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Prevalence of Substandard and Falsified Essential Medicines
Still an Incomplete Picture

Tim K. Mackey, MAS, PhD

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In a press release reporting updates from the recent 71st World Health Assembly of the World Health Organization (WHO), member state delegates called special attention to development of a 5-year roadmap aimed at improving access to safe, effective, and affordable medicines and vaccines, a health target contained in the United Nations' Sustainable Development Goals.[1] The WHO also highlighted one of the key impediments of progress toward this target, the increasing numbers of substandard and falsified medicines (SF medicines) that undermine global health, social and economic progress, and human development.

A Challenge Unresolved

Despite growing attention from a number of international organizations, including the WHO, the United Nations Office of Drugs and Crime, Interpol, and the World Customs Organization, the problem of falsified (ie, medical products deliberately and fraudulently misrepresenting their identity, composition, or source) and substandard (ie, authorized medical products that fail to meet their quality standards or specifications) medicines is not a recent phenomenon.[2] In fact, as early as 1988, the World Health Assembly called for international action against the illicit trade in "counterfeit" medicines (a term WHO has abandoned, as it refers to a violation of intellectual property).[2] More than 3 decades later, definitions have changed, resolutions have been adopted, reports have been issued, and new initiatives have been announced, but there remains a scarcity of empirical data on the actual prevalence, key characteristics, and economic impact of SF medicines.

The importance of collecting reliable and robust data on SF medicines cannot be understated. Without such data, it is nearly impossible to determine what medicines are at the highest risk of being fake or poor quality and what specific patient populations are most susceptible (which can vary country to country). Importantly, if we cannot measure the impact of SF medicines on patient morbidity and mortality, as well as their effect on related issues such as drug resistance and health system costs, developing and advocating for anti–SF medicine interventions (including targeted public health, regulatory, and policy approaches) is elusive.[3,4] The nature of the data also poses challenges. In the case of falsified medicines, transnational criminal networks are often involved, sources of data do not exist, or proxy data (eg, seizures of fake medicines, prosecutions of pharmaceutical crime) must be used.

A few global statistics on SF medicines have been reported, such as a recent WHO report estimating that 1 in 10 medical products in low- and middle-income countries (LMICs) are either falsified or substandard.[5] However, these estimates have significant limitations, such as lack of sufficient reporting sources, inconsistency in sampling methods, and variability in the type and quality of product testing (if any). In fact, WHO estimates rely on 1500 reports received since just 2013 to its Global Surveillance and Monitoring System for SF products, with the agency stating that their estimates are "likely just a small fraction of the total problem and many cases may be going unreported."[5]

Prevalence of SF Essential Medicines in LMICs

In response to some of these challenges, Ozawa and colleagues[6] conducted a systematic review and meta-analysis that sheds light on available evidence investigating (1) the quality of essential medicines, (2) the prevalence of SF essential medicines, and (3) estimates of the economic impact of SF medicines. Studies reporting medicine quality and prevalence were limited to those that had primary data, tested 50 samples or more, and studied LMICs. Furthermore, Ozawa et al assessed the quality and characteristics of the methods of sampling, pharmaceutical quality testing (eg, mass spectrometry, liquid chromatography), and overall quality of studies (scored using the Medicine Quality Assessment Reporting Guidelines). Economic studies were compiled separately and were examined for sources of data and methods used in calculations.

Results from the study provide a few new insights, but mostly validate what is already widely known. First, the majority of the 265 studies examined reported SF medicines from Africa (50.2%) and Asia (34.0%) and the majority (59.2%) were published in the last decade. These findings are not entirely surprising, given that most studies examined were for antimalarials or antibiotics, medicines commonly reported as falsified or substandard in these regions.[7,8] Based on results of a subset of these studies, the authors estimated the overall prevalence of poor-quality medicines to be 13.6% (19.1% for antimalarials and 12.4% for antibiotics).

One interesting finding was that studies with smaller sample sizes reported a statistically significant higher mean SF prevalence. This may mean that conducting targeted and purposeful sampling can lead to better detection of SF medicines but could also simply illustrate the wide degree of variation in prevalence depending on study design. Overall, the oversampling for anti-infectives as a therapeutic class likely skews the results, but given that these were the data available (only 17 studies examined "other drugs"), it might be more accurate to say that the study can generalize the prevalence of only SF antimalarials and antibiotics, not all essential medicines.

Ozawa et al[6] attempt to estimate the economic impact of SF medicines from 14 estimates that ranged from $10 billion to $200 billion. Estimates varied in what they measured, varied in scope (geographic coverage and categories of medicines included), and were often crude in calculation or did not adequately disclose methods. The root data source for 2 estimates could not even be identified.

An Incomplete Picture

The work of Ozawa et al[6] provides important validation of what is largely already known: SF medicines are an understudied problem, existing studies are of uneven quality and have high heterogeneity, and more evidence is needed to inform current and future actions. However, it is important to note that although the study is comprehensive, its narrow scope means it only provides a snapshot of the entire problem, as it is limited to studies conducted in LMICs and to those medicines classified as essential by the WHO.

Although SF medicines are a more significant problem in LMICs, their presence is not limited to countries with poor regulatory controls or weak pharmaceutical governance. In fact, SF medicines have infiltrated drug supply chains in countries of all economic levels, as evidenced by a 2015 study that analyzed both public and nonpublic data from the Pharmaceutical Security Institute's Counterfeit Incident System from 2009 to 2011.[3] In 2012, falsified versions of the anticancer drug bevacizumab (Avastin) were detected in the US drug supply chain, and the country is currently experiencing a counterfeit fentanyl crisis that has directly led to patient deaths.[9,10] Both represent real-world examples of falsified medicines endangering a high-income country.

What can be done to combat this form of public health crime? Ozawa et al[6] provide a hint by pointing to a disjointed effort and the need for standardization, but further exploration of solutions would have better translated study results into impact. For example, how can international legal frameworks, such as the MEDICRIME Convention (the only international binding treaty on SF

medicines) and the European Union's Falsified Medicines Directive, help standardize surveillance and reporting? Furthermore, how can disparate surveillance systems (eg, the Global Surveillance and Monitoring System and the Pharmaceutical Security Institute's Counterfeit Incident System) be bridged to provide a more complete picture of SF medicine detection and reporting from both public and private sources of data? Ozawa and colleagues mention the Sustainable Development Goals, universal health coverage, and the Global Health Security Agenda, which could act as global governance frameworks for SF medicine surveillance but remain immature in their application to the issue. Instead, this study simply reinforces that the global community has a long way to go in seeing and understanding the full picture of the problem of SF medicines.

ARTICLE INFORMATION

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Corresponding Author: Tim K. Mackey, MAS, PhD, Global Health Policy Institute, 8950 Villa La Jolla Dr, A124, La Jolla, CA 92037 (tmackey@ucsd.edu).

Author Affiliations: Division of Infectious Diseases and Global Public Health, Department of Anesthesiology, School of Medicine, University of California, San Diego; Global Health Policy Institute, San Diego, California; World Health Organization Collaborating Centre for Governance, Transparency and Accountability in the Pharmaceutical Sector, University of Toronto, Toronto, Ontario, Canada.

Conflict of Interest Disclosures: Dr Mackey is a noncompensated advisory board member for the Blockchain startup company FarmaTrust, which is working on technology solutions to falsified medicines. He has also previously received travel support from the World Health Organization and US Food and Drug Administration to attend and participate in technical meetings regarding falsified and substandard medicines. He has also acted as an expert consultant for the US Department of Justice on pharmaceutical diversion matters.

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