Critical Incentive Strategies for Accelerating R&D to Fight Against AMR

Greg Daniel, PhD, MPH
Deputy Director, Duke-Margolis Center for Health Policy
Clinical Professor, Fuqua School of Business
Adjunct Associate Professor, DPOP, UNC Eshelman School of Pharmacy

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To fight AMR, economic incentives are needed for development new therapies

• Inappropriate use of antibiotics drives resistance
  – Antibacterial drug resistance reduces the resources we have available to combat infections
  – Reducing misuse and overuse of antimicrobials will result in healthcare savings and slowing of antibacterial drug resistance

• Antimicrobial pipeline is critically thin
  – According to Pew Charitable Trusts, there are currently 41 antibiotics in phase I-III testing (in contrast, in 2015, there were 836 drugs in the pipeline for cancer)
  – Very few, if any, that target our most urgent needs will be approved
Economic challenges to antimicrobial development

• Appropriate stewardship means that sales volumes are low
• A lack of diagnostic tools leads to empiric treatment, which favors use of low-cost generics and contributes to inappropriate use
• A strong and effective generic market limits the cases where novel antimicrobials are needed and drives down prices
• Reimbursement for antibiotics does not reflect public health benefit

New models are needed to reward the development of innovative antimicrobial products while also supporting stewardship and appropriate use
U.S. efforts to combat antimicrobial resistance

**U.S. legislative activity**

- Generating Antibiotic Incentives Now (GAIN) [passed 2012]
- Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM)
  - Would provide add-on Medicare payments to innovative antibiotics as part of bundled DRG for inpatient care
  - Not included in final 21st Century Cures Act
- Re-Valuing Antimicrobial Products (REVAMP)
  - Would grant additional, transferable exclusivity for qualified antimicrobial products (legislation not yet introduced)
- Improving Access to Affordable Prescription Drugs Act
  - Establishes a monetary prize for antimicrobial developers who bring to market a qualified high priority drug in exchange for forfeiture of market exclusivity and reasonable pricing

**Other U.S. efforts on AMR**

- In 2014, the White House released the National Strategy for Combating Antibiotic-Resistant Bacteria (CARB)
  - Focused on discovery/development, prevention, surveillance, diagnostics, and global collaboration
- President’s Advisory Council on Combatting Antibiotic-Resistant Bacteria (PAC-CARB) formed in 2015
  - To address low ROI, recommended combination of general and targeted incentives, expanded push incentives, and adoption of a delinkage model
- Creation of CARB-X, a public-private partnership designed to support antimicrobial development at the preclinical stages
  - Focused on preclinical R&D and broadly promotes novel antimicrobial products
  - CARB-X will only fund projects through phase I clinical testing, leaving significant scientific and financial hurdles to clear prior to approval
Incentives for antimicrobials can support all stages in the development of priority antibiotics.

- **Push incentives**
  - Grant funding for R&D (e.g. NIH, CARB-X)
  - R&D tax credits
  - LPAD pathway

- **Pull incentives**
  - Public-private partnerships (BARDA)
  - Market exclusivity
  - Surveillance of infections and stewardship

**Stages of Development**
- Basic Research
- Preclinical
- Clinical Trials
- FDA Approval
- Post-Market
Global efforts have converged on market entry rewards

- **Chatham House** (an independent policy institute based in London), **DRIVE-AB** (an EU initiative comprised of 23 public and private partners), **The Review on Antimicrobial Resistance**, and **The German Global Union for Antibiotics Research and Development** recommended some form of a market entry (MER), which is designed to pay for vital antimicrobial drugs with public funds.

- The MER provides substantial additional revenues to reflect public health value quickly after approval, and removes the need for volume sales, which helps the developer recoup investments.
  - A form of ‘delinkage’, which removes the ‘link’ between development costs and revenues, the MER enables uncoupling of the ROI from the volume of drug sales.
Reinvigorating the antimicrobial pipeline with economic incentives: Duke-Margolis approach

Goals:
- Identify promising economic “pull” incentives, including reimbursement reforms, that encourage bringing priority antimicrobials to market, keeping them available when needed, and using them appropriately
- Outline a path for feasible implementation in the U.S. healthcare system

Strategy:
- Engage broad-based stakeholder and expert group to identify and develop promising models
- Examine outputs from DRIVE-AB, AMR Review Team, other global and U.S proposals
- Develop policy recommendations on the most viable economic incentives that could be implemented in U.S.
- Disseminate research findings through several public outlets, including publications and presentations at relevant meetings
Developing U.S. approaches aligned with global proposals

