Executive Summary

A STUDY ON THE PUBLIC HEALTH AND SOCIOECONOMIC IMPACT

of substandard and falsified medical products

World Health Organization

WHO/EMP/RHT/SAV/2017.02

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EXECUTIVE SUMMARY

Introduction

In 2015, the World Health Organization (WHO) Member State mechanism commissioned a study on the public health and socioeconomic impact of substandard and falsified medical products. This study is intended to be an advocacy document to highlight the scope and scale of the problem of substandard and falsified medical products and the harm they cause. It is published together with a report on the *WHO Global Surveillance and Monitoring System for substandard and falsified medical products* which provides context and suggests actions needed to prevent, detect and respond to substandard and falsified medical products.

WHO Member States, international organizations, procurement agencies, the pharmaceutical industry, health care professionals and civil society have all long recognized the unacceptable threat to public health posed by substandard and falsified medical products. However, providing accurate estimates of the scale of the problem and the harm caused is a significant challenge. These products are difficult to identify and deterioration in a patient's condition is rarely suspected to have been caused by a substandard or falsified medicine, but rather by the illness from which they are suffering.

The impact of substandard and falsified medical products is wide and varied, but not yet thoroughly understood. This study, together with its companion publication, aims to draw attention to the issue while emphasizing the need for considerable further research in order to better shape the urgently needed response.

Definitions of substandard and falsified medical products

A lack of clear, standardized definitions and a common global understanding has hindered research and international collaboration on this issue. In May 2017, following recommendations from the Member State mechanism, the World Health Assembly adopted a new simplified set of definitions as set out in Box 1.

Box 1: WHO definitions of substandard, unregistered/unlicensed and falsified medical products

Substandard medical products

Also called "out of specification", these are authorized medical products that fail to meet either their quality standards or their specifications, or both.

Unregistered/unlicensed medical products

Medical products that have not undergone evaluation and/or approval by the national or regional regulatory authority for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation.

Falsified medical products

Medical products that deliberately/fraudulently misrepresent their identity, composition or source.

Literature review – establishing the facts

Methodology

A literature review was carried out through a search of the academic literature, using the PubMed and MEDLINE databases. Papers published between 2007 and 2016 that reported on field studies or surveys of the quality of medicines were identified. Once papers for consideration had been gathered, they were screened against inclusion and exclusion criteria.

Results from the surveys

In total, 100 published papers and one publicly available database were included in this study. Those papers represented medicine quality surveys conducted in 88 WHO Member States involving 48 218 samples of medicines. The surveys were conducted in both the public and private supply chains. Sample sizes ranged from 10 to more than 15 000 and the surveys were either conducted using random or convenience sampling strategies. A range of analytical techniques were reported, with most samples undergoing laboratory analysis or analysis using the Minilab field testing technique. Medicines for the treatment of malaria and antibiotics accounted for 64.5% of the samples, which reflects important public health concerns regarding antimicrobial resistance and drug-resistant infections.

As seen in Table 1, low and middle income countries, based on the World Bank country classification of income level, appear disproportionately more than high income countries in the surveys. It should be noted that only 178 samples from high income countries were included; therefore no extrapolation for this group of countries was possible.

Table 1: Distribution by World Bank country classification by income level

World Bank country classification by income level	Number of countries surveyed	Total samples
Low income	19	11 156
Middle income	56	36 884
High income	13	178
TOTAL	**88**	**48 218**

Building from Table 1, the observed failure rates of samples from low and middle income countries are shown in Table 2.

Table 2: Aggregate observed failure rates by World Bank country classification by income level

World Bank country classification by income level	Samples tested	Failed samples	Percentage failure rate (95% CI)
Low income countries	11 156	1 166	10.5 (9.9–11.0)
Middle income countries	36 884	3 906	10.6 (10.3–10.9)

CI: confidence intervals.

The aggregate observed failure rate of tested samples of substandard and falsified medicines in low and middle income countries is approximately 10.5%.

One of the aims of this study was to try to estimate the current spending by countries on substandard and falsified products. However, the only publicly available data concerning the estimated total pharmaceutical sales stratified by low and middle income countries are limited: they are not disaggregated by therapeutic class and therefore do not permit accurate estimates of the cost.

However, if one were to use the unweighted combined estimates of market size for low and middle income countries (nearly US$ 300 billion) and the observed failure rates (approximately 10.5%) to calculate possible expenditure by these countries, the resulting total estimate is in the order of US$ 30 billion.

If this is even approximately correct, it highlights the urgent need to address this problem. It also highlights the need for better data on expenditure at country level to enable a more accurate estimate of the economic burden on these countries.

