Economic evaluation of antimicrobial usage surveillance in livestock

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Summary

There is increased pressure by governments and industry to develop national antimicrobial usage (ABU) surveillance programmes in animals. This article presents a methodological approach to conduct cost-effectiveness analysis (CEA) of such programmes.

We propose seven objectives of ABU surveillance: quantification of usage, detection of trends, detection of hotspots, identification of risk factors, facilitate research, evaluate impact of policies and disease, and demonstrate compliance with regulations. Achievement of these objectives should support decision process on interventions, generate trust, incentivise reduction in ABU and reduce the risk of antimicrobial resistance. CEA can be conducted for each objective by dividing the cost of the programme with the surveillance capacity (performance) to meet these objectives. We suggest that precision and accuracy of surveillance outputs can be used as performance indicators. Precision depends on the level of surveillance coverage (SC) and surveillance representativeness (SR). Accuracy is influenced by the quality of the farm records and SR. We argue that there is an increase in marginal cost per each unit increase of SC, SR and data quality. This is due to increasing difficulty to recruit farmers due to potential barriers such as staff capacity, capital availability, computing literacy and availability, and geographical difference, amongst other factors. We conduct a simulation model to test the approach using the quantification of ABU as primary objective, and we provide evidence of the application of the law of diminishing returns. CEA can be used

to support decisions regarding the level of coverage, representativeness and data quality required in ABU programmes.

Keywords

Antimicrobial usage – Cost-effectiveness analysis – Data collection – Data precision – Data quality – Livestock – National surveillance system.

Introduction

The increased use of antimicrobials is recognised as the main driver for the selection and spread of antimicrobial resistance (AMR) bacteria in humans and animals [1]. The monitoring of antimicrobial usage (ABU) through active surveillance programmes is being implemented or under consideration in most high-income countries. Setting ABU targets for animal farming is seen as one of the optimum strategies for reducing usage. However, data on ABU in European countries is often inferred from antimicrobial sales to pharmacies, wholesalers, and veterinarians. Whilst this method assumes nearly maximum coverage, data has low resolution and does not reflect accurate usage. This is because many farmers have a level of autonomy over treatment decisions [2, 3]. Furthermore, sales data has not yet being validated against prescriptions. As such on-farm records, required under legislation in the European Union and United Kingdom (UK), should provide the most accurate, high-quality data. However, the format of these is varied (paper or electronic) and not standardised, creating challenges for collating farm-level data on ABU. It has been recognised that central digitalisation of ABU is needed for efficient surveillance [4]. The Center for Disease Control guidelines on surveillance programmes, along with the World Health Organization, state that their costs should not be estimated alone, but judged relative to the effectiveness that these programmes can bring [5, 6].

Cost-effectiveness analysis (CEA) is a tool that has been applied extensively in animal health, production and welfare to economic evaluate interventions [7]. It has been proposed as a useful technique to evaluate disease surveillance in animals [8]. The aim of this study is

to present a cost-effectiveness approach that can aid the development of a digital national centralised surveillance programmes on ABU.

Setting objectives for a national antimicrobial usage surveillance programme for livestock production

According to the World Organisation for Animal Health, the objectives of ABU surveillance programmes are to provide:

a) an indication of trends over time

b) assess potential associations with AMR (and ensure targeted response) and

c) help manage risks through evaluation of the effectiveness of interventions [9].

The ABU monitoring programme implemented in the Netherlands includes objectives to set annual targets on ABU and benchmarking of farmers and veterinarians (identification of high users or prescribers) [10].

In Table I we propose seven objectives for the establishment of an ABU surveillance programme. The capacity of the programme to achieve these objectives needs to be considered at the design stage. Farmers could benefit in several ways:

a) through benchmarking, individual farmers can compare their usage to other similar farmers and help set targets;

b) the detection of ABU hotspots (area and individual level) will allow the establishment of targeted investigations and control measures to protect the farming community;

c) the outputs can be used to provide evidence of compliance, help generate trust and facilitate access to profitable markets; and

d) the programme can incentivise reduction in ABU and reduce the risk of AMR and their economic consequences.

