Funding the Fight Against Antimicrobial Resistance: Learnings from the UK and Sweden's Pilot Incentive Programmes

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Introduction

- The overuse and misuse of antimicrobials are major drivers of drug-resistant pathogens.
- Antimicrobial resistance (AMR) is a top global threat to human health, responsible for an estimated 1.27 million direct global deaths and 4.95 million indirect deaths in 2019.[1]
- Despite the substantial unmet need associated with rising rates of AMR, antimicrobial manufacturers face significant reimbursement challenges, which disincentivise innovation.
  - The traditional reimbursement model for pharmaceuticals is payment for volume sold; however, antimicrobials are typically reserved for use only when necessary as part of stewardship efforts, resulting in low sales volumes and poor return on investment.[2,3]
  - Additionally, reimbursement decision-making typically does not consider the elements of population-level or societal value relevant to antimicrobials.[4]
- In response to this increasing unmet need, decision-makers globally are implementing antimicrobial reimbursement incentives designed to encourage manufacturer investment in the research and development of antimicrobials, to ensure a pipeline of effective treatments while promoting their appropriate use to preserve efficacy.
- Several countries are undergoing pilot programmes to understand how such incentive schemes can be successfully implemented.

Objectives

- **Building on previous research outlining AMR policies and funding schemes[5-7] that established England and Sweden as forerunners in antimicrobial incentive development, our objective was to analyse the learnings from their respective reviews of the pilot programmes.**

Methods

- A keyword search and review of health agency websites were conducted to extract key characteristics of the pilot programmes for each country (e.g., eligibility, timeframe, funding).
  - England: National Institute for Health and Care Excellence (NICE)
  - Sweden: Public Health Agency of Sweden (PHAS) in collaboration with the Dental and Pharmaceutical Benefits Agency of Sweden
- Reports from each organisation were used to pull information on key pilot strengths and limitations into a table matrix to facilitate comparison.
- Information was synthesised to draw insights potentially applicable to other countries and future incentives.

Results

- Both pilot programmes are volume-delinked "pull incentives" where the value of the contract is independent of sales and is determined by the projected value of the antimicrobial to the health system (**Figure 1**).
  - In Sweden, manufacturers receive a guaranteed minimum income plus a 10% inventory incentive.
  - In England, manufacturers receive a fixed annual fee ranging from £5 to £20 million, dependent on eligibility score.

Figure 1. Overview of antimicrobial incentive pilot programmes in England and Sweden

	England	Sweden
Type of incentive model	Volume-delinked pull incentive • Subscription model of 3 years with potential extension for up to 15 years or until patent expiry • Maximum subscription payment of £10 million per year[a]	Volume-delinked pull incentive: • Guaranteed minimum income[b] • Inventory incentive: 10% of the annual guaranteed minimum income
Process for choosing antimicrobials	Public sector procurement process reviewed by NICE, NHSE&I, UK APRHAI, PHE, BSAC, and clinical experts based on a weighted scoring system including: • Unmet need,[c] including activity against the WHO's "critical priority pathogens" and key determinants of AMR, clinical severity and specific areas of unmet need • Product novelty • Antimicrobial stewardship • Antimicrobial surveillance • Surety of supply/manufacturing practices • Cost	Public sector procurement process reviewed by the PHAS and independent experts based on the following selection criteria: • EU commission-approved antimicrobial • Proven good activity against the WHO's "critical priority pathogens" • Infections in patients with limited treatment options or for ≥2 of the following: complicated intra-abdominal infections, complicated UTIs, hospital-acquired pneumonia • Bactericidal effect • Safety profile similar to β-lactam antibiotics • Additional stock/delivery/environmental requirements
Antimicrobials assessed in pilot programme	Two agents:[e] • Ceftazidime/avibactam • Cefiderocol	Five agents: • Imipenem/cilastatin/relebactam[f] • Ceftolozane/tazobactam • Meropenem/vaborbactam • Fosfomycin • Cefiderocol

