Fighting the fakes: tackling substandard and falsified medicines

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Poor-quality or fraudulent medicines are causing extensive humanitarian and economic harm, particularly on the African continent. These products are a global problem that requires a coordinated cross-border response, including enhanced regulatory capacities and surveillance, reporting and education.

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"There is no universal health coverage, no health security without access to quality medicines"[1]. A bold statement from the World Health Organization (WHO) Director General Dr Tedros Adhanom Ghebreyesus made in 2018, elevating the long-neglected and under-researched issue of substandard and falsified medical products (SFMPs) and binding it directly to the goals of universal health coverage, a key priority for the triple billion targets of WHO's General Programme of Work. The roots and consequences of SFMP circulation are global and require a global, coordinated, high-level, multi-sector response across education, prevention, detection and reporting mechanisms.

Substandard medicines are legal pharmaceutical products manufactured by registered companies that fail to meet quality standards or specifications and originate from poor manufacturing practices, supply chain gaps or inappropriate storage that lead to degradation of the active ingredients[2]. By contrast, falsified medicines result from the deliberate and fraudulent misrepresentation of the identity, composition or source of an authorized medical product, which is a crime.

WHO estimates that 1 in 10 medicines circulating in low-income and middle-income countries (LMICs) is either substandard or falsified[2]. The ratio of substandard to falsified medical products is difficult to determine, but substandard or low-quality drugs are likely to account for the majority of SFMPs[3]. Overall, the extent of SFMPs is poorly understood owing to limited research, methodological obstacles and current surveillance methods. However, both substandard and falsified medicines can cause enormous humanitarian and economic harm and require different regulatory and legislative mechanisms to protect patient safety.

The impact of SFMPs is vast (FIG. 1). First, they have a direct consequence on mortality and morbidity. WHO estimates that around 1 million people worldwide die every year from SFMPs owing to poor efficacy or adverse effects caused by contamination[4]. Treatment failure also prolongs disease and increases overall risk of morbidity and death. The WHO Global Surveillance and Monitoring System identified antibiotics and antimalarials as the most frequently reported medicines in the African region[2].

In 39 sub-Saharan African countries, 122,350 deaths were attributed to poor-quality antimalarials among children under 5 years of age and, in Nigeria alone, substandard antimalarials contributed to 74,188 deaths per year[5]. Other models estimate that >280,000 children in sub-Saharan Africa die every year owing to SFMPs for pneumonia or malaria[2]. Although antimalarials and antibiotics are the most commonly falsified medicines, all classes and categories are affected, including cheap generics[2]. Second, SFMPs increase the risk of antimicrobial and antimalarial resistance (AMR), which reduces drug efficacy and the market lifespan of an active compound[2]. Third, the economic burden owing to SFMPs is substantial. In the African region, poor-quality antimalarials were estimated to cost more than US$100 million per year in Zambia and more than US$800 million in Nigeria[6]. Limited health-care resources, particularly in low-income settings, are wasted on purchasing ineffective therapies and then treating complications. These additional costs, as well as those owing to AMR, are passed on to patients, health facilities, pharmaceutical companies and society[2]. Fourth, SFMPs contribute funding to organized criminal groups. The World Customs Organization estimates that the SFMP sector is worth up to US$200 billion[7] and that arising profits fund transnational crime and terrorism[8]. Crises such as the COVID-19 pandemic, war, natural disasters and pharmaceutical supply shortages exacerbate the SFMP issue, as SFMPs can be profitably used to fill the supply gap[8]. Finally, failing to tackle SFMPs erodes public trust in health-care systems and professionals[2], which can push patients towards informal care-seeking and self-medication from the internet or other unlicensed sources.

All regions of the world are affected by the increase in SFMPs, and their threat continues to grow online in high-income countries (HICs). However, Africa bears the heaviest burden with >75% of all SFMP alerts