If the surveillance is successful in reducing ABU and controlling risk hotspots, consumers and society will benefit through:

a) better public health protection, as risk of AMR is reduced;

b) increase trust and confidence on products; and

c) economic development associated with more efficient farm systems.

In Denmark and the Netherlands, such programmes have generated evidence on association between ABU and AMR leading to significant policy changes, including the ban of antibiotic growth promoters in 2006 [10, 11, 12].

Surveillance coverage and representativeness

Surveillance coverage is defined as 'the proportion of the population of interest (target population) that is included in the surveillance activity' [13]. Bertino defined representativeness as 'the degree of capacity of the sample to exhibit the characteristics of the parent (target) population' [14]. Lack of coverage will affect the precision of ABU estimates by the programme. Lack of representativeness can lead errors in accuracy of ABU estimates. Both will jeopardise the capacity of the programme to assess the magnitude of ABU and assess trends and the effectiveness of interventions. To minimise these errors, it is essential to have knowledge on the factors influencing ABU and the spread of the population amongst these (i.e. have good understanding of the population structure). Some of the factors that can potentially influence ABU and its recording by farmers are geographical region, seasonality, production systems, herd size, computing literacy of farmers, information technology (IT) capacity (e.g. presence of computer on farms and internet services), type of contract supplier, age/experience of farmer, among other factors. The importance of these will vary depending on the country. Many of these factors will influence disease prevalence, as some regions will

have different farm density, climates and even policy environment that facilitate or difficult disease spread. Boeckel *et al.* show how ABU does vary between countries and systems [15]. Curone *et al.* provide evidence that the Holstein Friesians breed is more susceptible to diseases, such as mastitis, than local breeds [16]. This will have hence an influence on ABU. Menéndez González *et al.* found that 32% of Swiss small dairy farms used paper recording, representing a substantial barrier for electronic surveillance [17].

The target farm population can be seen as a combination of vectors representing those factors influencing ABU and recording. Each vector will classify the population in different strata ($x \rightarrow x_1, x_2, \dots, x_n$). Based on this, measuring the level of representativeness becomes a useful indicator for subsequent CEA of the surveillance and understand the quality of the sample (Figure 1). Several authors have provided suggestions of representative indexes, such as Bertino [14].

Data quality

We define data quality as the capacity of the data to accurately reflect actual antimicrobial usage on farms. Data quality will be determined by missing and incorrect data. Missing data relates to the proportion of treatments that have not been recorded in the system. Incorrect data relates to the proportion of treatments recorded incorrectly, either because numbers were entered erroneously or because the wrong antimicrobial was recorded. Both type of errors can have a different impact on the accuracy of the final ABU measurement on the farm. Missing data will underestimate the level of ABU. For example, a farm that has only recorded 80% of their treatments, could result in a falsely reduce ABU. Incorrect data can increase or decrease the estimate, particularly if these data is associated to systematic errors as opposite to random errors. Hence some of the errors will have more important weight than others, and research to understand the magnitude and reasons is needed. Both errors can be used to estimate the proportion of total treatments recorded and recorded correctly (γ), as follow:

$$\gamma = [1 - Prop(missing\ data)][1 - Prop(incorrect\ data)] \quad \text{Eq. 2}$$

For example, $\gamma = 0.9$ indicates that full data has been recorded correctly for 90% of treatments implemented on the farm.

Several studies have identified the potential under-reporting of ABU in medicine records, including falsifying such records [18, 19, 20, 21]. A recent UK study found that on-farm records vary in quality, and as a result veterinary sales data are currently the most reliable source of information on ABU [22]. Menéndez González *et al.* study of small Swiss dairy farms found that antibiotic name and dosage were often inaccurate, with under- and over-dosing frequently observed [17]. Trauffler *et al.* study of Austrian pig farms showed that 14% of unrealistic drug amounts were present in farms records [23].

