% and 31%, respectively.20 Iron deficiency is exacerbated by the presence of intestinal parasites. MDHS (2015–2016) data showed that only 55% of women took deworming tablets during their most recent pregnancy.11

Immediate causes of anaemia in women of reproductive age in the WHO South-East Asia Region are nutritional deficiencies caused by inadequate diet; infections, particularly parasitic diseases; and genetic disorders such as thalassaemia.4 The prevalence of haemoglobinopathies – haemoglobin E, alpha-thalassaemia and beta-thalassaemia – is high among women of reproductive age in Myanmar.21 Intermediate causes of anaemia in women of reproductive age in the region include unsafe water and poor hygiene and sanitation.4 The MDHS (2015–2016) data show that 89% of urban households and 77% of rural households in Myanmar have access to an improved source of drinking water. Almost half of all households have an improved sanitation facility; however, less than 1% have a flush toilet linked to a sewer system.11 It is likely that anaemia is due to a combination of causes that coexist, with individual contributions varying in different settings. Since anaemia is the result of multiple factors, a better understanding of the factors discussed above will be important to understanding the main drivers of anaemia in the different geographical zones.

By contrast with socioeconomic factors, biological and pregnancy status were the main determining factors for anaemia in women of reproductive age. The significant role of these factors has been demonstrated in many settings. The policy of the Ministry of Health and Sports is to provide vitamin A

---

**Fig. 1.** The percentage of women of reproductive age in Myanmar with anaemia, by geographical zone (n = 12489)

<table>
<thead>
<tr>
<th>Geographical zone</th>
<th>No anaemia</th>
<th>Anaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hilly (n = 2097)</td>
<td>63.5</td>
<td>36.5</td>
</tr>
<tr>
<td>Coastal (n = 1469)</td>
<td>50.3</td>
<td>49.7</td>
</tr>
<tr>
<td>Delta (n = 4699)</td>
<td>48.4</td>
<td>51.6</td>
</tr>
<tr>
<td>Central plain (n = 4224)</td>
<td>48.1</td>
<td>51.9</td>
</tr>
</tbody>
</table>
Table 2. Determinants of anaemia in women of reproductive age (15–49 years) in Myanmar (n = 12 489)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total weighted sample (%)</th>
<th>Unadjusted analysis</th>
<th>Adjusted analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Geographical zone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hilly</td>
<td>2097 (16.8)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Coastal</td>
<td>1469 (11.8)</td>
<td>1.8</td>
<td>1.47–2.1***</td>
</tr>
<tr>
<td>Delta</td>
<td>4699 (37.6)</td>
<td>1.6</td>
<td>1.4–1.9***</td>
</tr>
<tr>
<td>Central plain</td>
<td>4224 (33.8)</td>
<td>1.6</td>
<td>1.4–1.9***</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>3554 (28.5)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>8935 (71.5)</td>
<td>1.0</td>
<td>0.87–1.1</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40 years</td>
<td>9235 (73.9)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>≥40 years</td>
<td>3254 (26.1)</td>
<td>1.2</td>
<td>1.11–1.34***</td>
</tr>
<tr>
<td>Educational status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary or below</td>
<td>6744 (54.0)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Above primary</td>
<td>5741 (46.0)</td>
<td>0.98</td>
<td>0.89–1.08</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not married</td>
<td>4942 (39.6)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>7547 (60.4)</td>
<td>0.83</td>
<td>0.75–0.91***</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not employed</td>
<td>4186 (33.5)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>8303 (66.5)</td>
<td>0.98</td>
<td>0.89–1.09</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight/thin</td>
<td>1876 (15.0)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>7520 (60.2)</td>
<td>0.85</td>
<td>0.75–0.96**</td>
</tr>
<tr>
<td>Overweight</td>
<td>2402 (19.3)</td>
<td>0.57</td>
<td>0.49–0.67***</td>
</tr>
<tr>
<td>Obese</td>
<td>691 (5.5)</td>
<td>0.54</td>
<td>0.44–0.67***</td>
</tr>
<tr>
<td>Wealth index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (poorest)</td>
<td>2223 (17.8)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2368 (19.0)</td>
<td>1.0</td>
<td>0.88–1.15</td>
</tr>
<tr>
<td>3</td>
<td>2590 (20.7)</td>
<td>0.9</td>
<td>0.86–1.15</td>
</tr>
<tr>
<td>4</td>
<td>2599 (20.8)</td>
<td>0.9</td>
<td>0.74–1.03</td>
</tr>
<tr>
<td>5 (richest)</td>
<td>2709 (21.7)</td>
<td>0.9</td>
<td>0.80–1.10</td>
</tr>
<tr>
<td>Pregnancy status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not pregnant</td>
<td>12 040 (96.4)</td>
<td>1.0</td>
<td>1.22–1.94***</td>
</tr>
<tr>
<td>Pregnant</td>
<td>449 (3.6)</td>
<td>1.54</td>
<td>1.14–1.94***</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>5099 (40.8)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2032 (16.3)</td>
<td>0.8</td>
<td>0.70–0.88***</td>
</tr>
<tr>
<td>2 or 3</td>
<td>3432 (27.5)</td>
<td>0.8</td>
<td>0.72–0.89***</td>
</tr>
<tr>
<td>4 or 5</td>
<td>1287 (10.3)</td>
<td>0.9</td>
<td>0.84–1.16</td>
</tr>
<tr>
<td>≥6</td>
<td>639 (5.1)</td>
<td>1.1</td>
<td>0.97–1.41</td>
</tr>
</tbody>
</table>

CI: confidence interval; OR: odds ratio.
*P < 0.05; **P < 0.01; ***P < 0.001.

Supplements to postpartum women (200 000 IU) within 42 days of their delivery; provide iron supplements (180 tablets during pregnancy) and deworming tablets (one tablet after the first trimester) to pregnant women; and offer education on eating iron-rich foods and avoiding parasites, to prevent anaemia. However, according to the MDHS (2015–2016) data, only 35%
of women aged 15–49 years who gave birth in the 5 years before the survey received vitamin A supplementation during the first 2 months after delivery. More than 40% of women did not take iron supplements for at least 90 days during their pregnancy and 12% took none.11

The Global Burden of Disease Study 2015 ranked iron-deficiency anaemia as the fourth-leading cause of years lost to disability worldwide.22 Anaemia has an impact on the health status of mothers and their children, and on the country’s productivity and overall socioeconomic development. More efforts should therefore be made to ensure that the government guidance on supplementation and advice for pregnant women is followed. Iron supplementation should also be expanded to cover non-pregnant women of reproductive age. There is also a need for health-care workers and allied personnel to improve communication and targeted messages on the important role of iron tablets for all women of reproductive age, as well as pregnant mothers, to prevent anaemia. This action could further support commitments to the Sustainable Development Goals,23 as well as the Global Nutrition Target 2025 for anaemia.2

This study has certain limitations. The 15 regions and states of Myanmar were clustered into four geographical zones to facilitate broad country-wide comparisons. Local approaches will require more detailed analysis of data at the state or regional level.

Conclusion
Anaemia still remains a major public health problem for women of reproductive age in Myanmar. There are geographical disparities in prevalence, and women in the coastal zone were the most vulnerable. Among the variables available for analysis, the main drivers were biological and pregnancy-related factors rather than socioeconomic factors. Further analyses on disparities at the state or regional level are needed, as well as on disparities in other health outcomes in Myanmar. Focusing on providing iron tablets for women of reproductive age, and improving provision to pregnant women, would be a simple and effective policy. Further work on holistic local development plans will be vital to reduce disparities among the regions and states of Myanmar.

Acknowledgements: This research is a product of the 2018 Subregional DHS Further Analysis Workshop, held in Pokhara, Nepal, 8–18 January 2018. The authors acknowledge Dr Thet Thet Mu (Deputy-Director General of Myanmar Ministry of Health and Sports), the United States Agency for International Development and ICF International for access to data and technical assistance.

Source of support: None.

Conflicts of interest: None declared.

Authorship: Both authors contributed equally to this paper.