Core Principles for Antimicrobial Economic Incentives

- Part of a comprehensive strategy to provide pull incentives in combination with other push incentives
- Provide public funding leveraged by private payments
- Provide developers with rapid access to funds upon market entry
- Be sustainable and dependable over entire drug development cycle
- Support and align with broader shifts in payment models to value and quality - away from volume and intensity
- Promote and reward innovation
- Promote stewardship so that antibiotics are sustainable over generations
- Promote access

Promote stewardship so that antibiotics are sustainable over generations
Increasing the value of health care delivery

• Traditional volume-based FFS payment scheme for drugs does not support high-value, appropriate use of antibiotics

• More emphasis on value and quality in care delivery in the U.S.
  – Shift from volume and intensity to patient- and episode-level alternative payment models (APMs) that enable more flexibility in how services are provided
  – Higher payments for better measured results and lower overall costs
  – Provide support for care coordination and innovative care delivery
  – Create new financial accountability for providers... Will affect incentives for use of costly therapies – particularly those with low impact on outcomes

• Creates new opportunities and motivation for how drugs are reimbursed
Duke-Margolis proposal: Market entry reward with shift to value-based reimbursement for antimicrobials

• The Priority Antimicrobial Value and Entry (PAVE) Award proposal combines a market entry reward with value-based payments

• Market entry reward payments phase down over time

• Continued eligibility for payment requires:
  • Reliable availability of drug
  • Continued sensitivity of priority organisms (CDC tracking)
  • Tracking/reporting appropriate prescribing
  • Data collection for post-market studies (if needed)
  • Shift to alternative payment models not volume based payment

• The PAVE Award model resolves the current conflict between the drivers of ROI and strong stewardship programs
  — Leverages private financing to reinforce “volume to value” shift

Key features:

  Strong incentive for innovation through a predictable entry reward
  Payers pay the same amount for drugs within a new structure
  Leverages public and private funds to accomplish delinkage while supporting stewardship and availability
  Directly incentivizes the shift from volume to value
Alternative Payment Models (APMs) for Antimicrobials

Traditional

Category 1
****
Fee for Service – No Link to Quality & Value

Category 2
****
Fee for Service – Link to Quality & Value

“Pay for Performance”

Category 3
****
APMs Built on Fee-for-Service Architecture

APMs linked to patient not services:

Limited

Most or all of manufacturer payment is per-episode or per-member, little FFS

More Complete

Part of manufacturer payment is per-episode or per-member, part is FFS

VALUE MEASURES FOR ALTERNATIVE PAYMENT MODELS FOR ANTIMICROBIALS

Effectiveness Measures: Sufficient drug supply, continued microbial sensitivity, better outcomes for patients with otherwise resistant infections

Appropriate Use Measures: Drug prescribed according to practice guidelines

Data Collection: Manufacturer supports data collection for post-market studies
Phased-in approach to the Priority Antimicrobial Value and Entry (PAVE) Award

*Level of revenue from payers is the same under current FFS model and new PAVE model*
Potential financing mechanism for the MER component of PAVE Award

- **Transferable exclusivity voucher (TEV)**
  - Provides financial incentives without relying on volume sales of antimicrobial
  - Potential to increase other drug prices, public and private drug spending – but some guardrails proposed to limit impacts
  - Does not address fee-for-service incentives for inefficient use of antimicrobials

- **Auction of multiple TEV(s) (with guardrails)**
- **User fees**
- **Per member per year fee on health plan members**
- **General tax revenue**
- **We do not plan to endorse a specific method – but seek to limit funds by leveraging and improving existing payments**

**Proposed “guardrails” for an antimicrobial transferable exclusivity voucher program**

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<tr>
<th>Challenges with TEV</th>
<th>Potential Solutions</th>
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<td>Increases cost in other areas of healthcare</td>
<td>Cap voucher (in value or duration)</td>
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| Can negatively affect the generic market (with TEV) | - Voucher will only be awarded to new drugs (not applicable for previously approved drugs)  
- Company that will be using the voucher must declare which drug the voucher will be used on at least 4 years prior to exclusivity expiration |
| Does not encourage stewardship | Link quality reporting requirements (e.g., efficacy, length of hospital stay) to receipt of voucher |
| Could be poorly targeted to needed antibiotics | Limit eligibility to drugs that meet criteria set by public/private partnership group, which will identify unmet need based on periodic reviews of infection rate, resistance, and the drug pipeline |

*Ten years after implementation of voucher program, the GAO could conduct a study to determine the effectiveness of the vouchers and whether the voucher program should continue*
Thank you