Calculation of the cost-effectiveness of the antimicrobial usage surveillance programme (CE_i)

For surveillance programmes, a CEA can be conducted for each of the objectives (i) of the surveillance, using a cost-effectiveness ratio (ACER):

$$\boldsymbol{objective\ specific\ CER_i} = \frac{\boldsymbol{Ct}}{\boldsymbol{K_i}} \qquad \text{Eq. 3}$$

Where Ct are the total costs of the surveillance and K indicate the performance of the programme for objective i. The incremental cost-effectiveness ratio (ICER) can also be calculated to assess the value of changes in key surveillance parameters, such as coverage and representativeness. The following equation illustrate the ICER for changes in surveillance coverage:

$$\boldsymbol{ICER} = \frac{\boldsymbol{Ct}_{X\%\ coverage} - \boldsymbol{Ct}_{10+X\%Coverage}}{\boldsymbol{K}_{at\ X\%\ coverage-}\ \boldsymbol{K}_{at\ 10+X\%\ coverage-}} \qquad \text{Eq. 4}$$

In this case, ICER will allow to understand the increase cost of each additional performance gained by increasing the surveillance coverage by 10%. ICER may represent a more useful approach to facilitate decision making on surveillance design.

The overall costs of the programme can be calculated as follow:

$$\boldsymbol{Ct} = \boldsymbol{Co} + \boldsymbol{Ctf} \qquad \text{Eq. 5}$$

Where Co are the total costs incurred by the institution organising and implementing the surveillance. This could be a national or regional government or an industry board. Cf are the total costs incurred by the farmers participating in the surveillance programme. The performance indicators (K) is defined based on the objectives set for the programme. This could be for example the power to identify trends in ABU, the precision of ABU measurement at national or farm or regional levels, etc.

Cost of the programme

Effectiveness of antimicrobials can be considered a public good, as the society benefits from proper use. Over-consumption of antimicrobials can also create negative externalities (i.e. AMR). At the same time, farmers benefit from antimicrobials as they are seen as essential for control of animal diseases and ensure efficient production. Hence, the assignment of costs of an ABU surveillance programme between industry and public requires careful consideration. In the Netherlands, these are implemented through public–private partnerships. In this section, we focus on the type of costs incurred for implemented such a surveillance programme [10].

The cost incurred by institutions organising and implementing the programme (Co) can be calculated as follow:

$$Co = Startup\ costs + \sum_{t=1}^{tmax}\left(\frac{Fixed\ costs + Variable\ costs}{(1+r)^t}\right) \qquad \text{Eq. 6}$$

The start-up costs are those expenses required before the programme starts. Variable costs and fixed costs are incurred in a yearly basis (t), with $tmax$ being the final year of the analysis. For some studies, this can be short term analysis (e.g. if evaluating cost-effectiveness of the surveillance in detecting trends) or long term (e.g. if evaluating impact of surveillance in reduction of AMR and public health consequences). The costs should be discounted into present value using the discount rate (r).

The type of costs are shown in Table II. The relevant start-up costs is the cost of developing an application interface that can extract data

from an existing software used by farmers. In most countries, there is a diversity of data recording software. A UK survey of dairy farms reported that eight different software were used by farmers for recording of ABU [24]. The number of farmers using each type of software will have an effect on the potential coverage of the surveillance.