References
5. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F et al. Global, regional, and national trends in anaemia and iron deficiency anaemia as the fourth-leading cause of years lost to disability worldwide.22 Anaemia has an impact on the health status of mothers and their children, and on the country’s productivity and overall socioeconomic development. More efforts should therefore be made to ensure that the government guidance on supplementation and advice for pregnant women is followed. Iron supplementation should also be expanded to cover non-pregnant women of reproductive age. There is also a need for health-care workers and allied personnel to improve communication and targeted messages on the important role of iron tablets for all women of reproductive age, as well as pregnant mothers, to prevent anaemia. This action could further support commitments to the Sustainable Development Goals,23 as well as the Global Nutrition Target 2025 for anaemia.2

This study has certain limitations. The 15 regions and states of Myanmar were clustered into four geographical zones to facilitate broad country-wide comparisons. Local approaches will require more detailed analysis of data at the state or regional level.

Conclusion
Anaemia still remains a major public health problem for women of reproductive age in Myanmar. There are geographical disparities in prevalence, and women in the coastal zone were the most vulnerable. Among the variables available for analysis, the main drivers were biological and pregnancy-related factors rather than socioeconomic factors. Further analyses on disparities at the state or regional level are needed, as well as on disparities in other health outcomes in Myanmar. Focusing on providing iron tablets for women of reproductive age, and improving provision to pregnant women, would be a simple and effective policy. Further work on holistic local development plans will be vital to reduce disparities among the regions and states of Myanmar.

Acknowledgements: This research is a product of the 2018 Subregional DHS Further Analysis Workshop, held in Pokhara, Nepal, 8–18 January 2018. The authors acknowledge Dr Thet Thet Mu (Deputy-Director General of Myanmar Ministry of Health and Sports), the United States Agency for International Development and ICF International for access to data and technical assistance.

Source of support: None.

Conflict of interest: None declared.

Authorship: Both authors contributed equally to this paper.

Win & Min Ko Ko: Disparities and determinants of anaemia among women in Myanmar


Factors associated with stillbirths in Haryana, India: a qualitative study

Preeti H Negandhi¹, Sutapa B Neogi¹, Ankan M Das¹, Sapna Chopra¹, Amit Phogat², Rupinder Sahota², Ravi Kant Gupta², Sanjay Zodpey¹, Rakesh Gupta³

¹Indian Institute of Public Health-Delhi (IIPH-D), Public Health Foundation of India (PHFI), Haryana, India, ²National Health Mission, State Government of Haryana, India, ³State Government of Haryana, India

Correspondence to: Dr Preeti H Negandhi (preeti.negandhi@iiphd.org)

Abstract

Background Each year, 2.6 million babies are stillborn worldwide, almost all in low- and middle-income countries. Several global initiatives, including the Sustainable Development Goals and the Every Newborn Action Plan, have contributed to a renewed focus on prevention of stillbirths. Despite being relatively wealthy, the state of Haryana in India has a significant stillbirth rate. This qualitative study explored the factors that might contribute to these stillbirths.

Methods This was a sub-study of a case–control study of factors associated with stillbirth in 15 of the 21 districts of Haryana in 2014–2015. A total of 43 in-depth interviews were conducted with mothers who had recently experienced a stillbirth, or with a family member. By use of reflexive and inductive qualitative methodology, the data set was coded to allow categories to emerge.

Results Two categories and several subcategories were identified. First, factors occurring before the woman reached a health-care facility were: lack of awareness of the mothers and family members; intake of sex-selection drugs during pregnancy, in order to have a male child; non-adherence to treatment for high blood pressure; lack of prior identification of an appropriate health-care facility for delivery; and transportation to a health-care facility for delivery. Second, factors occurring once the health-care facility was reached were: lack of timely and adequate management; and use of medication during labour.

Conclusion Intrapartum stillbirths are closely linked to the availability and accessibility of appropriate medical care. Timely and appropriate treatment and care, provided by a trained and skilled health worker during pregnancy and labour, as well as soon after delivery, is an absolute requirement for averting these stillbirths. This study underscores the importance of imparting and increasing awareness regarding factors that have a significant bearing on stillbirth and can be mitigated through prompt and adequate obstetric health-care services.

Keywords: India, prevention, qualitative, stillbirth, three delays model

Background

As defined by the World Health Organization (WHO) through its International statistical classification of diseases and related health problems (ICD-10),¹ a stillborn baby is one with no signs of life at or after 28 weeks of gestation. In 2015, the global stillbirth rate was estimated at 18.4 per 1000 births, with approximately 2.6 million stillbirths.² Most of these stillbirths were from low- and middle-income countries (98%), of which 77.4% were from sub-Saharan Africa and southern Asia.² The stillbirth rate in southern Asia was 25.5 per 1000 births.³ In 2015, India topped the list of countries with the highest number of stillbirths, at 592 000 (22.6% of the world’s stillbirths).² The burden of stillbirth was not emphasized during the Millennium Development Goals era of 1990–2015 but significant efforts have refocused international efforts. As part of the Sustainable Development Goals launched in 2015,³ it is being acknowledged that reduction and prevention of stillbirths would effectively contribute to the achievement of the SDG targets for reduction in under-5 mortality.⁴ Additionally, the Every Newborn Action Plan,⁵ launched in 2014, aims at reducing the stillbirth rate in every country to 10 or fewer per 1000 births, by ending preventable stillbirths by 2035. The vision is to improve the coverage of care of the mother and her baby during childbirth and the first few days after birth, as well as care of small and sick neonates, in order to have a
Stillbirths have higher negative psychosocial and economic effects on their families than live births. Several of the risk factors for stillbirth are particularly important in low- and middle-income countries, especially in rural settings. These risk factors include maternal age (<16 years or >35 years), parity, illiteracy, poor socioeconomic status, maternal malnutrition, maternal infections, pregnancy-induced anaemia, gestational diabetes, pregnancy-induced hypertension, inadequate health-care-seeking behaviour during pregnancy and labour, poor quality of antenatal and intrapartum care, unattended deliveries or deliveries by untrained health staff, delayed caesarean sections, and previous stillbirths. These have been previously documented as risk factors for stillbirth. In addition, a blend of certain social, medical and obstetric factors are associated with stillbirth.

Stillbirths in India are reported as part of the Ministry of Health and Family Welfare’s Health Management Information System, on a monthly basis. It is observed that there are very large variations across states and union territories in stillbirth numbers, as well as inconsistencies in the rates reported by different data sources, signalling the probability of inappropriate and insufficient recording and reporting of stillbirths by health-care workers at grass-roots level. This concern is greater in areas that are geographically rural, where a sizeable number of deliveries take place at home. Moreover, hospital-based data are mostly incomplete and obscure, and death certificates are seldom issued in these cases.

A verbal autopsy is an indirect interrogative method found to be helpful in such cases and is being utilized widely for determining the biomedical cause of fetal death, as well as to explore associated risk factors for framing suitable and effective interventions; information obtained from the immediate family of the stillborn child on the signs, symptoms and circumstances preceding death is used for this purpose.

Haryana, a wealthy state located in the northern part of India, has a relatively high stillbirth rate; as per the Sample Registration Survey of 2013, the rate in the state is 8 per 1000 births, compared with the nationwide average of 4 per 1000 births. Hence, an exploratory study was conducted in Haryana, with an objective to identify the factors that could have played a role in the stillbirth occurrences, based on the experiences of the mothers and their family members. This qualitative analysis was done in a subset of cases in a larger quantitative case–control study that investigated the risk factors associated with stillbirths, with a special focus on the intake of “sex-selection drugs.” Despite carrying a risk of severe fetal harm, use of these indigenous preparations that are thought to ensure birth of a male child is a common practice in north India. The aim of this study was to explore the participants’ experiences and perspectives regarding factors and circumstances that might have contributed to the outcome of their pregnancy.

Methods

Study setting and sample selection
This study was carried out in 15 of the 21 districts of Haryana (Ambala, Faridabad, Gurgaon, Hisar, Jhajjar, Karnal, Kurukshetra, Mahendergarh, Mewat, Palwal, Panchkula, Panipat, Rewari, Rohtak and Sonipat) between October 2014 and January 2015. These districts were chosen purposively to geographically cover the state. The study participants (mothers of stillborn babies) were selected from a list compiled by the National Health Mission (NHM) Haryana, as part of the ongoing Maternal Infant Death Reporting System (MIDRS). The MIDRS portal primarily captures facility-based stillbirths. Home-delivered stillbirths that are brought to the facilities soon after the delivery are also captured in the MIDRS system. This study restricted the enrolment of participants to two calendar months, August and September 2014, to avoid recall bias. For the case–control study, from the list of 825 stillbirths reported, 15–30 participants were randomly and proportionately selected from each of the 15 districts, resulting in 327 cases. From these cases, a convenience sample of women was selected for this qualitative study.

