A Future without Antibiotics

Anthony D. So, MD, MPA
IDEA (Innovation+Design Enabling Access) Initiative
ReAct—Action on Antibiotic Resistance
Johns Hopkins Bloomberg School of Public Health
anthony.so@jhu.edu

https://www.IgniteTheIDEA.org/ahcj2019

Disclaimer: This presentation represents views, opinions and positions expressed in my personal capacity, and these would not necessarily reflect the views of any third party, including the UN Interagency Coordination Group on Antimicrobial Resistance or the World Health Organization with which I might have affiliation.

At the Precipice of a Post-Antibiotic Era

- *United States:* 2 million with drugresistant infections, 23000 deaths in US per year (CDC, 2013)
- *Europe:* 33,000 attributable deaths from antibiotic-resistant bacteria (ECDC, 2019)
- Global: 700,000 attributable deaths globally to AMR (UK Review on AMR, 2014)

Table I

Global Deaths (Thousands) Due to Selected Infections Amenable to Antimicrobial Treatment (2013)³

Lower respiratory infections/pneumonia*	2,466
Tuberculosis	1,290
Malaria	855
Neonatal sepsis and infections	366
Meningitis	304
Intestinal infections*	221
Sexually transmitted infections*	142
Maternal sepsis and infections	24
TOTAL	5,668

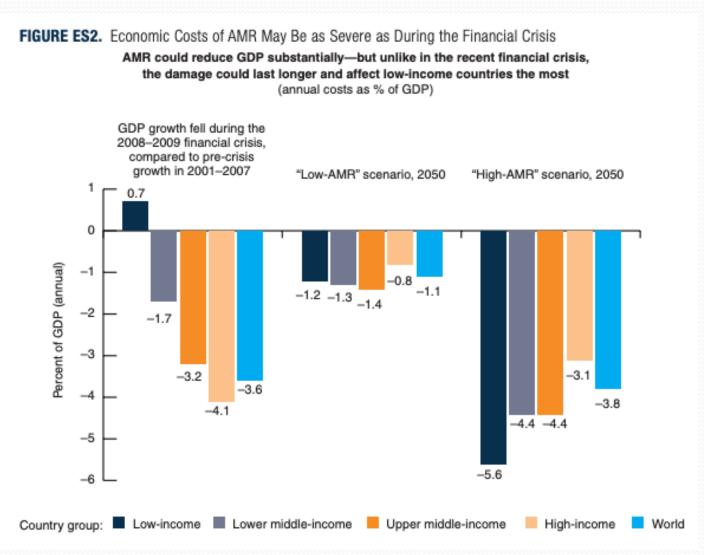
^{*}All ages, excludes viral aetiologies

Source: Table from Daulaire N, Bang A, Tomson G, Kalyango JN, Cars O. "Universal Access to Effective Antibiotics is Essential for Tackling Antibiotic Resistance. *J Law Med Ethics*, Summer 2015, pp. 17-21.

Forecasting the Future from AMR

If AMR is unchecked—

- Up to 10 million may die of drug-resistant infections annually in 2050 (UK Review on AMR, 2014)
- Up to 24 million more people would be forced into extreme poverty by 2030 (World Bank, 2017)
- In high AMR-impact scenario, 3.8% loss of annual GDP by 2050, with annual shortfall of \$3.4 trillion by 2030

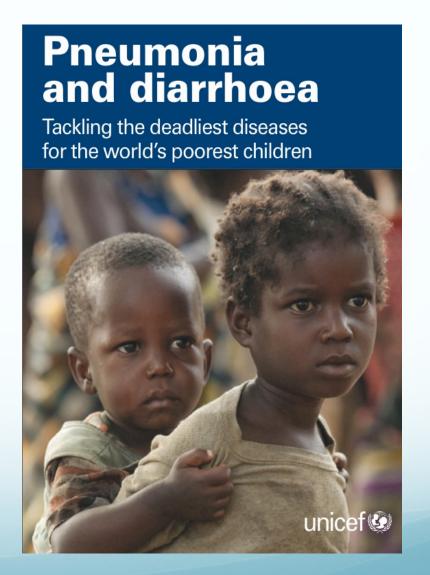


Source: World Bank, *Drug-Resistant Infections: A Threat to Our Economic Future*, March 2017.