The yearly fixed costs of the programmes are a combination of the annual staff cost needed for running the programme, including extracting the data from farms into the centralise system, cleaning and analysing the data, and produce the relevant reports; data storage costs; and the cost of maintaining equipment. If the programme is compulsory, the cost of staff needed to enforce the programme should be accounted. The yearly variable costs will vary depending on the number of farmers participating in the surveillance each year and on the number of farmers remaining to be recruited to achieve suitable coverage. The cost of training farmers can depend on the IT capacity of these. Those farmers that normally record data electronically before the implementation of the surveillance will require less training than those not recording and not familiar with computers. The cost of recruiting farmers will not be linear, but there will be an increase in the marginal cost of recruiting an additional farmer. Initially it will be relatively easy to recruit those new farms that have increased motivation, are highly accessible and have good IT capacity. After this, the effort to recruit new farmers will increasingly require larger costs, as farmers become more difficult to recruit. This may affect the representativeness of the surveillance, as those not willing to participate are likely to have different ABU practices than the rest. Figure 2 shows an example of the production function for with the total costs for the organising institution, where the slope of the curve will depend on the difficulty to recruit farmers in a country. Yet, over time, once reached the desire coverage level, the costs will remain constant.

The cost incurred by individual farmers will be different depending on the population strata and their year of participation in the programme (as experience will reduce cost). Many of the costs will depend on the

willingness of the farmer to pay for these. Low willingness to pay will impact participation and data quality if full costs required are not met. In addition, some farmers may have to incur an equipment and infrastructure costs to ensure that they have computer, membership to recording software, electricity, and internet connectivity on the farm. These represents the biggest barrier for ABU surveillance in low- and middle-income countries.

Calculation of performance

Each objective will require its own performance measurement. For example, performance can be measured based on the capacity to prevent AMR or the number of life saved and quality of life improved because of avoiding treatment failure in human and animals. Here, we however focus on the objective of the surveillance to quantify ABU at national level, which can be used to set targets, detect trends or as benchmarking for farmers. For this, accuracy and precision can represent utility, as the more precise and accurate the estimation is the better we can demonstrate changes in ABU and efficacy of policies or interventions. Hence, precision and accuracy will be the measures of surveillance performance.

To measure these performance indicators, we can start by measuring the ABU per kg at farm level for the i-th farm in the j-th strata. We denote this as c_{ij}, and is calculated as followed:

$$c_{ij} = \frac{\sum_q^k (ab_{iq})}{n_{ij}} \qquad \text{Eq. 7}$$

Where ab_{iq} is the quantity of ABU for the q-th treatment $(q_1, q_2, \dots, q_k)$, and n_{ij} denotes the herd size (in kg) for the i-th herd in strata j. The equation can be corrected to account for missing data as followed:

$$c_{ij\ corrected} = \frac{c_{ij}}{[1 - Prop\ (missing\ data)]} \qquad \text{Eq. 8}$$

The equation assumes that the treatments not entered have the same ABU distribution than those entered. If false data is assumed to follow a random error (e.g. typing mistake), then it may not require

correction. Yet, research to understand the nature and distribution of data quality is essential. Based on this, average ABU per kg (c) at each strata and national level can be estimated. The performance then can be calculated based on the magnitude of the range of c, so the precision of the final estimate which is equal its standard error (SE) and the accuracy based on data quality:

$$K_{precision} = SE\ (c) \qquad \text{Eq. 9}$$

$$K_{accuracy} = c_{Missing\ data \neq 0 \frac{and}{or} imperfect\ R} - c_{Missing\ data = 0\ and\ perfect\ R} \qquad \text{Eq. 10}$$

Where R denotes representativeness of the sample in the programme. Note that surveillance with low representativeness, can correct the accuracy of the measurement by calculating the weighted mean (weights based on the proportion of farms in the population within each strata). This will however increase standard errors of the final measurement, and reduce precision of the estimate.

Simulation of antimicrobial usage surveillance cost-effectiveness for a country

To illustrate the methodology, we simulated the population of dairy farmers in a country. The simulation generated a population of 8,040 farms dispersed in four different regions. We used only one type of strata for simplicity. The distribution of ABU from 40 English and Welsh farms based on farm record data [17], was used to establish usage in all farms in our simulation. The true average ABU per kg is 19.81 mg/kg (sd=7.48). Figure 3 shows the level of precision of the measurement of mean ABU per kg. For 10% and 50% coverage, which is shown as the confidence intervals based on SE. The figure shows the changes in accuracy due to reduction in data quality.