Data collection
For the case–control study, data were gathered by administration of a verbal autopsy tool, which was adapted from the validated 2012 WHO verbal autopsy instrument, with added questions on intake of sex-selection drugs. The tool was pretested before the study. For cases included in this qualitative study, this was followed by an in-depth interview. The interviews were conducted by two teams led by researchers with postgraduate degrees in public health (SC [female] and AMD [male]). These researchers were specifically recruited for this study, and a detailed orientation was given to the team members prior to data collection. They were also part of the pretesting of the tools, including the interview guide developed by the authors for the study.

At the beginning of the data-collection phase, two teams led by SC and AMD visited the households of potential participants, along with the field health workers who helped in facilitating the initial rapport with the participants. The main participants were the mothers of the stillborn babies. Confidentiality was maintained in every selected case but, given the social milieu in many Indian communities as a part of which daughters-in-law of the family are not allowed to speak to strangers alone, there were some cases in which the husband and/or mother-in-law also participated, at the mothers’ request. In one case of maternal death, her mother-in-law was interviewed. Using the pretested interview guide, the researcher asked each woman to narrate her own experiences and probed further to explore the sequence of events related to her pregnancy and delivery of the stillborn child. All the participants were interviewed in a uniform manner by the two teams and were asked questions based on themes in the interview guide, in order to minimize information bias. All interviews took place at the respective homes of the participants and were conducted in their local language. There were no refusals for the interviews. Field health workers accompanied the researchers and facilitated the home visits. Nobody other than the participants (and their husband and/or mother-in-law, where this occurred) and researchers were present during the interviews. Each interview was conducted over a duration of around 30 minutes, with no interview being repeated. Interviewers collected data pertaining to the mothers’ experiences before, as well as after, reaching a health-care facility, for hospital as well as home deliveries; this is because home-delivered stillbirths that are brought to the facilities soon

WHO South-East Asia Journal of Public Health | September 2018 | 7(2)
after the delivery are also captured in the MIDRS system, and thus were included in the list obtained for selecting the sample. Notes were collected on paper forms and a unique identification number was assigned to each participant. These notes were subsequently used for translation into English and further analyses. Considering the sensitive nature of the topic, audio recording of the interviews was not undertaken.

The two teams simultaneously conducted interviews with the participants. Alongside the data collection, these interviews were also translated from local language into English and categorized into different themes. Data collection was stopped once saturation was reached.

Analysis
The interviews were translated into English and coded manually. Two research staff coded the translated data. One member of research staff read every transcript in detail and arrived at a set of codes after exploring the various patterns that emerged from the data, based on the themes. The second researcher independently coded the transcripts to broadly guide the final analyses. Variations in coding the data were reflected upon and resolved among team members, through mutual discussions. A reflexive and inductive approach was utilized to code the material, allowing the codes and categories to emerge from within the data rather than by prior identification of categories.

Reporting
The COnsolidated criteria for REporting Qualitative research (COREQ) checklist was used as a guide to report the findings of the qualitative part of the study. Categories and subcategories were identified and presented. Some of the participants’ quotations are presented, to illustrate the categories and findings.

Ethical considerations
Before the study was initiated, due permission for conducting the study was obtained from the state and district authorities. The proposal was submitted to and approved by the Institutional Ethical Committee of the Indian Institute of Public Health, Delhi, before commencing the study. A participant information sheet and consent form were developed for the study. Prior to conducting the interviews, the information sheet was used to explain the study objectives to the participants, and written consent was obtained from each respondent. For the participants who were illiterate, verbal informed consent was taken and a literate family member signed as witness to the consent. The data collected were maintained by, and circulated only within, the research team. The researchers ensured that there was no linkage between the responses of the participants and their personal information, such as name, address and other details, thus suitably maintaining confidentiality.

Results
A total of 43 cases were included in this qualitative study, drawn from a sample of 327 cases. Of these 327 cases, the mean age of the mothers of stillborn children was 24.7 years (standard deviation [SD] 4.2 years) and that of the fathers was 27.9 years (SD 5 years). It was found that 38.8% (127) mothers of stillborn children had completed primary school, while 94 (28.7%) mothers had completed high or senior secondary school. The families of 203 stillborn children (62.1%) earned less than US$ 1527 annually, while 99 families (30.3%) of stillborn children earned between US$ 1527 and US$ 4581 annually. More than 90% of the mothers were home-makers.

The “three delays” model, originally proposed for pregnancy-related mortality, is commonly used to identify and categorize modifiable factors that are relevant to other adverse outcomes, including stillbirth and neonatal death. These are:

- **delay 1**: a delay in the decision to seek care. For example, a woman may labour at home for too long because she and/or her family are afraid to present for care, are concerned about the cost of care, or do not recognize developing problems;
- **delay 2**: a delay in reaching care. For example, a woman in labour may not be able to find or afford expedient transportation to a health-care facility;
- **delay 3**: a delay in receiving adequate care. For example, a woman in labour may arrive at a hospital without any clinicians available to provide care to her, or transfer between lower- and higher-level facilities may take too long to provide effective care and prevent stillbirth.

Analysis of the data collected identified several subcategories that were clustered broadly into two main categories: (i) factors occurring before the woman reached a health-care facility; and (ii) those relevant once the facility had been reached. Many of the findings in the first category related to delays 1 and 2 and those of the second category related to delay 3.

The findings are described next, illustrated as appropriate by quotes from participants. Where relevant to contextualization, selected data from the case–control study are also noted.

**Before reaching the health-care facility**

**Awareness of the mother/family members**

For participants in the study, the time taken to decide on the need to seek care was usually prolonged. Delay 1 in taking a decision to go to a health-care facility sets the immediate environment for the pregnant mothers and their fetuses that can result in a stillbirth. Primarily, this delay is a factor that is influenced by the level of awareness of the mother and her immediate family members. Some women who were aware that they needed medical assistance lacked the authority to make an informed decision regarding early care-seeking. In most Indian families, the elderly family members, who may not be fully aware of the medical situation, take these decisions. This first delay puts such women at higher risk of an adverse pregnancy outcome, as expressed by one of the participants:

> In the eighth month, I was having light pains. The pains relapsed at the beginning of the ninth month. For three consecutive days, I was in pain. My family members thought that it was happening because of the heat. (participant mother, 22 years, district 2)

While most participants chose to go directly to a health-care facility for check-ups, a few participants shared that after the onset of labour pain and/or if they felt that the baby was not
with high blood pressure, who had lost her baby, expressed that:

Intake of sex-selection drugs
Initially, there was reluctance on the part of most participants to divulge information regarding these preparations, but after probing further, some were found to have consumed sex-selection drugs in one form or another during their pregnancy, in order to have a male child. For instance, one participant said:

In the second month, I took medicines for having a boy. My mother-in-law got it for me. I took the medicines in the morning and evening for 7 days. (participant mother, 24 years, district 4)

These were generally obtained from local sources and consumed during the second month of pregnancy. Their responses reflected a complete absence of awareness by the mothers and/or their family members regarding the harmful effects of these preparations.

