



The use of antimicrobials in global pig production: A systematic review of methods for quantification



Angkana Lekagul^{a,b,*}, Viroj Tangcharoensathien^b, Shunmay Yeung^a

^a London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK

^b International Health Policy Programme, Ministry of Public Health, Nonthaburi 11000, Thailand

ABSTRACT

Background: Overuse of antimicrobials in both humans and animals is recognized as one of the main drivers of Antimicrobial Resistance (AMR); and the optimisation of their use has been advocated as a key strategy for dealing with AMR. The measurement of antimicrobial use is vital for the design, monitoring and evaluation of such strategies. This systematic review describes and compares methods and measurements used to quantify antimicrobial use in pigs in order to inform efforts to standardize measurement.

Methods: The peer-reviewed literature was systematically searched using four online databases: MEDLINE, ScienceDirect, Scopus and Web of Science. Eligibility criteria for inclusion in the review included: articles published in English, involving pigs of any age and types of production, providing quantitative data on antimicrobial use, containing a clear description of the methodology, and having moderate to high rank in the quality assessment.

Results: Of 2,362 abstracts reviewed, a total of 25 studies were included based on the eligibility criteria. All studies were published between 2001 and 2017. Twenty of the studies were conducted in eight European countries. Twelve studies estimated antimicrobial use and eight studies were primarily methodological papers comparing different methods or variables, or developing new methods. The two main sources of antimicrobial use data were farm surveys and national sales data.

A large variety of units of measurement was found. In this review, the ten measurements identified were categorized into four groups: 1) antimicrobials use measured by milligrams of active substance per animal weight; 2) antimicrobials use measured by daily dose per weight at treatment; 3) antimicrobial use measured by daily dose per treatment period; and 4) antimicrobials use measured by daily dose per period at risk of treatment.

Conclusion: There is no global standardized measurement of antimicrobial use in pigs. Given the importance of monitoring the use antimicrobials, we recommend that at a minimum, all countries should develop macro-level monitoring using national sales data and report use by milligram of active ingredients per Population Correcting Unit. Monitoring in specific animal species requires the development of systems to capture prescription at national or farm level. Findings from monitoring antimicrobial use may help to guide effective interventions for optimising use of antimicrobials, as recommended by the WHO Global Action Plan on AMR.

1. Background

Antimicrobial Resistance (AMR) is an increasingly serious threat to global public health. Overuse of antimicrobials can accelerate the

emergence of antimicrobial resistance (World Health Organization, 2015b). In livestock industries, large amounts of antimicrobials are used for both therapeutic and non-therapeutic purposes including growth promotion (Aarestrup, 2005). In response to global concerns

Abbreviations: ADD, animal daily dose; ADDD, animal defined daily dose; AMR, antimicrobial resistance; CASP, critical appraisal skills programme; DADD, defined animal daily dosage; DDD, defined daily dose; DDDA, daily doses animal; DDDvet, defined daily dose; DCDvet, defined course dose; DPD, daily product dose; EMA, european medicines agency; ESVAC, european surveillance of veterinary antimicrobial consumption; FAO, food and agriculture organization; nDDay, daily dose per animal year; OIE, organization for animal health; PCU, population correction unit; PDD, prescribed daily dose; PrDD, product-related daily doses; TI, treatment incidence; UDD, used daily dose; WHO, world health organisation

* Corresponding author at: London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK.

E-mail address: angkana@ihpp.thaigov.net (A. Lekagul).

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about AMR, in 2008, the World Organization for Animal Health (OIE) launched guidelines on the prudent use of antimicrobials in veterinary medicines, which describes the respective responsibilities of relevant stakeholders such as veterinarians, regulators, pharmaceutical industries, animal producers and consumers (World Organisation for Animal Health (OIE), 2008).

