TRANSFERABLE EXCLUSIVITY VOUCHERS: A SILVER BULLET?

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BACKGROUND

- Antimicrobial resistance (AMR) is one of the top 3 health threats identified by the EU's Health Emergency Preparedness and Response Authority (HERA)[1]
- AMR leads to an estimated 35k deaths and €1.5 Billion in healthcare costs and productivity loss in the EU. Cases of AMR have risen sharply over the last 5 years[1]
- Despite the obvious burden of AMR, pharmaceutical companies have been hesitant to invest in antimicrobial development due to limited return on investment due to low volumes and low prices
- The European Union (EU) has proposed a new regulation to replace Regulation 2004/726, introducing the concept of a transferable data exclusivity voucher (TEV) as an incentive for the development of priority antimicrobials[1]
- In brief, a TEV would allow a manufacturer to extend the patent on one of their drugs or sell this voucher to another company for the same purpose[1]
- This concept has been met with concerns centred around increased healthcare costs and an increased delay in access to medicines[2]
- In this research we review the literature to evaluate the positive and negative aspects of TEVs as an incentive to drive antimicrobial development

OBJECTIVE(S) AND METHODS

- To review the potential of TEVs in incentivising the development of new antimicrobials through a targeted literature review and critical appraisal of our findings

Targeted Literature Review

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Positive and negative criticisms of TEVs collated and reviewed

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Conclusions for the future of antimicrobial development incentives in Europe

WHAT IS A TRANSFERABLE EXCLUSIVITY VOUCHER (TEV)?

- TEVs, also known as transferable extension of exclusivity are just one of multiple 'pull' mechanisms proposed by policy-makers to combat the sparse pipeline for novel antibiotics
- 'Pull' mechanisms seek to reward a manufacturer for developing a product, while 'push' mechanisms provide an upfront incentive (e.g., a research grant) to work in the area[3]
- Theoretically TEVs would be granted to a manufacturer in exchange for the successful regulatory approval of a novel antimicrobial[4]
- The TEV would be applicable to a drug to delay the patent expiry in EU countries by up to 12 months, or be sold to another manufacturer[1]
- The current EU proposal is similar to one made in the US congress in 2018. The bill was never passed and has not been reintroduced[3]

CHALLENGES

Cost and Scale

- The estimated healthcare cost of the TEV ranges widely between $1 billion (industry sponsored reports[4,] and $3.2 billion (IE sales of AbbVie's blockbuster drug adalimumab – generic sales)[5] for which Europe would gain access to **one new antibiotic**
  - The highest estimates of TEV value assume that it would be applied to highest revenue drugs available. This assumption is logical as the owners of such drugs would reap the most value from the TEV, and therefore are likely to bid highest for it in a free market
    - Such drugs are unfortunately usually orphan drugs meaning that this cost burden would be borne by a relatively small group of patients
  - This is ***much*** higher than some other proposed pull incentives such as the ***global*** market entry reward of $1 billion, for which the EU share would be only ~$250 million
- According to the office of health economics in 2021, 15 new antibiotics were required to treat the 5 WHO & CDC defined "Critical + Urgent" pathogens[6]
  - Based on current pipelines and needs they estimated that an average of 1 TEV would be granted per year over 15 years
  - At $3+ billion each this would be a truly massive cost burden to EU health systems

No guaranteed access – a 'one off' transaction

- The current proposal only guarantees regulatory approval of an antibiotic and takes no account of HTA approval and price negotiations, which could impede access to the drug. Additionally, the manufacturer could go bankrupt, or the product could be removed from the market for safety reasons, all leaving healthcare systems out of pocket[5]
  - True access can take years to achieve. For example, at the start of 2023 only 3 European countries had access to meropenem/vaborbactam, a WHO essential reserve antibiotic approved 2 years earlier[4,5]

Better options for clinical value

- Currently in development antibiotics are unlikely to meet current European public health needs and so are of limited value. TEVs granted for such drugs would be a poor exchange
  - However, if the eligibility of antibiotics was more restrictive this would likely hamper the incentive for development, creating a no-win scenario[4]
- There is likely to be a diminishing return on new antibiotics with the demand for new antibiotics falling sharply as more enter the market[4,7]. This is matched by a corresponding fall in the value of TEVs as more are made available[6]
  - Unfortunately, this unpredictable fluctuation in TEV value in response to market forces is likely to be seen as an investment risk by manufacturers disincentivising investment in antibiotic development in the longer term
- The cost effectiveness of this approach is debatable.
  - Antibiotics developed as a result of this scheme would target specific resistant pathogens without impacting others, while investment of this scale in public health measures to combat all resistant pathogens would likely be of wider and more longstanding benefit[4]

OPPORTUNITIES

Multinational response

- Antimicrobial resistance is a multinational problem requiring a multinational response
- A coordinated approach using EU level legislative mechanisms has great potential to combat AMR compared to state level interventions[8]

Pull over push incentives

- The TEV is a pull incentive, meaning that reward is linked to delivery of the new antibiotic. This contrasts with much more prevalent push incentives which off cash up front to incentivise development[5,9]
- Pull incentives have the potential to be more cost effective as they are not paid unless the outcome is delivered[5,9]
- By placing the risk on the manufacturer, more efficient and effective drug development activity is incentivised vs push where free cash encourages waste[9]
  - This comes at a cost, however, as pull mechanisms require a greater reward to compensate for the increased risk[9]

Industry Support

- Industry buy-in is a crucial part of incentivising new antimicrobial development and industry have been generally supportive of the idea
- Industry argues that in combination, no need for upfront government spending, the large financial incentive, and the potential to benefit companies of all sizes make TEVs a desirable intervention to stimulate development[2,6]
- This contrasts with mostly negative outlook from academia and public bodies explored in this research

- High uncertainty persists around TEVs in Europe with a 5-fold difference between industry and academic forecasts of economic impact
- Similarly, there is no consensus on whether TEVs could effectively incentivise antimicrobial development in the medium and long term
- Investigation of possible 'guard-rails' to mitigate the risks of TEVs may collapse some of the uncertainty and increase confidence in this option
- Current incentives have not sufficiently driven antimicrobial development. A large scale, high risk – high reward solution should not be dismissed

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