The cost of the surveillance for the organising institution and the farmers were simulated, based on a function that reflects increase marginal costs of increasing participation of farmers in the programme. Cost-effectiveness was the calculate as in equations 3 and 4 using precision (the standard error) to measure performance.

If we assume perfect representativeness and data quality, the cost-effectiveness of the programme according to coverage is presented in Figure 4. The analysis shows that a small SE of 0.8 is achieve with 10% coverage only, with a small cost per 1 mg of SE. This SE error reduces significantly with increase coverage, while cost increases substantially after 40, 60 and 80% coverage reflecting the law of diminishing returns. Surveillance designers can use this to know the increase cost of the programme per unit of precision gain, and decide the most economically acceptable level of coverage needed.

We argue that achieving adequate representativeness and data quality will represent an increase cost to the programme and to farmers, and hence impact on the programme cost-effectiveness. This means that for the same level of coverage, a perfect representative sample will have smaller standard errors than a non-representative sample. A similar effect will occur with data quality, as increasing data quality will require training, incentives and regular validation, and hence increase programme costs. Considering level of acceptable representativeness and data quality in cost-effectiveness evaluation is an important factor.

Conclusions

The design of national surveillance programme requires multiple decisions which have important economic costs and performance consequences. A CEA can inform policymakers with decisions of trade-offs between increasing expenditure on surveillance and the gain in programme performance. Whether a given increase in performance is desired or useful will also be dependent on the programme manager. Grosbois *et al.* suggest that CEA should assess the cost associated with the probability that the information generated by the programme may lead to inappropriate interventions or no interventions [25].

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Table I

Proposed objectives of a national antimicrobial usage surveillance programme

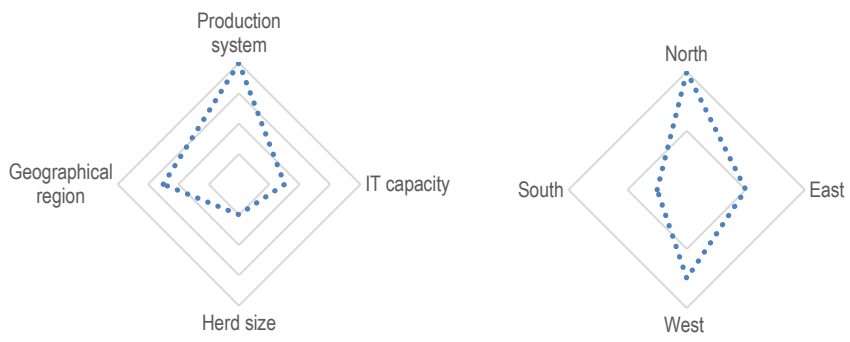
Objective	Reason
Quantify antimicrobial usage	Generates awareness of the magnitude of usage
	Allow comparison with other countries or regions
	Provide benchmarking data for farmers to set objectives
	Allow generating targets for reduction in usage
Detect trends and patterns	Understand whether usage is increasing or decreasing
	Detect seasonal variations in usage and the magnitude of variance
	Assess efficacy of policies or interventions
Detect hotspots	Identify areas with significant higher usage of antimicrobial
	Identify farmers and veterinarians that are high or very high users or prescribers
	Identify sudden localise increase in usage due to disease outbreak (real time surveillance required)
Identify risk factors	Determine the possible causes for antimicrobial usages
	Identify systems that are more likely to have increased usage
Facilitate research	Investigate association with antimicrobial resistance trends or emergence
	Understand links with animal and human health
Evaluate impact	Determine effectiveness of policies or interventions
	Allow determine impact of diseases
Allow compliance	Allow demonstrating compliance with industry targets
	Assess level of compliance with assurance standards
	Generate trust and facilitate trade