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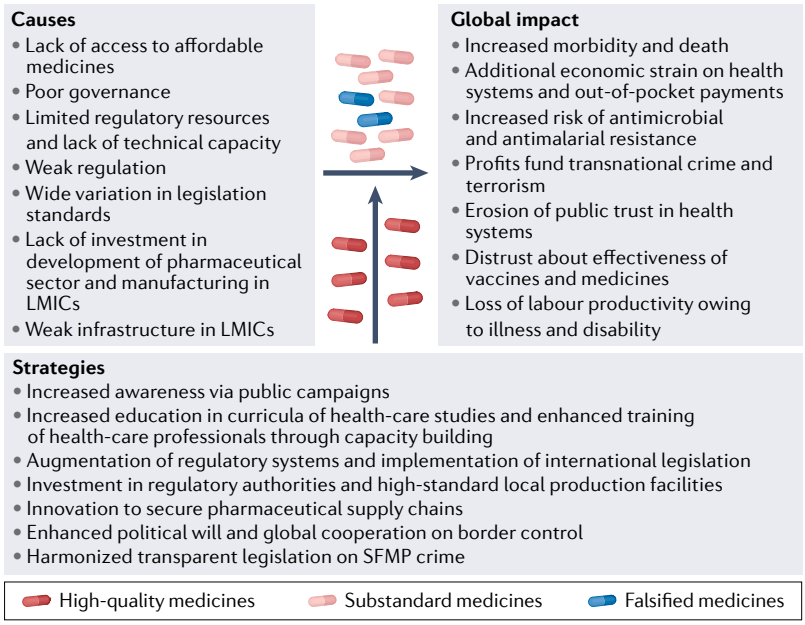

Fig. 1 | **Causes, effects and prevention of substandard and falsified medical product circulation.** Factors driving proliferation of substandard and falsified medical products (SFMPs) differ but overlap. SFMPs are most likely found at the intersection of constrained health-care access, fragmented supply chains with poor governance and low awareness. SFMP circulation has severe health, social and economic consequences, and strategies to improve prevention, detection and response require close and transparent international cooperation. LMICs, low-income and middle-income countries.

originating from the continent itself. Within Africa, detection rates of SFMPs vary widely and 0.8–89% SFMP prevalence has been reported[6]. Governance and regulatory capacity differ substantially among African regions, but lack of resources to support detection and reporting, and political pressures that may lead to under-reporting in some areas, may also contribute to this disparity[2]. HICs contribute to the problem by legally exporting substandard medicines that do not meet quality standards at their point of origin to regions with less stringent regulatory requirements. In addition, limited regulatory resources and lack of technical capacity, including trained staff, undermine the integrity of pharmaceutical supply chains and limit the ability of countries to safeguard population health[2]. In addition, investments and partnerships between local and foreign manufacturers are needed for LMIC pharmaceutical manufacturing companies to upgrade to international GMP standards[2]. As a result, some LMICs began to cooperate through mutual recognition agreements (MRAs) to share inspection costs and reduce the chances of receiving substandard products into their markets. However, MRAs can only work between national medicines regulatory authorities (NMRAs) if quality and inspection standards are harmonized.

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In 2020, seven African leaders placed SFMPs on the highest political agenda through the Lomé Initiative, a political declaration and legally binding agreement to criminalize the trafficking of SFMPs. In addition to this effort, as substandard medicines result from quality control issues[7], harmonized SFMP legislation across LMICs will be needed, coupled with the development of broader pharmaceutical manufacturing capabilities across Africa. A continental approach towards medicine regulation in Africa, akin to the European Medicines Agency, will enhance cooperation and is already underway. In 2019, the African Union countries signed a treaty to create the African Medicines Agency (AMA) to strengthen and modernize national regulatory systems. Investment into NMRAs and track and trace systems, as well as development of local production of safe and affordable medicines[2], will be needed in cooperation with the Africa Centres for Disease Control and Prevention to reduce the market opportunities for SFMP medicines to enter the supply chain.

Increased awareness around SFMPs is needed at all levels, including governments, health systems and the public, to stay vigilant against SFMPs. Campaigns, such as Fight the Fakes Alliance, Medicines We Can Trust and others, aimed at the general public and coupled with education and training for health workers increases SFMP reporting rates. Higher education institutes should engage in research around SFMPs and implement SFMP curricula in pharmacy, medical, nursing and other health courses.

Finally, to stay ahead of criminals and crises, constant innovation around securing the pharmaceutical supply chain is required, including the use of new incorruptible technologies such as blockchain[9]. The global goal should not just be fewer SFMPs on pharmacy shelves, but a healthier, safer and more equal world where access to quality medicines is a fundamental human right for all.

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Competing interests
I.A. led the Lancet Nigeria Commission funded by the Bill and Melinda Gates Foundation (to UCL); while the Lancet Nigeria Commission has a broad health systems focus, it does address the issue of self-sufficiency in medicines. O.Z.P. is Academic Chair of Fight the Fakes Alliance and Founder of the UCL Fight the Fakes Campaign.