Adherence to treatment for high blood pressure
In the case–control study, 14.7% (48) mothers of stillborn children reported a problem of high blood pressure during their pregnancy. Although treatment was initiated for most of them, compliance to continuation of the medication and completion of the regimen was not observed among many. This might be due to inadequate counselling from the health-care provider and/or lack of realization among the participants of the importance of treatment for high blood pressure during pregnancy. A woman with high blood pressure, who had lost her baby, expressed that:

My blood pressure was high from the beginning of my pregnancy, but I did not take any medicine. As soon as the ninth month began, I started to bleed but I did not go to the hospital. (participant mother, 22 years, district 11)

Lack of prior identification of an appropriate health-care facility for delivery
A majority of participating mothers and their family members had not pre-identified a health-care facility where they would want their baby to be delivered. As a result, when there were symptoms indicating an impending complication (e.g. not feeling the baby’s movement, excessive abdominal pain, bleeding, etc.), they would move from one health-care facility to another seeking treatment, rather than going to the same health-care facility that they used to visit for antenatal care, thereby delaying the correct and timely management of the case. A number of stillbirths might have been averted, had the pregnant mother and her family members taken a timely decision to avail appropriate health-care services and reached a suitable health-care facility in time to cater for their obstetric needs. One participant said:

In the eighth month, I suddenly started having pain. So we went to a local village doctor who said that the baby is not moving, and gave me some medicines for the pain. After 3–4 days, we casually went to a private hospital in [anonymized] for ultrasound, where we were told that the baby’s heartbeat is not there. So, we went to a private hospital in [anonymized], where they gave some medicines and I had a normal delivery soon after, but the baby was born dead. (participant mother, 21 years, district 12)

Transportation to a health-care facility
In Haryana, transportation is provided through a state-wide public sector free-of-cost referral transport scheme to transfer patients, including pregnant women, from their home to a public health facility or to a higher referral centre from a lower-level facility. Some participants gave very positive feedback regarding the available transport facilities, as mentioned by one of the participants:

It is very convenient. The ambulance came at the right time and took me to the hospital. (participant mother, 25 years, district 8)

Nevertheless, some others said that they faced trouble arranging for a vehicle and that they had problems contacting the ambulance service. Alternative means of transport had to be arranged in such cases. Another issue that emerged from the interviews was that some women were referred to different health facilities more than once on different pretexts (such as for ultrasound or for caesarean sections), which might have led to delay in the delivery of the child and subsequent stillbirth.

After reaching the health-care facility
Timely and adequate management
In general, as evident from the responses provided by participants, the health-care facilities are functional at all times. For many participants, the care and treatment they had received during their labour and delivery after reaching a facility was satisfactory. One respondent said:

I did not have any problem in the hospital. Everything happened easily there. (participant mother, 27 years, district 12)

However, some others narrated undesirable experiences they faced in the hospital, such as impolite and ignorant behaviour of the health-care staff. In the case–control study, mothers of 138 (42.2%) stillborn babies reported experiences where they felt very strongly that their baby was fine until they reached the health-care facility, but died after reaching there. This might have been either due to perceived negligence or delay in receiving appropriate care and services, or multiple referrals by the hospital health-care staff. During the in-depth interviews, one participant, while narrating her experience, said:

For the whole 9 months, I was okay. The ultrasound report was also normal. When the ninth month ended, we went to the hospital but they said that the mouth of the uterus had not opened yet. Then we went to a government hospital, they said that the delivery will be normal. They tried for 5 hours to deliver but the baby’s head got stuck. There, the health worker kept on trying to deliver the baby. The doctor was called
Negandhi et al.: Stillbirths in Haryana, India

later. He came and forced the baby out. The baby had marks on his head. (participant mother, 20 years, district 9)

Usually it is the prerogative of the hospital staff to decide whether to proceed with a normal delivery or operate on a mother. However, in this study it was found that a few mothers and their family members themselves had refused to be operated upon, despite having been advised for it, as the cost for the operation was too high in a private hospital and there was no time to go to another public sector health-care facility for the delivery. The experience of one of the mothers who faced this was as follows:

Doctor had said that an operation has to be done, but we said no. It took 10 hours to deliver. When the baby was born, it was dead. The doctor said that the baby got suffocated, as it could not come out in time. (participant mother, 35 years, district 3)

Referrals in the health system are intended to provide optimal care and services to the beneficiaries, for a favourable outcome. However, according to some participants, they acted as a barrier to timely care and safe deliveries. The experience of being referred to a different hospital after reaching a health-care facility had significantly led to delay in seeking care, as expressed by some participants. One mother said:

The eighth month had just started and I was having light pains. We called the ASHA1 and she came. She took me to the hospital. Nobody was there. Then we were told to go to another hospital. The doctor there told us that the baby is no more, and then referred us to another hospital. (participant mother, 22 years, district 1)

Use of medication during labour

When probed regarding the receipt of medications during labour before delivery, some mothers reported having been administered either oral or injectable medication during labour, but the details of the medications could not be ascertained through the interviews. They were not aware of the name or nature of the medication given. They assumed that the medications might have been given either to augment labour or to subside labour pains.

During the eighth month, my stomach started to pain in the night, we called the dai and she called a nurse who injected a medicine to subside the pains. The next day my stomach started to pain again, so we went to the doctor. He said that the baby had died during the night. (participant mother, 24 years, district 6)

The day I was to deliver, since morning 5 am, I started to have pains. So we called the ASHA worker but it would have taken a lot of time for the car to come. Until then we called a dai. She came and gave me two injections because my pains had subsided by then. After that my baby was delivered at home around 8 pm but was born dead. (participant mother, 20 years, district 6)

While it is a protocol in health-care facilities to use injectable medication to induce labour, it should be given under supervision, with an efficient maternal and fetal monitoring system available for appropriate management, including caesarean section if required. Unfortunately, women reported such incidents of augmentation of labour before they reached the facilities or in facilities without availability of operative services. One family member explained a disastrous incident in which the mother died after a stillbirth delivery:

At the end of the ninth month, she started to have labour pains. The baby was alive when it was about to get delivered. The doctor also said that the baby is alive and its heart beat is there. But the baby was born dead. She was given a lot of injections; 30 minutes after the baby was born, she started bleeding. We also transfused a bottle of blood but she died within 4 hours. (participant mother-in-law, 20 years (mother), district 6)

Discussion

This study explored participants’ individual experiences related to the events that led to their stillbirth, and their perceptions regarding factors and circumstances that might have led to the stillbirth. The major categories that emerged from the interviews of the mothers were: lack of awareness of the mothers and family members; intake of sex-selection drugs during pregnancy, in order to have a male child; non-adherence to treatment for high blood pressure; lack of prior identification of an appropriate health-care facility for delivery; transportation to a health-care facility for delivery; lack of timely and adequate management after reaching the health-care facility; and use of medication during labour. In the quantitative part of the study, the factors that emerged as significant risk factors for stillbirths included history of previous stillbirths, preterm births at <37 gestational weeks, complications during labour, and history of intake of sex-selection drugs during pregnancy.

Many participants, despite having complications during pregnancy such as high blood pressure, were unaware of the consequences of their symptoms and therefore did not consider these a reason for seeking health care. The level of education, not only of the pregnant women, but also of their family members, along with other factors such as poverty and poor familial support, tend to influence mothers’ decision-making and demand for timely health care. In some cases, a dai was consulted prior to deciding to take the pregnant woman to a health facility. The knowledge and awareness of the dai regarding maternal and newborn health also play a critical role in decisions made by the mothers and their family members during pregnancy, thereby contributing to the first delay in seeking professional obstetric health-care services for early diagnosis and care.

Good antenatal care with the recommended number of visits is an important component of prevention of antepartum stillbirths. This care includes regular monitoring of the well-
being of the pregnant woman and the baby throughout the duration of the pregnancy, so that any complications present can be identified in a timely way for appropriate action, and averted. Each 1% increase in the proportion of women completing at least four antenatal visits has been shown to reduce the intrapartum stillbirth rate by 0.16 per 1000 births. In this study, although it was observed that some mothers had visited antenatal clinics and were diagnosed with pregnancy complications such as high blood pressure, compliance with the advice of the treating doctor and/or the treatment was poor. The quantitative component of the study also showed that the mothers of stillborn babies were almost twice as likely to have had high blood pressure during pregnancy as compared to the controls. Previously conducted studies have reported poor compliance during pregnancy to long-term therapies, globally, with variations depending on the cost of treatment, availability of health-care facilities and awareness of patients about the importance of adherence to medication. High blood pressure during pregnancy or labour is associated with increased risk of maternal and perinatal adverse outcomes, with between 5.6% and 9.4% of pregnancies complicated by high blood pressure leading to stillbirths. This suggests that adherence to antihypertensive medication during gestation favourably influences maternal and fetal health outcomes.

Apart from the medical causes and complications that have a direct role in the occurrence of stillbirths, there are certain social factors that might also have a contributory role. Consumption of locally available indigenous preparations for a male child is one such factor. It is observed that a strong desire for a male child compels families to resort to such practices. The fact that data on this issue are usually kept confidential and obscure by the community and local health-care providers worsens the problem further. Analytical studies on both major and minor congenital anomalies, as well as stillbirths, indicate a strong association between the intake of sex-selection drugs and these adverse pregnancy outcomes.

