

**INTERVENTIONS AGAINST ANTIMICROBIAL RESISTANCE:  
A REVIEW OF THE LITERATURE AND EXPLORATION OF  
MODELLING COST-EFFECTIVENESS**

**A report prepared for the Global Forum for Health Research**

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# EXECUTIVE SUMMARY

## 1. Introduction

Antimicrobial resistance (AMR) is one of the biggest challenges to face global public health at the beginning of the third millennium. However, there is little accurate information concerning many aspects of AMR, in particular, the cost and/or effectiveness of various strategies that may prevent the emergence of AMR and/or limit the transmission of resistant organisms, or resistance determinants. The Global Forum for Health Research therefore provided funding to:

1. Review current knowledge concerning the cost and/or effectiveness of (medical) interventions aimed at reducing the emergence and transmission of AMR in humans; and
2. Explore the feasibility of, and issues involved in, the development of an economic model to assess the cost-effectiveness of interventions to address AMR in humans.

## 2. Literature review – Methodology

A systematic literature review was undertaken to describe and critically appraise studies reporting on: (i) the costs and/or effectiveness of strategies to prevent, and control the spread of, AMR; and (ii) the cost of resistance. Literature was identified through contact with key international figures and institutions in the field of AMR, and through searching major electronic bibliographic databases. Approximately 155 studies were reviewed, following clearly defined inclusion and exclusion, and quality assessment, strategies. Meta-analysis was inappropriate, and thus a qualitative overview provided.

## 3. Literature review – Results

From this review it would appear that most studies:

1. Are from the developed world (principally the United States);
2. Are mostly hospital/other institution-based, with few community level interventions;
3. Are concerned with control of transmission as opposed to prevention of emergence;
4. Cover “micro” interventions, such as hand washing, but not more “macro” policy interventions, such as legislation, global control of drug availability, tax/subsidy; and
5. Do not measure the cost impact of AMR to the health service, patients or society.

There were few studies examining strategies to reduce AMR in developing countries, although several focusing upon prescribing were reviewed. This may be a reflection of pharmaceuticals being widely available at a community level (with few restrictions governing their availability) and, as a consequence, much inappropriate prescribing. Given the focus on prescribing, it is not surprising that analysis tended to be concentrated at the community level.

Overall, there appears to be no definitive evidence (cost and/or effectiveness), which suggests that one specific control measure (or combination) is particularly more successful than another in containing the spread of AMR. In addition, many interventions that impinge on levels of antimicrobial usage, and thus ultimately levels of resistance, are also not currently subject to such formal evaluation.

#### **4. Modelling cost-effectiveness — techniques and methods**

Modelling is an extrapolation of the main parameters that influence the phenomenon of interest, and then a construction of relationships between these parameters. There are six main forms of modelling in common use that might be applied to AMR:

1. Decision-analytic models;
2. Markov-chain models;
3. Monte-Carlo simulation;
4. Mathematical models;
5. Statistical models;
6. Macro-economic models.

These forms of modelling differ in their theoretical and methodological basis, the purpose for which they are designed, the manner of presentation and the level of data required. The theoretical and methodological features of each of these forms of model are summarized in chapter 4.

#### **5. Modelling cost-effectiveness — factors in model development**

In considering the range of possible approaches to modelling for AMR there are several specific factors that are important in determining which is most suitable:

1. Contextual factors, such as socio-economic environment, type of health care system and demographic characteristics of the population;
2. Policy goal of the intervention, such as a focus upon resistance or infection, micro or macro intervention and the prevention of emergence or transmission of AMR;
3. Outcome of interest, referring to focusing more widely upon resistance or health;
4. Temporal factors and the role of changes over time;
5. Extent of endogeneity of parameters within the model (i.e. those explained by the model);
6. Discounting of future costs and benefits; and
7. Handling uncertainty, in both the development of new antimicrobials and the development of resistance.

These will determine the relevant parameters to be collected, and how the relationships between them will be constructed. These factors are outlined in chapter 5.

## 6. Modelling cost-effectiveness — “minimum” data set

As well as the broader structural issues, outlined in chapter 5, there is a requirement for specification of variables of importance and the collection of data related to them. Although these will vary according to the final model structure, there will likely be a “minimum data set” of variables that would be required whatever the specific model developed. Chapter 6 considers the variables that would most likely comprise such a “minimum data set” within categories of:

1. Epidemiological or clinical factors relating to resistance;
2. Cost factors relating to resistance;
3. Pattern of antimicrobial usage;
4. Impact on AMR in humans from non-human consumption of antimicrobials; and
5. Information concerning the costs and effectiveness of the policy evaluated.

## 7. Discussion and research agenda

In terms of the current literature, there is a narrow focus upon the closed hospital system and concentrating upon the effects of policies aimed at reducing *transmission* rather than *emergence* of resistance. However, although it will be easier to identify the outcome of strategies aimed at reducing transmission in a closed environment, these are not likely to produce an optimal long-term outcome (i.e. a stable balance of the costs and benefits of antimicrobial use). This is because of the possible irreversibility of AMR and the potentially severe harm that could be imposed as a result. Yet, given the increasing importance of evidence-based medicine, strategies that have been evaluated using experimental methods and well-conducted economic evaluations, may be prioritized above these policies, which are much more difficult to evaluate. This is a danger that should be avoided both by awareness among policy-makers of the relative challenges associated with evaluating different types of policy, and by awareness among the research community of the importance of evaluating policies that may potentially be more important, even if the rigour with which they can be evaluated is smaller than for the potentially less important policies.

Overall, there appears to be no definitive evidence (cost and/or effectiveness) that suggests that one specific control measure (nor indeed a combination of measures) is particularly successful in containing the spread of AMR. Although it would seem that surveillance is a basic pre-requisite to tackling AMR, in the absence of evidence it is difficult to go further in making recommendations, or in suggesting priorities for research among those interventions assessed here. Readers are referred to the WHO Global Strategy for the Containment of Antimicrobial Resistance as presenting the most current and complete “best advice” on interventions to tackle AMR, how these should be implemented, and research priorities.

In terms of developing a model to assess the cost-effectiveness of strategies to tackle AMR, the appropriate and desirable model will need to satisfy four broad criteria of feasibility, sensitivity, relevance and flexibility. Considering these criteria, and this review of modelling as applied to AMR, two broad options are outlined:

1. A “macro-model” approach that attempts to integrate factors within a broad-based model aiming to assess strategies on a more “global” level; and

2. A “suite” of micro sub-models, each “embedded” within a given set of primary parameters, such as country, disease and level of intervention (e.g. hospital or community), which determine which of the “suite” of sub-models is most appropriate for that context.

A definitive recommendation concerning which form of modelling to pursue is not possible at present, as it depends upon both feasibility and relevance to the question and context concerned. However, it is clear that there needs to be further research into the modelling of AMR. Although such a model will require substantial investment of time and resources, the potential benefits of such a model, if accurately specified and incorporating quality data, could be vast in terms of the potential health benefit to current and future generations.