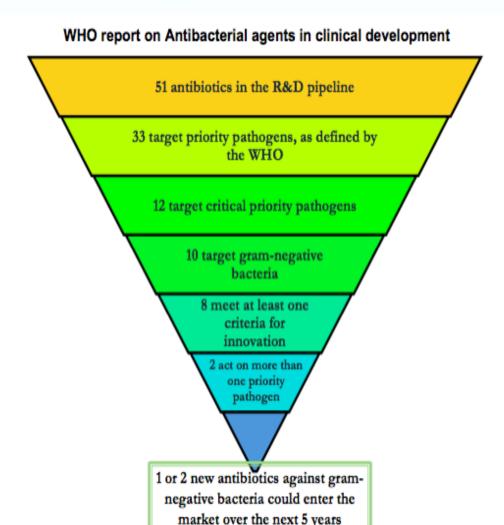
Access, but not Excess

Pneumonia: Fewer than one in three children with suspected pneumonia received antibiotics when necessary.

Diarrhea: Fewer than two in five children received appropriate treatment with oral rehydration therapy and continued feeding, yet many received unnecessary antibiotics.



Antibiotics in the Pipeline



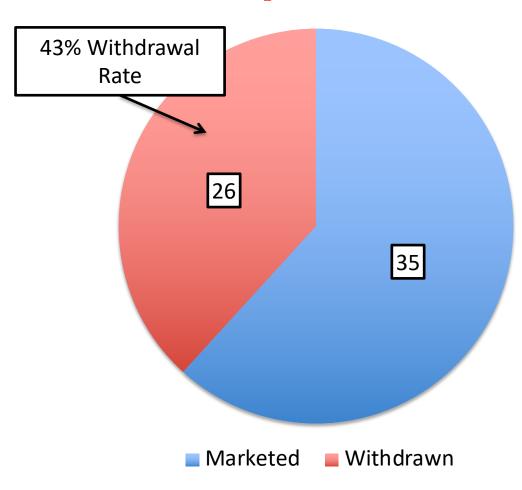
- Existing antibiotics on market vs. Antibiotics in the R&D pipeline
- Dearth of novel antibiotics against Gram-negative pathogens
- To prime the pump, push or pull?

Source: WHO, Antibacterial Agents in Clinical Development: An analysis of the antibacterial clinical development pipeline, including tuberculosis, 2017.

Are higher drug prices the solution?

- The price of doxycycline increased from \$20 for 500 tablets to \$1,849, a ninety-fold hike between October 2013 and April 2014.
- First-in-class antibiotics—linezolid and daptomycin—came to market without new incentives, commanding prices of \$3,172 and \$5,990, and average annual US sales of \$648 million and \$708 million, respectively.
- TOBI (tobramycin inhalation solution), as an orphan drug for treating cystic fibrosis patients with *Pseudomonas* lung infections, has risen from \$26,782 in 2009 to \$45,856 per patient per year in 2013.
- But what about Achaogen's Plazomicin, a once daily infusion costing \$944 a day, with treatment courses of 5-14 days, approved for the indication of complicated urinary tract infections (estimated 3 million cases of cUTI in hospital settings in the U.S. each year)?

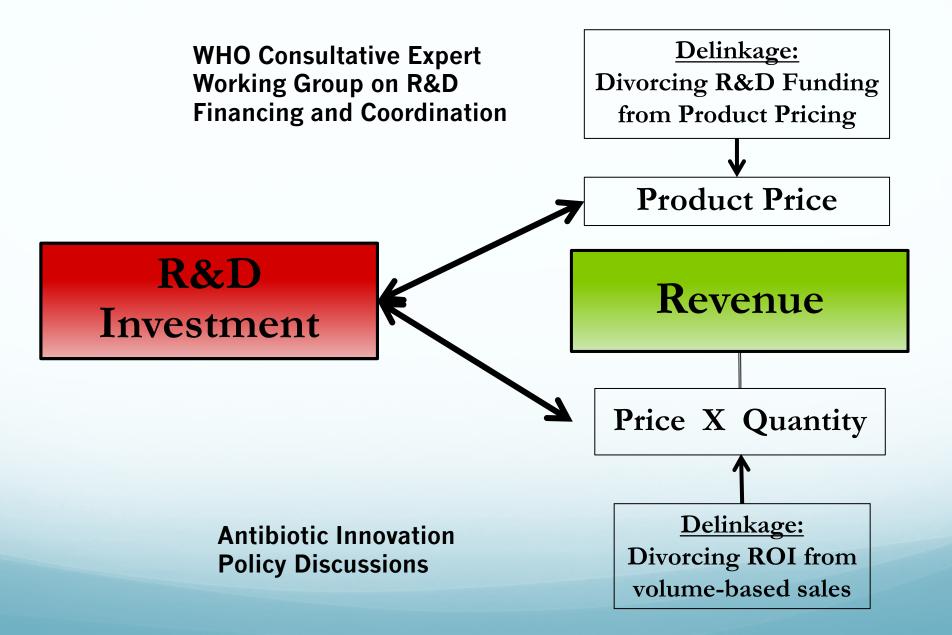
What is the role of therapeutic competition to market failure?