Table II

Potential costs incurred in the development and implementation of a MCSP

	Cost incurred by the organising institution	Cost incurred by farmers
Start-up costs	Costs to access the funding needed	Equipment (i.e. computes)**
	Costs of designing the programme	
	Costs of experts required for the design and review of the programme	
	Costs for programme approval and validation	
	Costs of equipment or technology (inc. developing an application interface to extract data from farmers)	
	Costs of setting enforcement mechanism*	
Fixed costs	Permanent staff costs	Equipment maintenance**
	Cost of maintaining equipment	Recording software subscription**
	Storage costs	Internet access**
		Electricity**
Variable costs	Costs of training new farmers	Staff time (opportunity cost)
	Cost of communicating results	Training costs
	Cost of recruiting new farmers	
	Cost of enforcement*	
	Cost of incentivising data collection	

* Only applicable for compulsory programmes
** Only for those farmers lacking such cost before the programme



IT: information technology

Figure 1

Example of representativeness index of a hypothetical antimicrobial usage surveillance in a country

The left figure shows the representativeness for different factors, while the right figure shows the representativeness of different strata within one factor (in this case geographical region). In the example, the surveillance achieves good representation in IT capacity and herd size but is potentially deficient in production systems and geographical regions. In terms of regions, the areas with poorer representativeness are the North and the West

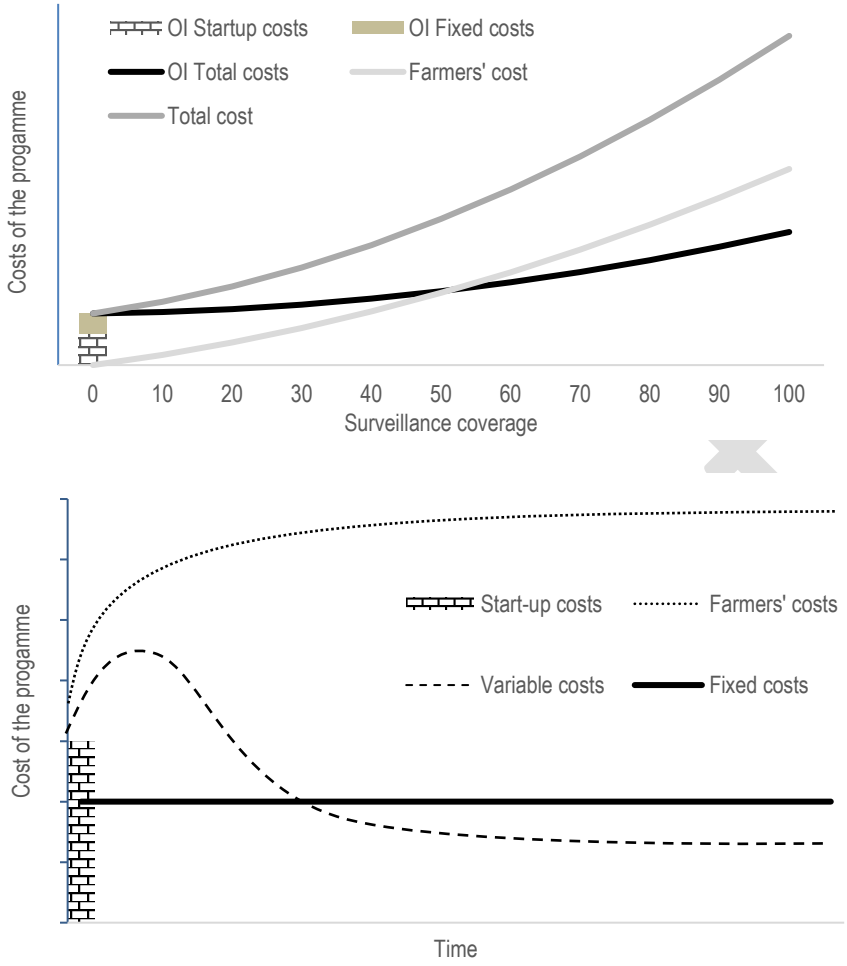


Figure 2

Example of the costs of National surveillance antimicrobial usage programme

Top figure shows the costs incurred by the organising institution (OI) and by farmers depending on surveillance coverage. Bottom figure shows the evolution of cost over time

