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Combatting Antimicrobial Resistance: Economic Incentives for Innovation and Stewardship

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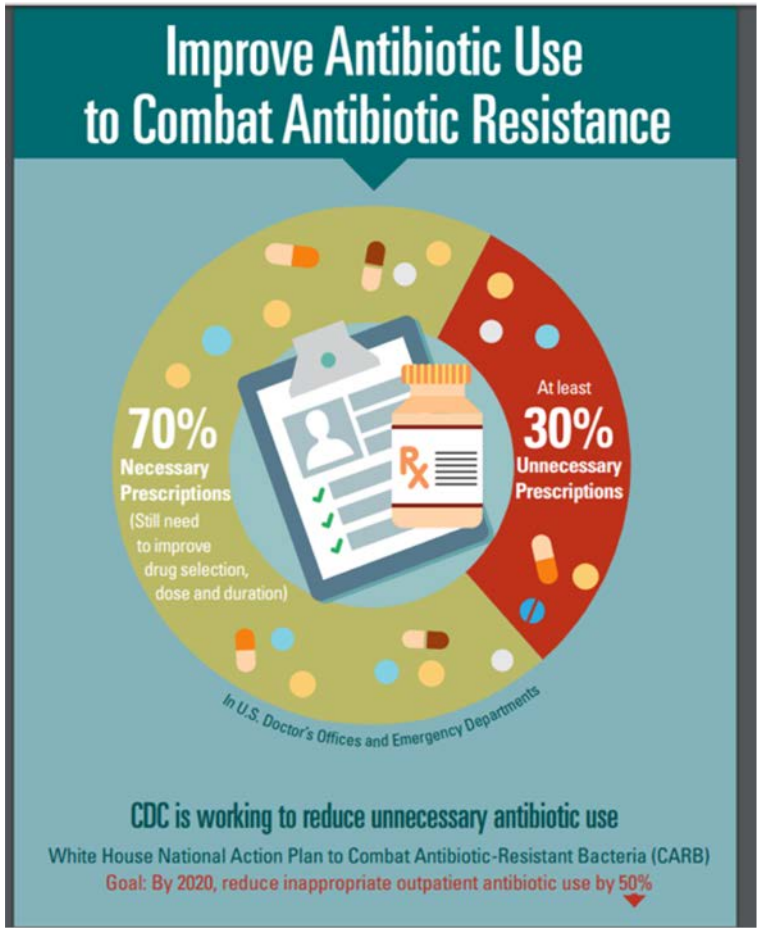
Inappropriate use of antibiotics drives resistance

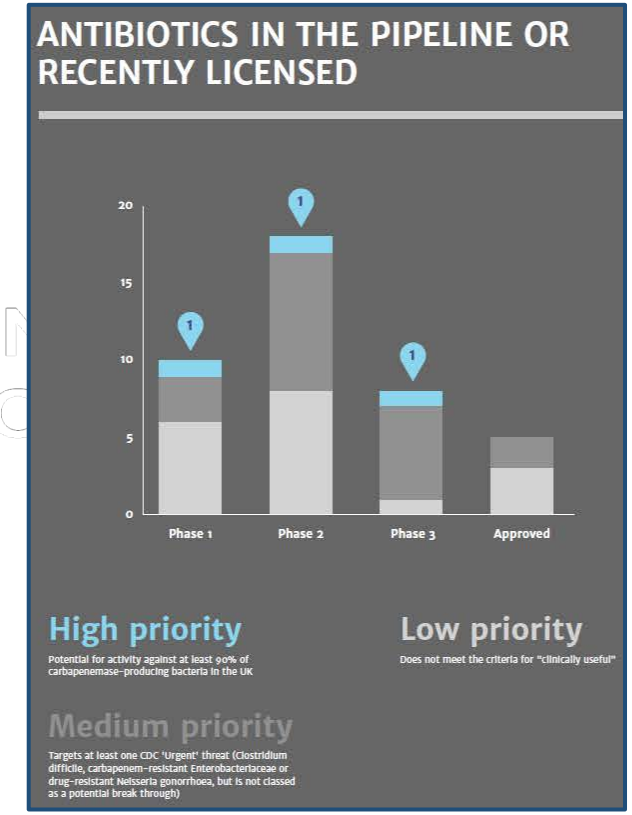
- In 2009, **antibiotic expenditures in the U.S. in all healthcare settings totaled $10.7 billion**
- **One third of antibiotic prescribing is inappropriate**
- Reducing misuse and overuse of antimicrobials reduces health care spending and slows antibacterial drug resistance
- Antibacterial drug resistance reduces the resources we have available to combat infections