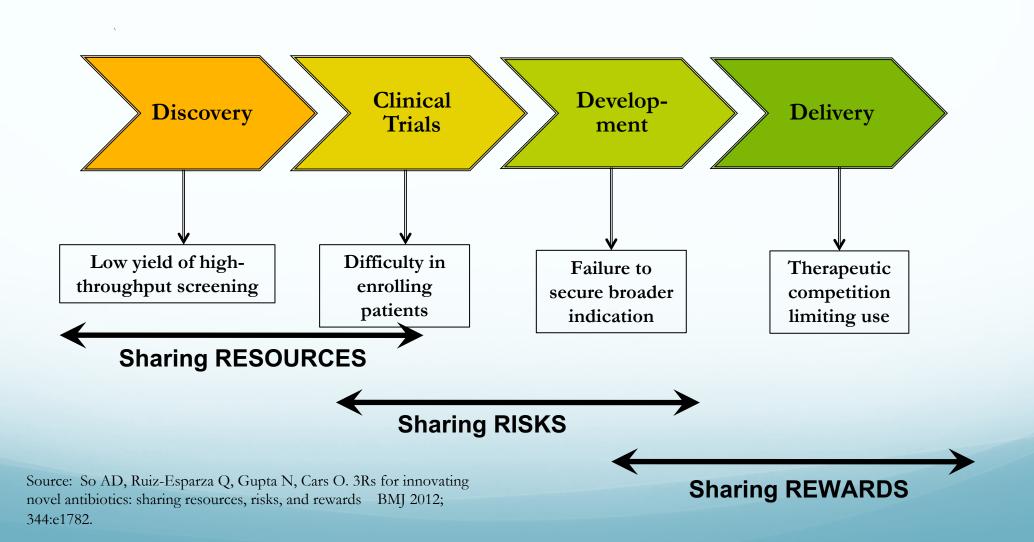
- Over 40% of systemic antibiotics were withdrawn from the market between 1980-2009.
- 20 out of 26 of these withdrawals were not for safety reasons. All of these drugs were from existing classes of antibiotics.
- Rate of antibiotic withdrawal is over three times greater than other therapeutic categories.

Source: Outterson K, Powers JH, Seoane-Vazquez E, Rodriguez-Monguio R, and Kesselheim AS. Approval and Withdrawal of New Antibiotics and Other Antiinfectives in the U.S., 1980-2009. *Journal of Law, Medicine & Ethics* Fall 2013, pp. 688-696.

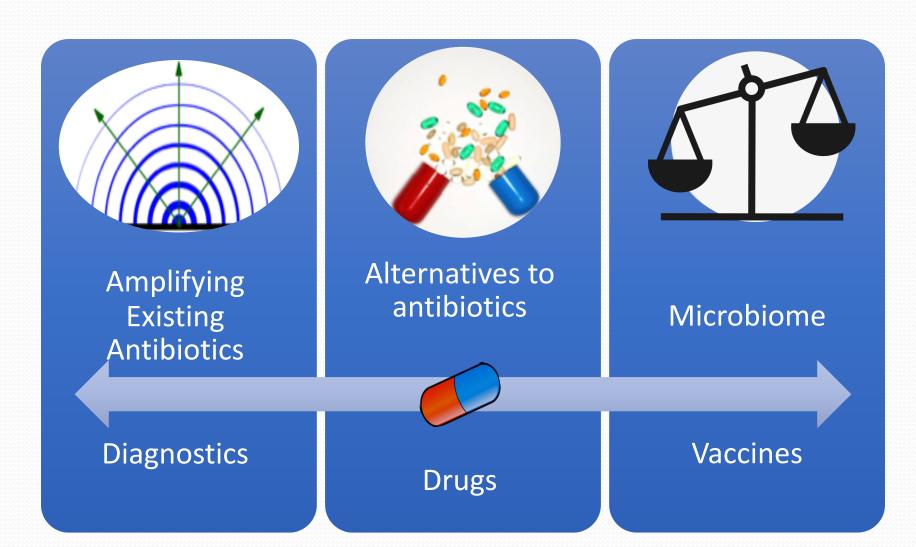
Incentives and Innovation Ecosystem



Reengineering the Value Chain for Antibiotic Innovation – The 3Rs



Complements and Substitutes for Antibiotics







https://www.lgniteTheIDEA.org/ahcj2019