Transport was not a major issue in Haryana with regard to the second delay. However, reaching an appropriate health-care facility took longer than the usual time required to reach a health-care facility, particularly when care was sought from higher levels of health-care facilities, as these are usually located closer to the district headquarters, which are distant from the rural residences of the pregnant women. Prevailing delay in deciding to seek care, and the added delay in reaching a health-care facility, both significantly contribute to the delay in accessing timely care and services. Studies have shown that improvement in transport services leads to increased access to maternal and child health services, which can subsequently lead to reduction in the rates of maternal and neonatal death and stillbirth.

Guidelines for emergency obstetric care have been laid out by the Ministry of Health and Family Welfare, Government of India, but not all public health-care facilities follow them diligently. Multiple referrals during labour indicate that there is a lack of motivation to implement the protocol for care and referral within each level of the health system, thereby accentuating the need for sufficient communication and training at all these levels within the system. This also highlights the fact that there is either a lack of availability of appropriate intrapartum services and skilled personnel at the lower levels of health-care facilities within the public health system, or there is a lack of competence and confidence among the health-care service providers to deliver prompt and adequate services. In Sri Lanka, the availability of effective health-care services, provided by sufficiently trained health personnel in primary health-care centres, has invited early and efficient management of high-risk maternal and child cases, contributing to significant reduction in the number of referrals.

Women who do not receive skilled care at delivery, and who do not have access to emergency obstetric care, are among those at greater risk for stillbirths. Intrapartum stillbirths are closely linked to the availability and accessibility of appropriate medical care. In the present study, a number of stillbirths were perceived by the participants to be intrapartum and could have been averted. Thus, correct diagnosis, followed by timely and appropriate treatment and care provided by a skilled health worker during labour and delivery and immediately after delivery, are vital if stillbirth rates are to be reduced. Hospital-based studies suggest that 25–62% of intrapartum stillbirths are avoidable with improved obstetric care and more rapid responses to intrapartum complications, including reducing delays in seeking care.

In this study, both oral and injectable medications were reportedly given to almost all participants who were admitted to hospital for delivery. However, accurate information on the indication for the medication was not clear. This was primarily because of undocumented practice of giving medications that might be oxytocin, misoprostol, antibiotics or vitamins. Studies conducted in the past have reported increased risk of stillbirth with unwarranted use of oxytocic drugs.

This study highlights deplorable but preventable instances of stillbirth. Although the study features the need for appropriate decision-making and highlights the importance of antenatal and intrapartum care in efficiently managing pregnancy complications and outcomes, it has some limitations. The participants from the study belonged predominantly to rural areas, which might have caused selection bias. Secondly, during the interviews, the mothers were the primary participants, who were helped by their mothers-in-law or husbands in some instances. This might have introduced reporting bias and the data may have been misrepresented. In addition to that, given the tragic outcome, faults and delays in care-seeking on the part of the family may not have been fully revealed by the participants and their family members.

Every stillbirth is a personal tragedy for the family involved and everything possible should be done to minimize the frequency of this devastating occurrence. The objective of this study was to look into all the possible factors for both antepartum and intrapartum stillbirths. While more data related to antepartum factors for stillbirths were extracted, it was difficult to obtain specific health-system-related data for factors related to intrapartum stillbirths, owing to the scarcity of adequate medical records. It was also not possible to categorize each stillbirth as antepartum or intrapartum, since there is no system yet in India to record and report stillbirths as fresh or macerated. The timing for conducting the interviews was no more than 3–4 months after the delivery, thereby minimizing recall bias. They could not have been conducted immediately after the event, owing to its sensitive nature.

This study underscores the importance of imparting information and increasing awareness regarding factors that have a significant bearing on stillbirth, and the critical need...
for prompt and adequate obstetric health-care services to minimize the number of stillbirths.

Source of support: The study received funding from the National Health Mission, Haryana, India.

Conflict of interest: None declared.

Authorship: PHN and SBN designed and coordinated the overall study, analysed the data and drafted the manuscript. AMD and SC designed the tools, pre-tested them, collected the data and helped with the analyses. AP and RS helped with designing the overall study and drafting the manuscript. RKG, SZ and RG coordinated with the research team to facilitate data collection, gave critical inputs and helped with finalization of the manuscript.


References


Negandhi et al.: Stillbirths in Haryana, India


Successes and challenges of expansion of environmental poliovirus surveillance in the WHO South-East Asia Region

Aarti Garg, Sirima Pattamadilok, Sunil Bahl
World Health Organization Regional Office for South-East Asia, New Delhi, India
Correspondence to: Dr Aarti Garg (garga@who.int; aartidewan.79@gmail.com)

Abstract
The last decade has witnessed an exponential expansion of environmental surveillance (ES) of poliovirus in sewage samples in the World Health Organization (WHO) South-East Asia Region. This has grown from only three sites in Mumbai, India in 2001 to 56 sites in 2017 in Bangladesh, India, Indonesia, Myanmar, Nepal and Thailand. ES is critical to the region in providing evidence of silent transmission of vaccine-derived poliovirus and Sabin-like poliovirus type 2 – especially since the global "switch" to cease use of oral polio vaccine type 2 – and for monitoring the effectiveness of containment activities. This targeted expansion of ES to supplement surveillance for acute flaccid paralysis (AFP) required quality assurance in ES procedures, improvements in the sensitivity of the laboratory-based surveillance system, and establishment of real-time data analysis for evidence-based programmes. ES in the region has provided documentary evidence for the absence of indigenous wild poliovirus in circulation and no importations via international travellers. Post-switch, while no vaccine-derived poliovirus was detected from AFP cases, ES identified five ambiguous vaccine-derived polioviruses in 2016 and early 2017, with no evidence of circulation. Future challenges include monitoring for vaccine-derived poliovirus strains shed for a prolonged time by immunodeficient individuals, and expanding ES to areas lacking sewage networks. To maintain the polio-free status of the WHO South-East Asia Region and achieve a world free of poliomyelitis, critical evaluation of immunization coverage, continued performance of surveillance for acute flaccid paralysis, and enhanced analysis of sewage samples to detect any breach in containment are essential.

Keywords: environmental surveillance, poliovirus, South-East Asia Region

Background
The World Health Organization (WHO) South-East Asia Region was certified as being polio free on 27 March 2014, 3 years after the last case due to wild poliovirus (WPV) was reported in the region.1 Along with maintaining polio-free status, the region has made unprecedented progress towards the global goal of polio eradication,2 by sustaining high overall population immunity against polio, surveillance of certification-standard acute flaccid paralysis (AFP), and outbreak response preparedness. AFP surveillance in children under 15 years of age remains the gold standard for polio surveillance, and in selected locations it is supplemented with environmental surveillance (ES).

ES for poliovirus is the monitoring of poliovirus transmission in human populations by examining environmental specimens that are potentially contaminated by human faeces. The rationale for testing sewage for poliovirus is that, once infected with poliovirus, individuals shed large amounts of the virus in their faeces for several weeks, irrespective of whether they have symptoms.3 Poliovirus infection may be symptomatic in only 0.1% to 1% of infected individuals, or even less in partially immune groups.4 Testing of stool and sewage samples includes genomic sequencing to characterize poliovirus isolates; the results are used to map poliovirus transmission and identify gaps in AFP surveillance. Overall immunization rates may conceal unvaccinated individuals, who are susceptible to infections on coming into contact with the circulating poliovirus strains, and hence pose a continued risk of poliovirus spread. Thus, early detection of poliovirus circulation is critical for an effective response to outbreaks and to prevent further spread of the virus.

The aim of this paper is to assess the supplementary role of ES in the ongoing AFP surveillance and highlight the current challenges in expansion of ES in the WHO South-East Asia Region.
Establishment and expansion of environmental surveillance

In the WHO South-East Asia Region, ES has been based on meticulous risk analysis, taking into consideration the chances of importations; past history of poliovirus circulation; identification of high-risk areas of low routine immunization coverage; and environmental and social factors, including the demographic profile.

In India, ES was initiated in 2001 with sewage sampling conducted weekly from three sites in Mumbai, Maharashtra. Nearly a decade later in 2010, five ES sites were established in New Delhi. Since 2010, the number of sewage sampling sites in India has more than quadrupled, from eight sites in one state and one union territory in 2010 to 42 sites in seven states and one union territory in 2017.