From Suda et al, *J. Antimicrob. Chemother.* (2013)

The antimicrobial drug pipeline is thin

- Few drug candidates in the pipeline
  - Pew Charitable Trusts identified 48 antibiotics currently in phase I-III testing (in contrast, in 2015, there were 836 drugs in the pipeline for cancer)
  - Very few drugs in development for most urgent AMR needs
- Low ROI for antimicrobials relative to public health benefits
  - Clinical trial challenges
  - Lack of rapid diagnostics
  - Effective stewardship leads to low sales volumes
  - Most health benefits accrue to patients who never need to be treated and who can undergo other procedures because effective antimicrobials exist



From "Securing New Drugs for Future Generations: The Pipeline of Antibiotics", The Review on Antimicrobial Resistance. May 2015

Emerging global consensus to address AMR

- **Chatham House**, the Royal Institute of International Affairs, an independent policy institute based in London, released a report on business models for antimicrobial development in Oct. 2015
- **The Review on Antimicrobial Resistance** was commissioned by, and reports to, the UK Prime Minister, released a final report on May 19th, 2016
- The German **Global Union for Antibiotics Research and Development** report (Feb. 2017) identified actions to improve needed development
- **DRIVE-AB**, 16 public and 7 private partners from 12 countries, released a final report (Jan. 2018)

- Convergence of principles:
  - Provide funding to support R&D on antimicrobials
  - Implement pull incentives that delink reimbursement from sales volume
  - Coordinate globally on surveillance and development efforts