Measuring antimicrobial use is critical to understanding the magnitude and profile of antimicrobial resistance in countries. Measurement is the first step to detecting whether there is excessive and inappropriate use and monitoring whether policies aimed at optimizing use are successful. Recognising this, international organizations such as FAO, OIE and WHO, have recommended that countries develop systems for monitoring antimicrobial consumption (World Health Organization, 2015a, OIE, 2016; FAO, 2016). The World Health Organization (WHO) guidelines defines antimicrobial “consumption” data captured from aggregate sales data such as form importer, local manufacturer or wholesales, whilst data on antimicrobial “use” are collected from patient-level data such as medical records and prescriptions (World Health Organization, 2017). Whilst there has been significant progress in the monitoring of antimicrobial use and consumption in the human health sector, action in the animal health sector has lagged behind (Schar et al., 2018). Some European countries established national programs for the surveillance of antimicrobial consumption in animals for more than 20 years ago, specifically DANMAP in Denmark in 1995 (Statens Serum Institut, 2012), MARAN in Netherlands in 1998 (Anonymous, 2012) and SWEDRES-SVARM (SWEDRES and SVARM, 2014). The European Medicines Agency established the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project in 2009 (Agency, 2017). ESVAC compiles, verifies and reports on antimicrobial consumption of veterinary antimicrobial agents in 29 European countries. Data are collected through a network of national focal points. Furthermore, ESVAC has been striving to set up a standardised methodology to allow for cross country comparisons. The monitoring of antimicrobial consumption serves various objectives. It monitors time trends of antimicrobial use, compares use by different antimicrobial classes, identifies high users and promotes more prudent use, and studies the association between level of usage and bacterial resistance (Collineau et al., 2017).

Currently, there is a wide variation in the availability and type of data, methods and use measurement across countries. The lack of uniformity hampers cross-country comparisons (Collineau et al., 2017). In order to guide the strengthening of existing monitoring systems and the development of new ones to facilitate cross-country comparisons, it is essential to understand the different existing methods, their strengths, limitations and operational feasibility.

This systematic review will describe and compare methods and measurement to quantify antimicrobial use in pigs, in order to contribute to the process of future guideline development of monitoring the antimicrobial use.

2. Method

2.1. Scope of study and research question

The operational definitions of the terms used in this review are as follows.

Term	Definition
Antimicrobials	According to OIE definition, an antimicrobial is considered as a naturally occurring, semi-synthetic or synthetic substance that exhibits antimicrobial activity (it kills or inhibits the growth of micro-organisms) at concentrations attainable <i>in vivo</i> . Anti-helminthic and

substances classed as disinfectants or antiseptics are excluded from this definition (World Organisation for Animal Health (OIE), 2015).

Pig	The term refers to all stages of swine production including breeding and gestation, farrowing (from birth to weaning), nursery and feeding and finishing.
Use and consumption	As explained above WHO defines “use” data as estimates derived from patient-level data. It may focus on how and why antimicrobials are being used by health care providers and patients. “Consumption” data are usually reported when information on antimicrobial use in patients is not available. It can be collected from several sources such as import data, wholesale data or aggregated health insurance data. Consumption data provides a proxy estimate of the use of antimicrobials (World Health Organization, 2017). However, in this study, for simplicity the term “use” is applied to refer to both use at farm level and consumption at aggregate national or sub-national level.
Biomass	The weight or total quantity of living organisms of one animal species or of all the species in the community. Using biomass for antimicrobial consumption aims to compare the weight of animals between different species and between human and animals.

This review covers use of antimicrobials in pigs, with the following research question: “What methods and measurements are used to quantify the use of antimicrobials?”

2.2. Search strategy

2.2.1. SPIDER tool

A “SPIDER” tool was applied in order to specifically identify relevant quantitative and mixed-method studies. It covers the Sample, Phenomenon of interest, Design, Evaluation and Research type (Cooke et al., 2012).

S: 1) Surveys based on end-point antimicrobial usage: veterinary prescription, usage by pig farmer

2) Antimicrobial sales data (from pharmaceutical operators, such as importer, manufacturer, wholesaler)

P and I: Antimicrobial use in pigs D: Observational studies, intervention studies

E: Methods used for the measurement of antimicrobial use R: Quantitative study

2.2.2. Eligibility assessment of studies and inclusion criteria

The following inclusion criteria were considered:

- (i) the paper was published in, or translated into, the English language,
- (ii) the study involved pigs of any age and type of production,
- (iii) the study provided quantitative data on antimicrobial use with a focus or clear explanation of the methodology in pigs or other food producing animals including pigs,
- (iv) The study had moderate to high ranking of a quality assessment.

2.2.3. Search protocol

Literature on the use of antimicrobials in pigs was systematically

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