In addition to India, ES has been ongoing for more than a decade in Indonesia. This started in 2004, as a part of a feasibility study of inactivated poliovirus vaccine (IPV) at one site in Yogyakarta. Since 2016, the data from the Yogyakarta site have been shared with programme experts for strengthening the surveillance of poliovirus in the region. The National Polio Laboratory, located at Bandung, conducts viral isolation, intratypic differentiation and genomic sequencing of poliovirus isolates from sewage samples collected from both Bandung and Yogyakarta. The Bandung laboratory also supports the genetic analysis of poliovirus isolates from ES samples processed in polio laboratories at Surabaya and Jakarta. Focused expansion of ES in Indonesia was seen with establishment of sewage sampling sites, one each at Jakarta (2016) and Surabaya (2017), and supported by the Regional Polio Laboratory Network of Indonesia.

In Bangladesh, ES was started in September 2015. The two sewage sampling sites at Dhaka and Gazipur were selected for monitoring susceptible populations, after careful analysis of wastewater flow routes in areas where AFP surveillance was suboptimal, silent virus circulation was suspected, and there was a high risk of importations, specifically during the large religious mass gatherings that occur annually in Dhaka.

Myanmar established ES during November 2017, with sampling sites in Yangon Region and Rakhine State to strengthen the ongoing poliovirus surveillance activities. There was a need to establish ES subsequent to an outbreak of circulating vaccine-derived poliovirus (cVDPV) type 2 in 2015, to provide concrete documentary evidence of no poliovirus circulation in the community.

The setting up of a sewage concentration laboratory in Nepal during 2017, led to establishment of an innovative mechanism to expand ES in those Member States that do not have facilities for detection of poliovirus within the country. After initial concentration using the two-phase separation method, the sewage collected from three sites in Kathmandu district in Nepal is shipped to the regional reference laboratory in Bangkok, Thailand, for viral isolation and analysis.

Since November 2016, ES in Thailand has been conducted at two sites, one each at Din Daeng district, Bangkok, and Samut Sakhon Province. Inner Bangkok is a high-volume traveller zone, so catchment areas are used to ensure high vigilance for any poliovirus importations into the country, which is necessary for maintaining the country’s polio-free status. The Samut Sakhon site has a large number of labour immigrants from neighbouring Myanmar. Information regarding the immune status of the migratory population is usually insufficient and so initiation of ES led to enhanced confidence in the ability of the existing system of surveillance to detect any poliovirus importation/circulation in the catchment area.

The last decade has witnessed an exponential expansion of ES of poliovirus in sewage samples in the WHO South-East Asia Region, from only three sites in Mumbai, India, in 2001, to 56 sites in 2017, located in six Member States, namely Bangladesh, India, Indonesia, Myanmar, Nepal and Thailand. This strategic expansion of ES is encouraging and indicates that the region is preparing for the post-certification era and contributing to building a polio-free world at a commendable pace.

The Polio Laboratory Network: the backbone of surveillance

Laboratory support for ES was established by building on the capacity of selected polio laboratories from among the pre-existing Global Polio Laboratory Network of 16 laboratories in the region. The laboratories support viral isolation, intratypic differentiation and genomic sequencing of poliovirus isolates from sewage sludge, and in addition there are two laboratories in India (Hyderabad and Patna) and one in Nepal performing sewage concentration only, as shown in Table 1.

Table 1. The Polio Laboratory Network in the WHO South-East Asia Region, January 2016 to January 2017

<table>
<thead>
<tr>
<th>Country and laboratory</th>
<th>Areas covered by sampling site(s)</th>
<th>Processes supported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country and laboratory</td>
<td>Areas covered by sampling site(s)</td>
<td>Processes supported</td>
</tr>
<tr>
<td>India</td>
<td>Mumbai</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Ahmedabad</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Delhi</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Kolkata</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Lucknow</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Patna</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Hyderabad</td>
<td>Yes</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>Dhaka</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Bandung</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Jakarta</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Surabaya</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Bangkok</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Yangon</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Nepal</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Source: Epidata team, Immunization Vaccine Unit, WHO Regional Office for South-East Asia.
Outcomes of expansion of environmental surveillance

All countries in the WHO South-East Asia Region established case-based AFP surveillance in 1997. More than 50,000 sites are currently participating in the reporting of AFP cases and the surveillance system is instrumental in generating real-time, credible data that help the programme to prioritize and guide immunization activities and future strategies. The non-polio AFP rate in the WHO South-East Asia Region in 2017 was 6.29 per 100,000 population under 15 years of age, which exceeds the globally recommended target of 2 per 100,000. A total of 2567 sewage samples were collected from the 56 sewage sampling sites in the region during 2016–2017 and processed at laboratories supporting ES (see Table 2 and Fig. 1).

Indication of wild polio-free status

Wild poliovirus types 2 and 3 (WPV2 and WPV3) have been isolated from sewage samples since 2001 in India. A gradual decline in isolation frequency and, finally, complete absence of WPV in sewage samples has been observed from the ES data in the region. During 2010, the last WPV1 and WPV3 strains were detected in sewage samples, while there was no WPV2 recovered even in sewage samples during 2010, indicating that there was no circulation of WPV2 in the region (see Fig. 1).

Vaccine-derived poliovirus in sewage samples

Since 2010, the sewage samples have detected 43 instances of ambiguous vaccine-derived poliovirus (aVDPV) type 2 in the region – all in India (see Fig. 2). Furthermore, only two occurrences of aVDPV type 1 and a single case of aVDPV type 3 have been reported from India via ES during the last decade in the entire WHO South-East Asia Region.

In April 2016, there was a globally synchronized “switch” from trivalent to bivalent oral polio vaccine. Following withdrawal of the oral polio vaccine type 2 strain (OPV2), ES was used to closely monitor poliovirus type 2 in sewage samples. While no VDPV type 2 was detected in AFP cases, sewage specimens indicated ambiguous vaccine-derived poliovirus type 2 (aVDPV2) in the region. A total of seven aVDPV2 cases were detected in sewage samples from India – Telangana (2), West Bengal (1) and Delhi (4) – between April 2016 and December 2017 (see Fig. 2). All VDPVs detected by ES were adequately investigated to establish genetic linkages, and no circulation of poliovirus in the region was evident.

Tracking of circulation of Sabin-like poliovirus type 2 subsequent to withdrawal of oral polio vaccine type 2 in April 2016

During the pre-switch period (January to April 2016), Sabin-like poliovirus type 2 (Sabin-like PV2) was detected through both AFP and ES; after the switch, Sabin-like PV2 was reported primarily in ES samples. A total of 134 instances of Sabin-like PV2 were reported from the region during 2016, post switch. The ES reported 81/134 Sabin-like PV2 isolates from April to December 2016 during laboratory investigations. The stool samples from 49 AFP cases isolated Sabin-like PV2 during April to May 2016. Even though detection of Sabin-like PV2 in stool samples from AFP cases was confined to only 1 month post switch, the detection in sewage specimens continued for almost 10 months following the withdrawal of trivalent oral polio vaccine. The ES samples collected from two sites in India between August and December 2016 reported Sabin-like PV2 with zero nucleotide changes, thus indicating recent introduction of the poliovirus.

Discussion

ES contributes to monitoring the effectiveness of polio vaccination strategies and also indicates the progress achieved in bringing the world to the brink of eradicating WPVs. The ongoing ES in the WHO South-East Asia Region is highly valuable, as it provides documentary evidence for the absence of indigenous WPV in circulation and no importations via international travellers (see Fig. 1). The post-switch tracking of poliovirus type 2 during 2016, using the existing surveillance set-up in the region, underscores the importance of ES in identifying poliovirus transmission in the absence of concomitant cases of paralytic polio, which is in agreement with studies from Egypt, Finland, Japan, India and Pakistan. The results from ES data in the region are in line with global findings that ES provides sensitive detection of poliovirus transmission, which might occur in the absence of detected AFP cases, as, for example in Pakistan, polioviruses were isolated from sewage samples before the detection of a case of paralytic poliomyelitis.