Discussion on key limitations of available data

This study highlights the following limitations that should be borne in mind when considering the results:

- use of heterogeneous definitions for substandard and falsified medical products;
- literature review limited to English language and to literature in the public domain;
- lack of systematically collected data with sufficient sample sizes and random sampling design;

- currently, publicly available market data do not disaggregate by therapeutic category and by country or income level;
- likely biases introduced by different testing technologies (e.g. some methods are able to identify the presence or absence of an active pharmaceutical ingredient (API), but cannot quantify it reliably);
- uneven distribution across therapeutic categories and geographical regions;
- limited availability of prevalence or economic data;
- no existing broad methodological guidelines to help attribute health impacts to substandard and falsified medical products and;
- exclusion of medical products distributed and sold through e-commerce.

An important limitation was that studies that focused exclusively on samples obtained from e-outlets were excluded from the literature review. This represents a gap in knowledge on the impact of a source of medical products that is not only used by consumers and businesses in high and middle income countries, but is increasingly important in low income countries too. Although some studies have been conducted, further research is required to accurately assess the scale of this fast growing issue, particularly in terms of the quality of products being offered.

Estimates made from the surveys included in this study can only be used as one source of information providing an indicator of the scale of the problem. There is a need for far greater homogeneity in study protocols and future research to more accurately estimate the threat posed by substandard and falsified medical products.

Impact models

Insufficient research has been conducted to enable the health impact of substandard and falsified medical products to be estimated. WHO commissioned the development of two models focused specifically on childhood pneumonia and on malaria in sub-Saharan Africa. These models were developed for WHO by the University of Edinburgh (childhood pneumonia model) and the London School of Hygiene and Tropical Medicine (malaria in sub-Saharan Africa model). Both models have highlighted that the results are likely to underrepresent the true impact of substandard and falsified medical products in both disease areas, owing to the lack of exhaustive data and the challenges of incorporating all impact factors into a single model.

The two models summarized below demonstrate that it is possible to estimate the impact of substandard and falsified medical products, but to do so requires sound estimates of the prevalence of those products, the burden of disease and case management at patient level.

Model 1: Childhood pneumonia

A team from the University of Edinburgh was commissioned by WHO to investigate the impact of the use of substandard and falsified antibiotics in the treatment of childhood pneumonia. This model provides a first estimation of the potential impact of substandard and falsified antibiotics on mortality from pneumonia among children aged 0 to 5 years.

The estimation of the impact of substandard and falsified antibiotics on childhood pneumonia mortality considered different levels of global prevalence of substandard and falsified antibiotics used for the treatment of this illness. Table 3 summarizes the estimates for excess deaths from severe pneumonia due to substandard and falsified antibiotics at prevalence levels of 1%, 5% and 10% (assuming that use of substandard and falsified medicines results in a two-fold or a four-fold increase in case fatality rate (CFR)).

Table 3: Impact of substandard and falsified medical products on childhood pneumonia

Prevalence of substandard and falsified products (percentage)	Number of excess deaths in most likely scenario (two-fold increase in CFR)	Number of excess deaths in alternative scenario (four-fold increase in CFR)
1	8 688	18 372
5	37 018	85 438
10	72 430	169 271

CFR: case fatality rate.

Based on a 10% prevalence of substandard and falsified antibiotics, this model estimates that:

- **Up to 72 430 deaths from childhood pneumonia can be attributed to the use of substandard and falsified antibiotics that have reduced antibiotic activity.**
- **This increases up to 169 271 deaths if substandard and falsified antibiotics have no activity.**

The full model details the limitations of the available data and the modelling approach adopted.

Model 2: Malaria

A team from the London School of Hygiene and Tropical Medicine was commissioned by WHO to investigate the health and economic cost of substandard and falsified medical products for first-line treatment of uncomplicated *Plasmodium falciparum* malaria in sub-Saharan Africa.

The prevalence of substandard and falsified antimalarials was based on a literature review of studies of antimalarial quality in sub-Saharan Africa. The analysis modelled the incremental impact of their prevalence on treatment effectiveness. Health impact was measured in terms of deaths and disability-adjusted life years, and economic impact in terms of patient and provider costs related to additional treatment and further care needed due to failure of initial treatment. Table 4 summarizes these estimates.

Table 4: Health and economic impact due to reduced effectiveness of substandard and falsified antimalarial products

	Incremental health impact (deaths)		Incremental economic impact (US$2017)	
	WMR* cases	**CHAI cases**	**WMR cases**	**CHAI* cases**
Base case	72,000 (40,000-98,000)	266,906 (147,000-364,000)	12,100,000 (6,700,000-16,500,000)	44,700,000 (24,800,000-60,800,000)
CFR adjusted case	31,000 (17,000-43,000)	116,000 (64,000-158,000)	10,400,000 (5,800,000-14,200,000)	38,500,000 (21,400,000-52,400,000)

CFR: case fatality rate.

