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## Review

## Measuring antibiotic consumption in low-income countries: a systematic review and integrative approach

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## ABSTRACT

Antibiotic resistance is a global issue. Risk factors specific to low-income countries (LICs), including non-prescribed antibiotic use, place them at risk for the emergence of resistance and make them important targets for reducing the burden of resistance worldwide. Responding to this threat in LICs means first having access to appropriate antibiotic consumption data. A PubMed search was conducted for studies examining antibiotic consumption in the community in LICs. For the articles included in the analysis, the methodologies used, type of data gathered and methodological appropriateness in responding to specific LIC data needs were noted. Of the 487 articles identified by the search strategy, 27 were retained for final analysis. Four main investigative methods were identified, including pharmacy/hospital document reviews, the simulated client method, observed prescribing encounters/patient exit interviews and community surveys. Observed encounters and exit interviews are well adapted to answering a number of important questions surrounding antibiotic consumption but may include bias and miss some sources of non-prescribed antibiotics. Community surveys are the only approach able to fully account for non-prescribed antibiotics and should be used as the first step in an integrative approach towards antibiotic consumption measurement and monitoring in LICs. Antibiotic consumption data needed for programmes to control use must take into account the LIC context. An integrated and adaptive approach beginning with community surveys responds to the various data needs and difficulties of LIC contexts and may help facilitate the investigation and optimisation of antibiotic consumption in these settings.

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## 1. Introduction

Resistance to antibiotics is a global issue. High levels of resistance have been reported both in high-income countries and low-income countries (LICs), leading the World Health Organization (WHO) to call this issue a 'global health security threat' [1]. A number of specific risk factors exist for the development and spread of resistance in LICs, including substandard hygiene and living conditions, misuse of antibiotics, over-the-counter and parallel market access, and counterfeit or poor quality drugs [2,3]. The role of LICs in the emergence and rapid spread of resistance is highlighted by the worldwide spread of carbapenem-resistant New Delhi metallo- $\beta$ -lactamase 1 (NDM-1)-producing Enterobacteriaceae [4]. The adverse effects of antibiotic resistance are particularly worrisome in LICs where infectious disease rates are significantly higher than devel-

oped countries and where access to second- or third-line antibiotics is often limited [5]. Steps to control rising resistance are urgently needed, including programmes to monitor and control antibiotic consumption in LICs where consumption is growing rapidly [6,7].

The WHO has developed a global strategy to reduce antibiotic resistance and lower consumption and suggests a number of potential intervention targets, including the general population, antibiotic providers, hospitals and government policies [8]. Prioritising these interventions requires reliable data on issues such as frequency and amount of antibiotic use, patient and provider knowledge, drug source and quality, healthcare-seeking behaviour and reasons for antibiotic use. Reliable consumption information is also needed to monitor trends, to evaluate the impact of interventions, and importantly, to generate the political will to deal with this issue [9].

In LICs, these data can be unreliable or non-existent. Furthermore, gathering comprehensive data is complicated by the large number of non-prescribed and parallel market sources available in many of these countries [2,3].

Purchasing antibiotics without a prescription, including from non-medical sources, is common in many LICs and can account for as much as 100% of consumption among certain populations [3,10].

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Non-prescribed antibiotics are also a driving factor in increasing global antibiotic consumption [11]. Methods capable of accounting for non-prescribed antibiotic sources are thus important to accurately measure consumption in these contexts.

Current reports of consumption in LICs rely on diverse methodologies, making comparison difficult. The WHO has published guidelines on investigating medicine use by consumers and in health facilities. Numerous methodologies are detailed and analysed but no clear roadmap for investigation of community antibiotic consumption is presented [12,13].

Here we review currently used methodologies for antibiotic consumption measurement in LICs and propose an integrative and adaptive approach to respond to this issue.

## 2. Search methods

To investigate the methods used for measuring antibiotic consumption in LICs, a literature review was conducted by searching PubMed (last search 30 September 2015) using the search terms 'antibiotic', 'antibiotic consumption', 'developing country', 'low-income country', 'non-prescription antibiotic', 'community' and 'survey'. The search terms 'infection' and 'tuberculosis' were excluded and the search was limited to articles published since 1990. Reports on measuring antibiotic or drug use, including WHO reports, were also examined and references from these reports were screened for inclusion, as were selected articles from the author's library. LICs were defined as countries classified by the World Bank as 'Low-income economies' or 'Lower-middle-income economies' [14].

Inclusion criteria included measures of community and/or outpatient antibiotic consumption. Studies measuring only hospital inpatient use or limited to only one pathology were excluded. Identified articles were first screened by title and abstract, followed by full reading of the retained articles. For articles included in the analysis, the methodologies used, type of data gathered and methodological appropriateness for desired data as discussed were noted.