Table 2. Environmental surveillance in the WHO South-East Asia Region, April 2016 to December 2017

<table>
<thead>
<tr>
<th>Countries with environmental surveillance activities</th>
<th>Number of sites for collection of sewage samples</th>
<th>Number of sewage samples collected</th>
<th>Total number of samples with vaccine-derived poliovirus</th>
<th>Total number of samples with Sabin-like poliovirus type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>4</td>
<td>193</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>India</td>
<td>42</td>
<td>2229</td>
<td>7</td>
<td>134</td>
</tr>
<tr>
<td>Indonesia</td>
<td>2</td>
<td>18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nepal</td>
<td>4</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myanmar</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thailand</td>
<td>2</td>
<td>109</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>2567</td>
<td>7</td>
<td>134</td>
</tr>
</tbody>
</table>

Source: Epidata team, Immunization Vaccine Unit, WHO Regional Office for South-East Asia.
### Fig. 1. Environmental surveillance of poliovirus detected in sewage samples in the WHO South-East Asia Region since 2010 – data as of January 2018

<table>
<thead>
<tr>
<th>Year</th>
<th>Week</th>
<th>Country</th>
<th>States/Cities</th>
<th>No. of Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>1</td>
<td>India, Mumbai</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>India, Delhi</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>India, Bihar</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>India, West Bengal</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>1</td>
<td>India, Mumbai</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>India, Delhi</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>India, Bihar</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>1</td>
<td>India, Mumbai</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>India, Delhi</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>India, Bihar</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>1</td>
<td>India, Mumbai</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>India, Delhi</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>India, Bihar</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>1</td>
<td>India, Mumbai</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>India, Delhi</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>India, Bihar</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>India, Punjab</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>India, Punjab</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>India, Punjab</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>1</td>
<td>India, Mumbai</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>India, Delhi</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>India, Bihar</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>India, West Bengal</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>India, Punjab</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>India, Punjab</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>India, Punjab</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>India, Punjab</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>1</td>
<td>India, Mumbai</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>India, Delhi</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>India, Bihar</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>India, West Bengal</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>India, West Bengal</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>India, West Bengal</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>India, Telangana</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>India, Telangana</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>India, Telangana</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>India, Telangana</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>India, Uttar Pradesh</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>38</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>41</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>43</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>44</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>46</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>47</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>49</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>51</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>52</td>
<td>India, Uttar Pradesh</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

**Wild poliovirus types:**
- **Wild poliovirus type 1**
- **Wild poliovirus type 2**
- **Wild poliovirus type 3**
- **Wild poliovirus negative**

**Vaccine-derived polioviruses:**
- **Type 1 vaccine-derived poliovirus**
- **Type 2 vaccine-derived poliovirus**
- **Type 3 vaccine-derived poliovirus**
- **Sabin-like poliovirus type 1**
- **Sabin-like poliovirus type 2**
- **Sabin-like poliovirus type 3**
- **Sabin-like poliovirus type 1 and 3**

**Non-polio enteroviruses:**
- **Non-polio enterovirus**
- **Sampling not scheduled**
- **Samples not collected**

**Notes:** For India: ES samples positive for Sabin-like poliovirus 1 and 3 and non-polio enterovirus are recorded as negative for wild poliovirus and labelled accordingly. For Bangladesh, Indonesia, Myanmar, Nepal and Thailand: in weeks where non-polio enterovirus was detected in addition to Sabin-like poliovirus 1, Sabin-like poliovirus 3, or both Sabin-like poliovirus 1 and 3, from different sewage collection sites in the country, the figure shows only the relevant Sabin-like poliovirus result.

**Source:** adapted from World Health Organization Regional Office for South-East Asia. Vaccine Preventable Disease Surveillance Archives (updates) (http://www.searo.who.int/immunization/data/archive/en/).

---

**Garg et al.: Environmental poliovirus surveillance in the WHO South-East Asia Region**

---

**WHO South-East Asia Journal of Public Health | September 2018 | 7(2)**
The critical role of ES in detection of Sabin-like PV2 in circulation in India during 2016, indicating reintroduction of trivalent oral polio vaccine post switch, further highlights the potential of ES in providing documentary evidence for any breach in containment.9,15,16

The vaccine-derived polioviruses (VDPVs) pose a high risk for re-emergence of polio. While no VDPV has been detected from AFP cases in the region following the switch, sewage samples tested from India confirmed four aVDPVs after April 2016 and a single aVDPV in March 2017. All poliovirus sequences from VDPVs detected in ES were analysed and determined to be not genetically linked, indicating that there was no evidence of circulation in the region. Detailed subnational risk assessments and a rapid surveillance review confirmed that population immunity against poliovirus type 2 was very high and did not warrant the use of monovalent OPV2; however, a mop-up response with a fractional dose of IPV was conducted in one of the areas concerned (Hyderabad), to mitigate the risk of spread of the VDPV2 during the third quarter of 2016.16,17 The VDPVs detected in sewage confirm that ES is a very sensitive tool for monitoring circulation of poliovirus strains in the community.

Furthermore, the possibility of poliovirus circulation in populations using only IPV remains, as described in Israel for WPV, thus representing a possible source of polio re-emergence.18 Poliomyelitis has been a notifiable disease in Israel since 1950 and the last case of WPV1 was reported during 1988. Routine ES detected the importation of WPV1 into Israel in 2013 and sustained transmission that could mainly be explained by exclusive immunization of all birth cohorts since 2005 with a routine IPV-only regimen. The fact that no cases of paralytic poliomyelitis occurred is most likely attributable to the high IPV coverage of the cohorts of children aged 0–10 years, combined with early warning provided by ES and the resulting response.18

In situations where IPV supplies are interrupted and vaccine coverage is suboptimal, it is imperative to identify the immunodeficiency-associated vaccine-derived poliovirus (iVDPV) strains in circulation. Immunocompetent individuals excrete polio vaccine viruses for up to 2–3 months, whereas prolonged excretion of VDPV for 6 months up to more than 10 years has been found in persons with primary humoral immunodeficiency.19 VDPV strains from immunodeficient individuals (iVDPVs) have not yet been implicated in outbreaks in the same way that cVDPVs have, although globally there has been some evidence of local virus transmission from patients to unvaccinated children.19 Risks posed by iVDPV strains in the region remain unknown because currently there is no organized way to ascertain the number of immunodeficient, long-term iVDPV excretors in the region. Thus, further monitoring is warranted to secure eradication of poliovirus, including iVDPVs. Provided antibody titres and immunization coverage are maintained, it is likely that populations will remain protected against paralytic disease.

Over time, as OPV2-naive cohorts accumulate, the risk of generating new cVDPVs will increase, following exposure to (i) immunodeficient, long-term iVDPVexcretors; (ii) virus inadvertently released from a manufacturing facility/laboratory; or (iii) monovalent OPV2 use in response to outbreak. Thus, to prevent paralysis caused by VDPVs, it is critical to establish the absence of vaccine viruses from the environment. Hence, there is an urgent need to systematically enhance the quality of surveillance and closely track any new circulation of poliovirus type 2, to safeguard against potential widespread transmission.
Currently, the roadmap for targeted ES expansion is based on risk analysis, at both national and subnational level in the region. The risk status is dynamic and dependent upon changes in virus epidemiology, immunization coverage and surveillance status, making it a daunting task to identify an appropriate site for sewage sampling. ES expansion at subnational levels is rife with challenges, particularly in remote areas with open defecation, pit latrines, septic tanks and an absence of well-established sewage systems.

The mapping of sewage lines and understanding the sewage systems require close coordination with departments beyond health, such as departments of public work; water and sanitation; industrial waste management; and the environment. This calls for closer collaboration and fostering of synergies among various agencies beyond health, to maintain polio-free status in the region. The isolation of poliovirus from sewage samples is complex, as the odds of having various serotypes mixed in a given sample are high. It is critical to augment the capacity of laboratories, to ensure that optimal sensitivity in detecting polioviruses from sewage specimens is sustained.

The strong programmatic performances for polio eradication have been backed by data from AFP surveillance. Data quality for ES poses a challenge, owing to inconsistent and incomplete data from all administrative levels, and the rapid evolution of protocols for ES sample processing. Most laboratories have adopted the latest two-phase concentration method, though some, along with adopting new techniques, are still following methods that have been in use for a long time, to allow comparative analysis of results.

For real-time, data-based informed decisions, it is necessary to establish robust data analysis at regional, national and subnational level, with widespread sharing of results, and increased capacity at all levels for data management.