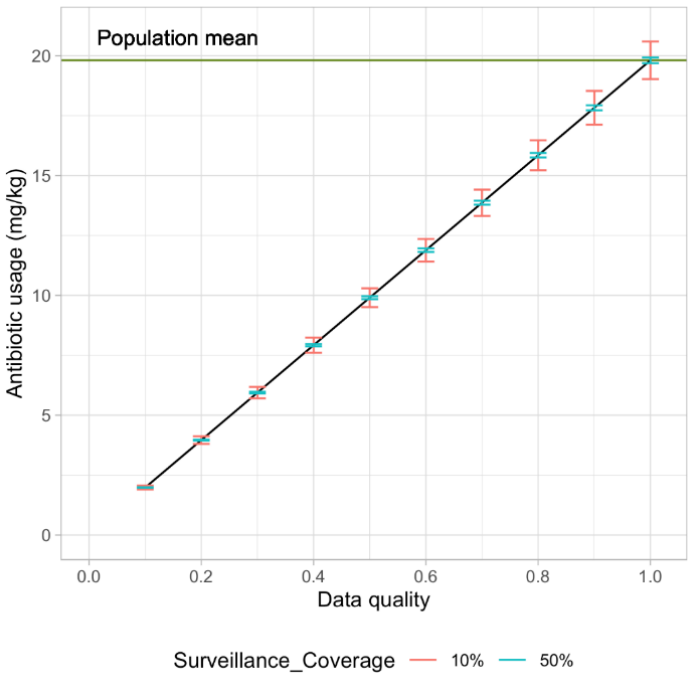


Figure 3

Estimation of mean antimicrobial usage from a national surveillance programme with 10% and 50% farm coverage, and depending on data quality of farms records

The horizontal line shows the true mean in the population

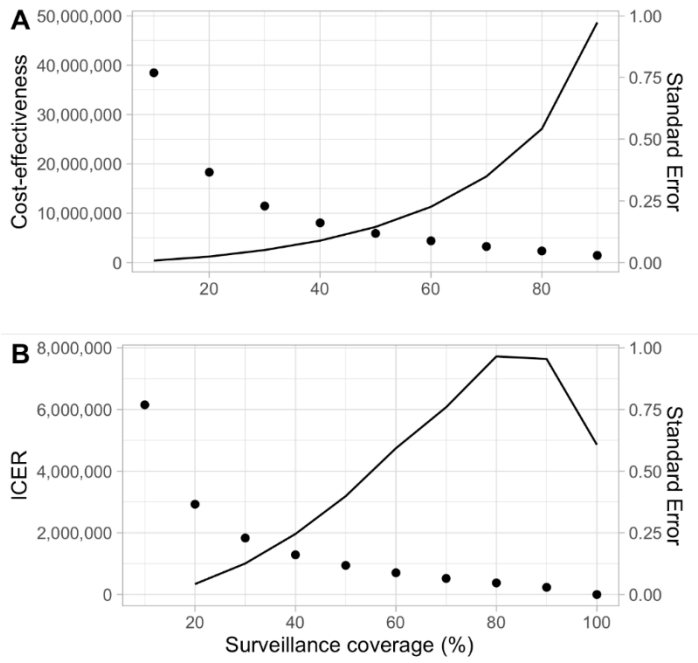


Figure 4

Average cost-effectiveness ratio (ACER) (top) and incremental cost-effectiveness ratio (ICER) (bottom) of surveillance programme on antimicrobial usage in animal farms with different level of surveillance