*WMR: World Malaria Report; CHAI: Clinton Health Access Initiative.

For both the base case and CFR-adjusted case, it is estimated that incremental deaths in sub-Saharan Africa due to substandard and falsified antimalarials comprise:

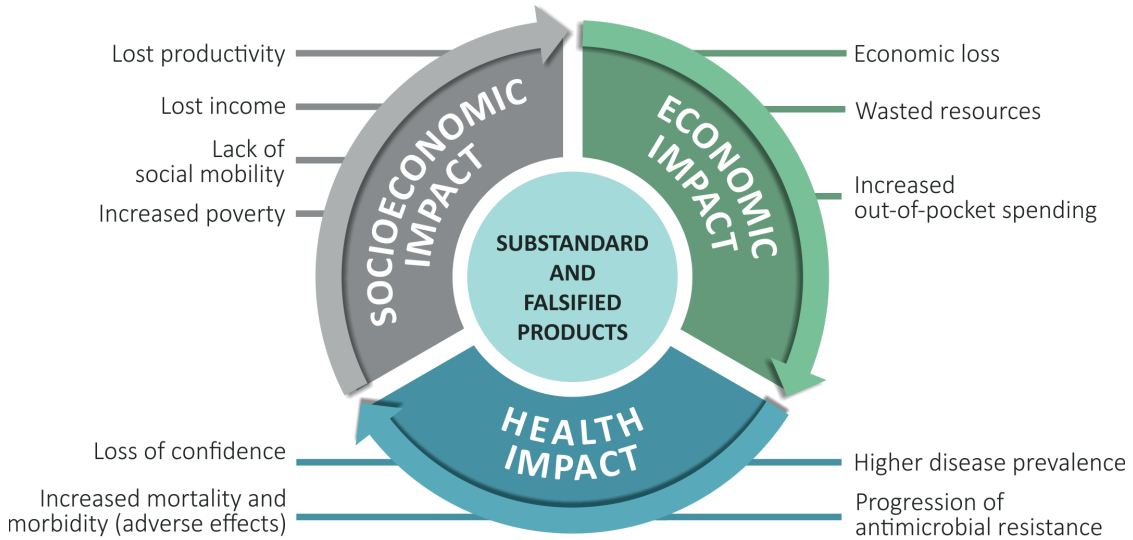
- **approximately 2.1% to 4.9% of total malaria deaths, or**
- **approximately 3.8% to 8.9% of malaria deaths relating to patients seeking treatment.**

The full model details the limitations of the available data and the modelling approach adopted.

Key areas for consideration

The study is a step towards gaining a better understanding about the socioeconomic and public health impact of substandard and falsified medical products (summarized in Fig. 1), but there is more to be done.

Fig. 1: Impact of substandard and falsified medical products



Conclusion

This study has focused on published surveys conducted between 2007 and 2016 and has applied strict criteria to the use of the publicly available data. It has highlighted limitations, gaps in the data and further research required to more accurately estimate the scope and scale of the problem of substandard and falsified medical products and the harm they cause. However, it is clear that substandard and falsified medical products pose a very significant threat to health and undermine the ability to treat and prevent disease. To complete this picture, better reporting systems and greater transparency within and between countries is required, together with wide multistakeholder and effective public and private sector engagement. It will also require removal of barriers to the sharing of information, allowing more rigorous data analysis and research to enable identification and effective response to the weaknesses, vulnerabilities and medicines at most risk.

It is well recognized that investing in public health generates cost-effective health outcomes and contributes to wider sustainability, with economic, social and environmental benefits.[1] Substandard and falsified medical products are widespread and they affect all regions, income levels and therapeutic categories. They undermine investments in health systems, efforts to reduce the burden of disease and waste precious resources.

The public health response to this issue must be scaled up, with policy decisions reached at the global level translating into actions on the ground. This will require appropriate financial and human resources. Strengthening regulatory capacity and systems is a key step and a sound investment in safeguarding the manufacture, distribution and supply of medical products.

Taken in conjunction with the report on the *WHO Global Surveillance and Monitoring Surveillance System for substandard and falsified medical products*, it is hoped that these two publications will provide the impetus to make a compelling case to governments for prioritizing the prevention, detection and response to substandard and falsified medical products as a "good buy" for health.

1 The case for investing in public health: A public health summary report for EPHO 8. Copenhagen: WHO Regional Office for Europe; 2014 (http://www.euro.who.int/__data/assets/pdf_file/0009/278073/Case-Investing-Public-Health.pdf).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