[a]Annual fee based on the calculation of England's fair share of the financial incentive needed per new antimicrobial proposed by the UK team leading the project.; [b]Guaranteed minimum income is based on the following calculation: (volume of stock set aside for Sweden based on medical need in a worst-case scenario) x (template price per pack) x (1.5).; [c]Clinical unmet need has the highest weighting.; [d]The WHO Bacterial Priority Pathogens List categorises pathogens into critical, high, and medium priority groups to inform research and development and public health interventions.[8]; [e]Ceftazidime/avibactam was an existing antimicrobial and cefiderocol was a new-to-market antimicrobial.; [f]Imipenem/cilastatin/relebactam is now included in the permanent programme along with avibactam/ceftazidime.
Abbreviations: AMR = antimicrobial resistance; APRHAI = Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection; BSAC = British Society for Antimicrobial Chemotherapy; NHSE&I = National Health Service England and Improvement; NICE = National Institute for Health and Care Excellence; PHAS = Public Health Agency of Sweden; PHE = Public Health England

Results (cont.)

- Both pilots use qualitative criteria to select eligible antimicrobials with a focus on assessing the unmet need.
- Key learnings were **similar** across the pilots (**Figure 2**).
  - Agreement to focus on antimicrobials targeting the WHO pathogen priority list.
  - The need for incentive flexibility over time and by product, including new and updated eligibility assessments and procurements to reflect the evolving AMR landscape and clinical needs.
  - In Sweden, the programme facilitated earlier access to new antimicrobials compared with other European countries.
- Key limitations **differed** by pilot (**Figure 2**).
  - In England, the pilot's complexity and resource intensiveness were challenging for both manufacturers and agencies.
  - In Sweden, the volume requirements led to stock exceeding the medical need and resulting wastage, which was later adjusted so stock is based on previous sales.

Figure 2. Key learnings and limitations of antimicrobial incentive pilot programmes in England and Sweden

	England	Sweden
Pilot strengths and/or learnings	• Opportunity for manufacturers to engage in dialogue with NHSE&I • Antimicrobial stewardship requirements • Focus on MDR WHO pathogen priority list • Clinical and non-clinical selection criteria • Large support for the purpose, execution and outputs • Qualitative framework appropriate for antimicrobials	• Most of the pilot's principles were appropriate and effective • Sweden gained access to all four newly approved antibiotics earlier than other comparable European countries • Two antimicrobials have good sales above the threshold to qualify for this programme[a], but both are still marketed and available • Pilot programme has since been made permanent

Pilot limitations and/or aspects to improve/adjust	• Time-consuming and resource-intensive process with complex evaluation
	• All products meeting eligibility criteria should be included
	• Need for a flexible cap that varies based on how well products meet selection criteria
	• Need to account for instances of high drug usage
	• Investment for antimicrobials outside of the selection criteria might be disincentivised
	• Product novelty should extend beyond the chemical entity (e.g., mode of delivery)
		• Pilot model had requirements for storage volume which were too extensive and led to wastage
		• Need for a flexible model which includes the possibility of:
		  – Adjusting the compensation level and updating procurements based on market evolution
		  – Excluding or not renewing the procurement of certain products with very low demand/clinical need
		  – Reducing the compensation or terminating the agreement early if requirements are not met
		• Two antibiotics did not qualify for procurement renewal due to low clinical demand[b]

[a]If an antimicrobial has annual sales >SEK 6 million, the PHAS has the right to terminate the agreement early; [b]If an antimicrobial has been marketed for ≥2 years and has annual sales <SEK 450,000, the PHAS has the right to terminate the agreement.
Abbreviations: AMR = antimicrobial resistance; APRHAI = Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection; BSAC = British Society for Antimicrobial Chemotherapy; MDR = multidrug resistant; NHSE&I = National Health Service England & Improvement; NICE = National Institute for Health & Care Excellence; PHAS = Public Health Agency of Sweden; UTI = urinary tract infection

Conclusions

- **Learnings from both pilot programmes underscore the need to establish and refine antimicrobial procurement processes.**
- **Ongoing dialogue between stakeholders is vital based on the complexity and novelty of such evaluations.**
- **Nations and healthcare systems must consider their contribution to the global AMR effort when developing their incentives.**
- **Future consultation with manufacturers would determine the impact of incentives on antimicrobial investment.**

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Disclosures

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