

WHEN IT COMES TO INCENTIVES FOR ANTIMICROBIAL DEVELOPMENT – IS A UNITED FRONT ESSENTIAL?

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BACKGROUND/INTRODUCTION

- ▶ Antimicrobials are medicines to be used against infections; antimicrobial resistance (AMR) occurs naturally as bacteria and viruses’ genetics mutate over time to become stronger, this can make infectious diseases hard to control [1,2]
- ▶ Human factors, like the misuse of antimicrobials, have accelerated the rate of resistance globally. Some of the most commonly used antibiotics are now becoming redundant as resistant microbes soar. In 2019 it was estimated 1.2 million people died from antibiotic-resistant bacterial infections. Antimicrobial resistance is a threat to global health [1,2]
- ▶ The development of new antimicrobials with the current payment methods is not something seen to be commercially attractive to industry
- ▶ There has been significant research into the health economic challenges of antimicrobial development and the market failures are well documented. In response to this the number of incentive programmes and payment methods being developed has also increased. But with so many initiatives several approaches are also becoming apparent [3].

OBJECTIVES

- ▶ Given that this is a problem that transcends borders and health systems, we explore the need for a unified approach.
- ▶ We seek to address the conceptual question “Is it sufficient for a number of innovative countries – such as the UK – to develop new assessment and payment models or does there need to be real change at an international level?”

METHODS

- ▶ This is a conceptual exploration of whether the market failures will be addressed by individual country initiatives and the imperative for a more global approach.
- ▶ The current and proposed approaches for reimbursement of antimicrobials in a selection of countries were evaluated for impact on these challenges and marked subjectively on how far they address the market failures.
- ▶ The implications of having different approaches across markets is discussed in light of its impact on the incentives to develop novel antimicrobials
- ▶ A targeted literature review was conducted to assess the number of different approaches being either discussed or implemented, and whether a united approach can be applied from any of the current ideas.

RESULTS

- ▶ In this review we found governments have been developing incentives both for their countries and with other countries, however, there were differences to all the approaches and whether they are truly incentivising (**Table 1**).
- ▶ On a country level, a large majority of countries have an action plan for tackling AMR, but not as many have an action plan for addressing the market failures [3].
- ▶ The UK, France, Sweden Germany and the US have tried to either implement acts or pilot new payment schemes to incentivise new development [4-6].
- ▶ Additionally, there were some collaborations involving multiple countries; including the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), the WHO, the EU4Health programme and the EFPIA.[7-8]
- ▶ In one survey of several countries interviewed it was found 11/13 would prefer a multinational incentive, that is, one where countries may opt in, so long as it is independent from national health technology assessment, medicine pricing, and reimbursement processes [9].
- ▶ Given the seemingly preferred approach by countries for a collaborative method, the results of this literature review highlighted there was no clear winner
- ▶ The key initiatives can be grouped into 4 types of approach as follows:
 - ▶ Subscription based / annual guaranteed payment
 - ▶ Variations on some exemption from reference pricing
 - ▶ Extension of patents
 - ▶ Funding the research

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RESULTS CONT.

Table 1 Summary of incentives

AMR scheme	Summary approach
JPIAMR [7]	Coordinating national public investments including in transnational research, 29 nations with support from the EC
EFPIA [8]	Suggestion to extend time available on patents for new antimicrobials
UK [5]	NICE pilot. Delinked model to assess long-term value, with an annual payment system based on new valuing
Sweden [6]	PHAS pilot. Antibiotics made available in return for state guaranteed annual revenue
France [2,3]	Guaranteed a price no lower than the lowest across 4 reference countries, if moderate’ or higher added therapeutic benefit is gained
Germany [2,3]	Antibiotics exempt from internal reference pricing on an ad hoc basis
USA [2,3]	Several Acts to help fund innovative research and increase reimbursement in hospitals

Key: JPIAMR: Joint Programming Initiative on Antimicrobial Resistance, EFPIA: European Federation of Pharmaceutical Industries and Associations, PHAS: SE Public health agency EC: European Commission

DISCUSSION

Comparing the schemes

- ▶ Initiatives have impact by incentivising innovation, though the incentive is not always complete with just a promise of reimbursement. We compare the approaches here (**Table 2**).
- ▶ The Swedish pilot has not presented results so therefore cannot be compared too closely. However, the promise of an annual payment much like the NICE pilot which used a subscription-based model, is certainly a good approach. Similarly, France and Germany guaranteeing a certain level of pricing is also helpful. But one of the key issues with new antimicrobials is how they are valued versus comparators as well.
- ▶ The NICE pilot involved industry and as a result some concerns were raised that predicted usage had been underestimated in the subscription model. This highlights the continued need for collaboration between industry and governments.
- ▶ Joint collaborations between countries are a great approach, however to date, haven’t achieved the progression the pilot schemes present.
- ▶ The final approach of government level funding of research is one we saw work well during he Covid-19 pandemic, with vaccines being developed rapidly. While this could have the highest impact, this approach does ultimately result in high cost and risk for governments and is unlikely to fit with every country’s finances.

Table 2 Summary of the pros, cons and potential impact of initiatives

AMR scheme	Pros +	Cons –	Potential Impact
JPIAMR [7]	A great initiative to bring countries together	No real united action to find a resolution to market failures has come from it yet	MODERATE IMPACT
EFPIA [8]	A collaborative group could have a wide impact. Idea to increase time industry can make money	No real impact yet	MINOR IMPACT
UK [5]	A guarantee of reimbursement and a new way to value the new technologies. This method will likely work very well for the UK. It could be applied well in other HTA markets	Unclear if it could work globally	STRONG IMPACT
Sweden [6]	A guarantee of reimbursement	Uncertainty on how the value is ascertained while the pilot is ongoing	UNSURE
France [2,3]	A guarantee reimbursement will be no lower than the lowest reference countries	Uncertainty on how to receive enough benefit	MODERATE IMPACT
Germany [2,3]	A guaranteed list price can be reimbursed	Uncertainty on how value will be measured, guaranteed price is “ad hoc” implying not all will receive. Industry could charge a lot	MODERATE IMPACT
USA [2,3]	Funding research is a positive step and would incentivize.	Funding research costs more and is a risk for governments. Not clear if reimbursement promises apply nationally.	MODERATE IMPACT

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CONCLUSIONS

- ▶ It’s clear that several methods exist, and which is the right route to follow is naturally country specific, but when it comes to healthcare interventions, policies need to service the patients as well.
- ▶ There has been positive development toward incentives to correct the market failures impacting new antimicrobial technologies, in particular the recent NICE pilot provides a strong base. The way the NICE pilot values the technologies is likely to work well in the UK and could potentially be adapted by other HTA markets, however the concept of the subscription model for payment could be adapted far wider, even in non-HTA markets.
- ▶ However, for many markets despite the certainty of reimbursement, the suggested approaches still present companies with uncertainty over how the new technologies may be valued. This is where its important industry do not proceed with a new antimicrobial unless it has improved outcomes versus comparators.
- ▶ Initiatives to align country approaches and bring industry to discussions will be important in ensuring that the appropriate incentives are established.