U.S. efforts to combat antimicrobial resistance

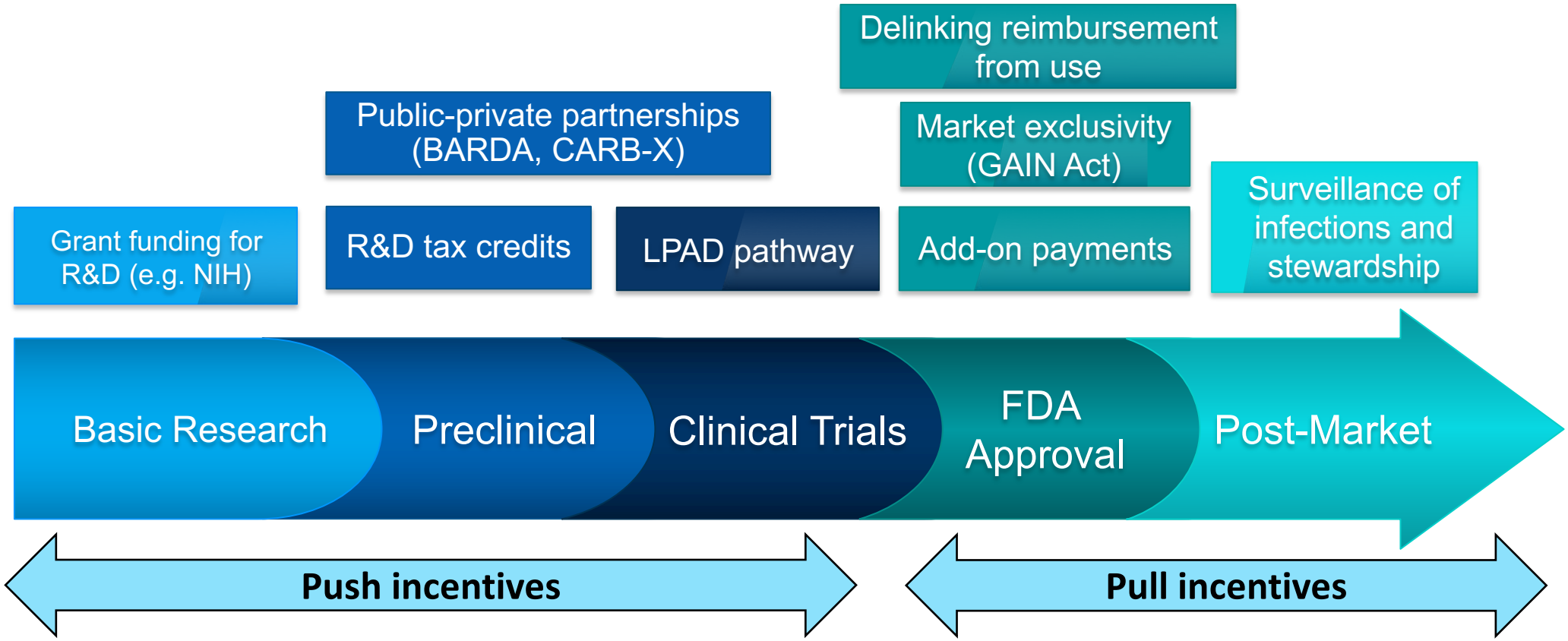
U.S. legislative activity

- Generating Antibiotic Incentives Now (GAIN) Act of 2012
- 21st Century Cures Act: Limited Population Antibacterial Drug (LPAD) pathway
- 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
- 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

Other U.S. efforts on AMR

- In 2014, the White House released the National Strategy for Combating Antibiotic-Resistant Bacteria (CARB)
- 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
- CARB-X and BARDA, public-private partnerships designed to support antimicrobial development at the preclinical and clinical stages
  - Broadly promotes novel antimicrobial products
  - CARB-X funds projects through phase I clinical testing, and BARDA provides fund during clinical phases

Incentives to address AMR can support all stages in the development and use of priority antimicrobials



Status of “pull” incentives for development of priority antimicrobial drugs

- **Multiple recommendations for global market entry rewards (MER) – to reflect public health benefits of priority antimicrobials**
  - Large award (~$1-4B globally) upon drug launch needed for ROI and ‘delinkage’ from sales volume
  - Budgetary, regulatory, and other challenges of adequate public funding and management in US
- **Transferable exclusivity voucher (TEV)**
  - Provides financial incentives without relying on volume sales of antimicrobial
  - Without guardrails, will increase price of another drug, and public and private drug spending Does not address fee-for-service incentives for inefficient use of antimicrobials
- **Desirable features of alternative approach:**
  - Leverage existing antimicrobial payments to limit need for public funding
  - Limit increases in other drug prices and spending
  - Reinforce trend toward paying for value in health care

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.

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

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 <u>better measured results and lower overall costs</u>
  - 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

Overview of value-based model

- Delinked payments would align with global recommendations on AMR
- An independent panel would set eligibility criteria that is aligned with current unmet medical need, and would provide a list of desired R&D targets
- Benchmark payments would reward innovation in a tiered manner upon market entry
- Continued payments would be dependent on
  - Drug availability
  - Proper stewardship
  - Population-based APM contracts with payers

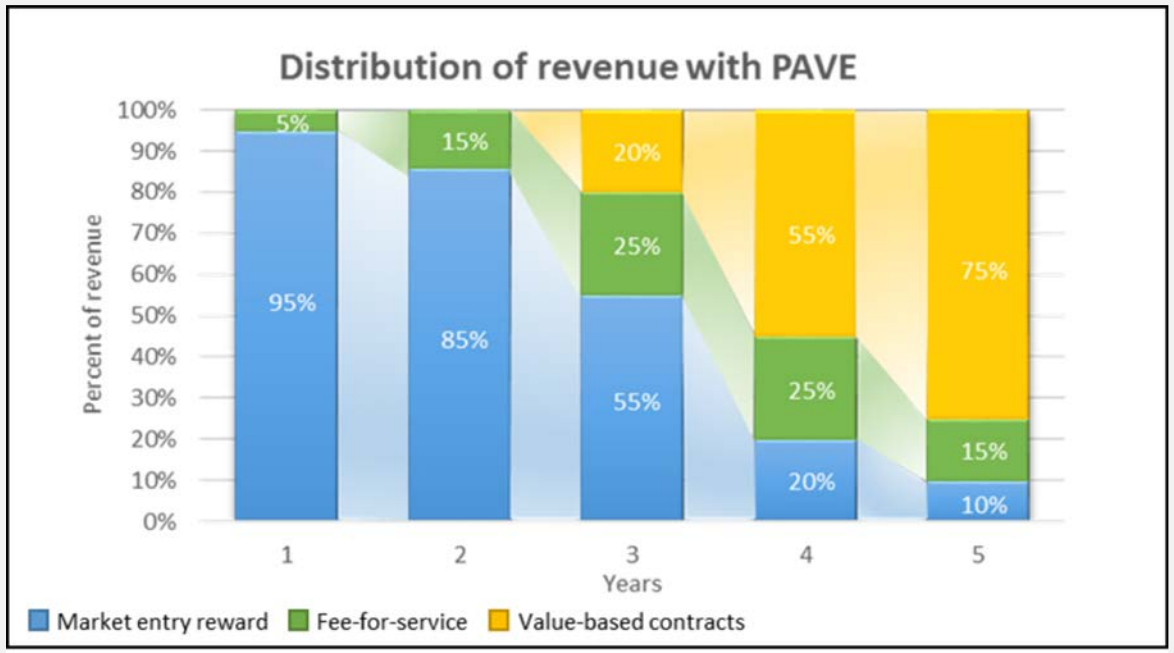
Phased-in approach to value-based reimbursement