## 3. Results and methodology review

Of the 487 studies identified through the search strategy, 37 were selected for full reading. Of these, 27 were retained in the final analysis (Fig. 1). Four main investigative methods were identified from the literature search results, including pharmacy/hospital document reviews, the simulated client method, observed prescribing encounters/patient exit interviews, and community surveys. The articles including methods used and main measures can be seen in [Supplementary Table S1](#).

One of the simplest ways to investigate antibiotic use in a community is to review pharmacy or hospital records or prescription documents [15–21].

In Vellore, India, Chandy et al collected antibiotic sales records from participating pharmacies and rural hospitals [19]. Data allowed for the calculation of defined daily doses (DDDs) dispensed per 100 patients along with the proportion of antibiotics dispensed by pharmacy type and location. DDDs are a standardised measure of drug quantity developed by the WHO to allow for easy comparison between drugs and across healthcare settings. Kotwani et al collected bulk purchase information from participating pharmacies in Delhi, India, and calculated consumption as DDDs purchased per 1000 population. The authors also identified antibiotic proportions and compared proportions between structure types [21].

Outpatient and prescription records were analysed for participating centres in South Africa (Brits and Durban) by Holloway et al [20]. The proportion of patients with a prescribed antibiotic and the proportion of prescriptions with an antibiotic were calculated along with DDDs per 100 patients attending the facility. Trends in antibiotics used by facility type were also analysed [20]. A recent review

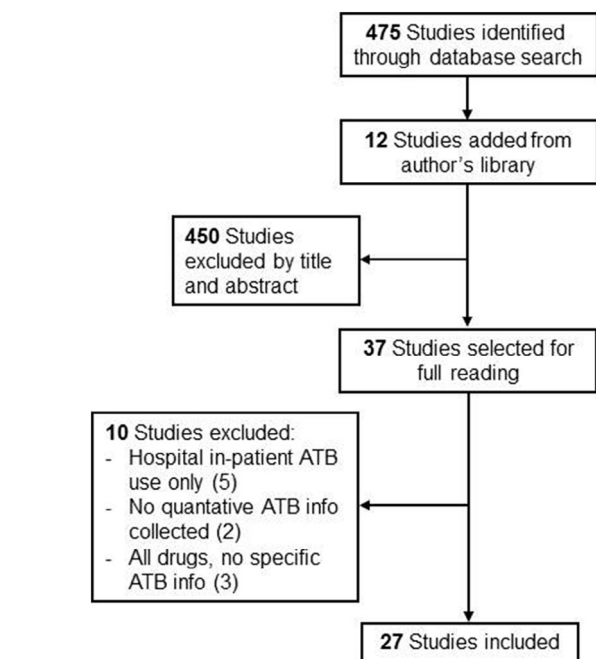


Fig. 1. Flowchart of literature search. ATB, antibiotic.

of global antibiotic use and trends also used pharmacy sales records to estimate country-level antibiotic consumption [7].

The major strength of these methods is that these types of data take relatively little time to gather, making them a potential candidate for surveillance. Antibiotic type, proportion and DDDs can be easily calculated. A number of weaknesses also exist with these methods. First, the choice of pharmacies or health centres is not random. Only those facilities with appropriate data willing to participate can be included, which may bias results [20]. In the case of bulk purchase studies, these data may not correspond directly with purchased or consumed antibiotics. This method also makes it difficult to determine community-level consumption, as relating participating pharmacies to a well-defined population is difficult.

Importantly, potential sources of non-prescribed antibiotics outside pharmacies are not measured and no information is available on the proportion of antibiotics sold in the pharmacy without a prescription. The limited information gathered on important aspects such as symptoms or patient knowledge, attitudes and beliefs along with potential biases related to this approach must be taken into account when using this method.

The simulated client method involves trained field workers posing as clients of pharmacies or health centres. The field worker will present symptoms (either their own or those of another person), ask for medication and measure the reaction of the medication provider [18,22–24]. Measures can include medication delivered, recommendations or information given [13].

In Bolivia, Bartoloni et al trained six 'actors' to describe various episodes and patient profiles to all pharmacies in a rural town [18]. Actors asked for medication without a prescription and the main outcomes included the proportion of visits resulting in the purchase of an antibiotic without a prescription. A similar study in Vietnam trained field workers to pose as the mother of a child suffering from either respiratory symptoms or diarrhoea and to ask for medication without a prescription [23]. This technique has also been used in developed countries. In Spain, Llor and Cots used this technique both to estimate the proportion of pharmacies providing antibiotics without a prescription and to gather information about dispenser attitudes and beliefs about non-prescribed antibiotics [25].

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