To ensure the highest standards in laboratory-supported ES, it is of paramount importance to delineate indicators for ascertaining quality in ES procedures. An accreditation checklist has been finalized and piloted by the WHO Global Polio Laboratory Network. There is an urgent need to develop appropriate proficiency test panels for implementing quality control measures.

The containment requirements of the third edition of the WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use (GAPII) add further complexities to handling potentially infectious material, especially sewage specimens at the poliovirus-non-essential laboratory facilities, which process new specimens that contain, or might contain, polioviruses, and adopt a non-retention policy. There is a strong need to assess and minimize the laboratory-associated risk in compliance with containment practices at laboratories exclusively supporting concentration of sewage samples, because these laboratories in the region are currently not included in the WHO-accredited Regional Polio Laboratory Network.

As progress is made and moves closer to eradication, ES assumes higher significance and it is very important to overcome the challenges in strengthening and expanding ES in the region.

Conclusion
Globally, polio eradication is currently at a critical stage, so continued and sustained efforts are ongoing in the region to maintain and further improve the sensitivity of the surveillance system. As we move closer to a polio-free world, sensitive AFP surveillance becomes increasingly critical and, as the number of reported polio cases declines, ES will continue to be an important supplement to AFP surveillance. Maintenance of the region’s polio-free status requires promotion of: (i) expansion of ES to identify early indication of new importations into the region; (ii) expansion in high-risk areas where populations are at a particular risk of VDPV emergence; (iii) documentation of the elimination of Sabin-like viruses following the sequential withdrawal of polio vaccine types 1 and 3 in the near future; (iv) supportive documentation for the certification of polio eradication; and (v) in view of the increasing importance of effective ES during the post-certification period, strengthening of sustainable laboratory resources and maintenance of specialized laboratory skills to optimize sensitivity in detection from sewage samples.

Acknowledgements: We thank Mr Deepak Dhongde, data management associate, WHO Regional Office for South-East Asia, and experts from the Regional Polio Laboratory Network, for their contribution to the programme and help in guiding the process of regional polio-eradication activities.

Source of support: None.

Conflict of interest: None declared.

Authorship: AG wrote the article and subsequent revisions, SP reviewed sections relevant to the Regional Laboratory Network, SB reviewed the overall paper.


References


The journal is published in April and September each year. A series of invited, peer-reviewed Perspectives is published in each issue. In addition, the journal publishes Original research articles, Reviews, and Policy and practice papers that have potential to promote public health in the World Health Organization South-East Asia Region. We invite papers on communicable and noncommunicable diseases, epidemiology, health administration, health economics, health promotion, health systems, maternal and child health, occupational and environmental health, primary health care, public health, public health nutrition and social and preventive medicine. Manuscripts must be original, and should not be published or be under consideration for publication in any substantial form in any other publication. Submitted articles are peer-reviewed anonymously and confidentially before acceptance for publication. All published manuscripts are the property of the World Health Organization.

Articles can be submitted online at http://www.searo.who.int/publications/journals/seajph/en/.

Manuscript preparation
Articles for submission must be typed double spaced (including references) using 12 point font, with a margin of at least 2 cm on every side. The Recommendations for the conduct, reporting, editing and publication of scholarly work in medical journals ("Uniform Requirements"; http://www.icmje.org/recommendations/) should be consulted before submission of the manuscript. All articles should mention how ethical aspects of the study relating to humans and/or animals have been addressed. When reporting experiments on human subjects, authors must indicate whether the procedures followed were in accordance with the Helsinki Declaration (http://www.wma.net/en/20activities/10ethics/10helsinki/index.html).

Title page
This page should contain the title of the manuscript, the name of all authors (first name, middle initials and surname), a short/running title (not more than 40 characters including spaces), the name(s) of the institution(s) where the work has been carried out, and the email address of the corresponding author. One of the authors should be identified as the corresponding author and guarantor of the paper, who will take responsibility for the article as a whole. In a multi-author paper, a brief statement of the contribution of each author is also required. Any conflicts of interest and the source of any support in the form of grants, equipment, drugs etc. must also be stated. Any acknowledgements should also be noted on the title page; the corresponding author should obtain written permission from any individual acknowledged. The word count of the abstract and main text, and number of references, figures and tables should also be noted at the bottom of the title page.

Text
The main text of the paper should begin with the title and an abstract. The abstract for an Original research article should be structured: Background, Methods, Results, Conclusion. The main text should follow the IMRD format, i.e. Background, Methods, Results and Discussion. A single-paragraph Conclusion may be added as a subsection at the end of the Discussion, if desired. Abstracts for other article types should be unstructured, and informative subheadings should be used in the main text. Manuscripts should be written in a manner that can be understood by a broad public health readership.

References
Only original references should be included. Signed permission is required for use of data from persons cited in personal communications. The ANSI standard style, as adapted by the United States National Library of Medicine, should be followed (http://www.nlm.nih.gov/bsd/uniform_requirements.html). References should be numbered and listed consecutively in the order in which they are first cited in the text and should be identified in the text, tables and legends by Arabic numerals as superscripts. The full list of references placed at the end of the main text of the paper should include surnames and initials of all authors up to six (if more than six, only the first six are given, followed by et al.), the title of the paper, the journal title abbreviation according to the style of Index Medicus, year of publication, volume number, first and last page number, and doi number, if available. References for books should give the surnames and initials of the authors, book title, place of publication, publisher and year; citation of chapters in a multiple author book should include the surname and initials of the authors, chapter title, and names and initials of editors, book title, place of publication, publisher and year, and first and last page numbers of the chapter. For citing website references, the authors' surnames and initials, title of the article, website address, and date on which the website was accessed should be given.

Tables and figures
All tables and figures must be cited in the text in the order in which they appear. The tables/figures must be self-explanatory and must not duplicate information in the text. Each table and figure must have a title and be numbered with Arabic numerals. Figures should be prepared using standard computer software and submitted in a modifiable format. A descriptive legend must accompany each figure and should define all abbreviations used, in alphabetical order. Abbreviations in tables should also be defined in alphabetical order, in a separate table footnote.
WHO South-East Asia Journal of Public Health

Volume 7, Issue 2, September 2018, 59–128

Editorial
Accelerating access to essential medicines in the WHO South-East Asia Region: opportunities for greater engagement and better evidence
Poonam Khetrapal Singh, Phyllida Travis

Perspective
Approaches to improving access to essential cancer medicines in the WHO South-East Asia Region
Meenakshi V Chivukula, Klara Tisocki

Access to pain relief and essential opioids in the WHO South-East Asia Region: challenges in implementing drug reforms
Nandini Vallahal, MR Rajagopal, Suraj Perera, Farzana Khan, Bishnu Dutta Paudel, Klara Tisocki

Addressing the threat of antibiotic resistance in Thailand: monitoring population knowledge and awareness
Virjoj Tangcharoensathien, Angkana Sommanustweechai, Sunicha Chaivatik, Hatairat Kosiyaporn, Klara Tisocki

National introduction of fractional-dose inactivated polio vaccine in Sri Lanka following the global “switch”
Deeza Gamage, Samitha Ginige, Paba Palihawadana

Improving access to assistive technologies: challenges and solutions in low- and middle-income countries
Virjoj Tangcharoensathien, Wocana Witthayapipopsakul, Shaheda Viriyathom, Walaiporn Paatcharanarumol

Original research
Essential cancer medicines in the national lists of countries of the WHO South-East Asia Region: a descriptive assessment
Meenakshi V Chivukula, Klara Tisocki

Pricing policies for generic medicines in Australia, New Zealand, the Republic of Korea and Singapore: patent expiry and influence on atorvastatin price
Elizabeth E Roughead, Dong-Sook Kim, Benjamin Ong, Anna Kemp-Casey

Geographical disparities and determinants of anaemia among women of reproductive age in Myanmar: analysis of the 2015–2016 Myanmar Demographic and Health Survey
Hla Hla Win, Min Ko Ko

Factors associated with stillbirths in Haryana, India: a qualitative study
Preeti H Negandhi, Sutapa B Neogi, Ankan M Das, Sapna Chopra, Amit Phogat, Rupinder Sahota, Ravi Kant Gupta, Sanjay Zodpey, Rakesh Gupta

Policy and practice
Successes and challenges of expansion of environmental poliovirus surveillance in the WHO South-East Asia Region
Aarti Garg, Sirima Pattamadilok, Sunil Bahl