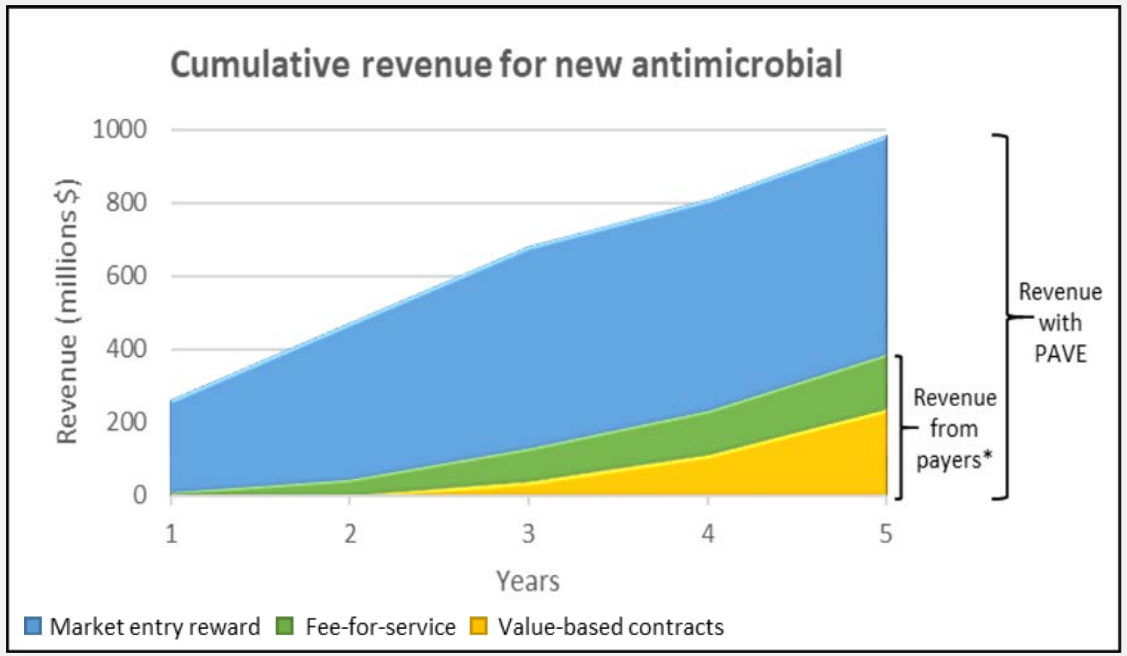
- The Priority Antimicrobial Value and Entry (PAVE) Award proposal combines a market entry reward with value-based payments
- Population-based payment effectively delinks reimbursement from the volume of drug used
- Aligning payments for high-priority antibiotics with effective use would encourage all parties to support stewardship
- 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

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

Policy guardrails and outstanding issues

Guardrails must be in place to ensure value for all stakeholders:

- Payments for antimicrobial would link to:
  - Continued data collection on drug's use to determine value
  - Manufacturer commitment to guarantee drug's availability
- Payers and providers must enact strong stewardship guidelines
  - Should be clear protocol for appropriate drug use
  - Must be careful pricing to discourage inappropriate use

Special considerations and outstanding issues:

- Some conditions may be too infrequent to benefit from PAVE Award
  - Should consider a MER-only option for drugs for rare infections
- Implementation will be dependent on measurement of value
  - Measures for value should build on those available today, including measures that would pertain to ongoing availability, utility and access measures, and use data
- Initial payer participation could be challenging
  - Long-term cost-saving is difficult to account for in near-term payments
- Antimicrobial use in inpatient vs. outpatient settings
  - The guidelines and outcomes governing the PAVE Award model for high-priority inpatient antimicrobials may need adjustments to be applicable in the outpatient setting

Thank you!

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