

Reigniting innovation in antibiotics

When to Push and when to Pull

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Slides happily shared – just drop me a note!

The opinions in this presentation are my own and not necessarily those of any group with which I work.

Disclosures

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- He sits on the scientific advisory boards of Bugworks Research, Inc.; Basilea Pharmaceutica; Forge Therapeutics, Inc.; Novo Holdings; and Roche Pharma Research & Early Development
- He is a shareholder in AstraZeneca Pharmaceuticals; F2G, Ltd; Advent Life Sciences; Zikani Therapeutics; and Bugworks Research, Inc.
- He has received consulting fees from Phico Therapeutics; ABAC Therapeutics; Polyphor, Ltd.; Heptares Therapeutics, Ltd.; Gangagen, Ltd.; Meiji Seika Pharma; Basilea Pharmaceutica International Ltd.; Allecra Therapeutics GmbH; Forge Therapeutics, Inc.; SinSa Labs; AtoxBio; Peptilogics; F. Hoffmann-LaRoche, Ltd.; Novo Holdings; Innocoll; Vedanta; Progenity; Nosopharm SA; Roivant Sciences; and Shionogi Inc.
- The opinions expressed are his own and do not necessarily reflect the opinion of any of the groups with which he works.



Agenda

Antibiotics are the fire extinguishers
of medicine

How far in advance do we have to
plan?

Push and Pull: How and How much?

Pop Quiz: Have you used a fire extinguisher today?



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*Let's be more concrete.
Are you using a fire extinguisher right now?*

Fundamental starting points

- Antibiotics enable all of health care:
 - Safety net for surgery, cancer therapy, and essentially everything else
 - Fire extinguishers (or fire departments) of medicine
 - Infrastructure for civilization

- Stated differently...

Antibiotic benefits go beyond simple use

But, we don't (yet) have an agreed way to capture that value



*Antibiotics are the
fire extinguishers of
medicine!*

- **Enabling value:** Many surgical and medical procedures rely on prophylaxis with effective antibiotics.
- **Option or insurance value:** We may want to have an antibiotic in reserve before we really need it, so it's ready if resistance arises or worsens.
- **Diversity value:** Having multiple antibiotics may reduce selection pressure and delay resistance.



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Antibiotics are the fire extinguishers
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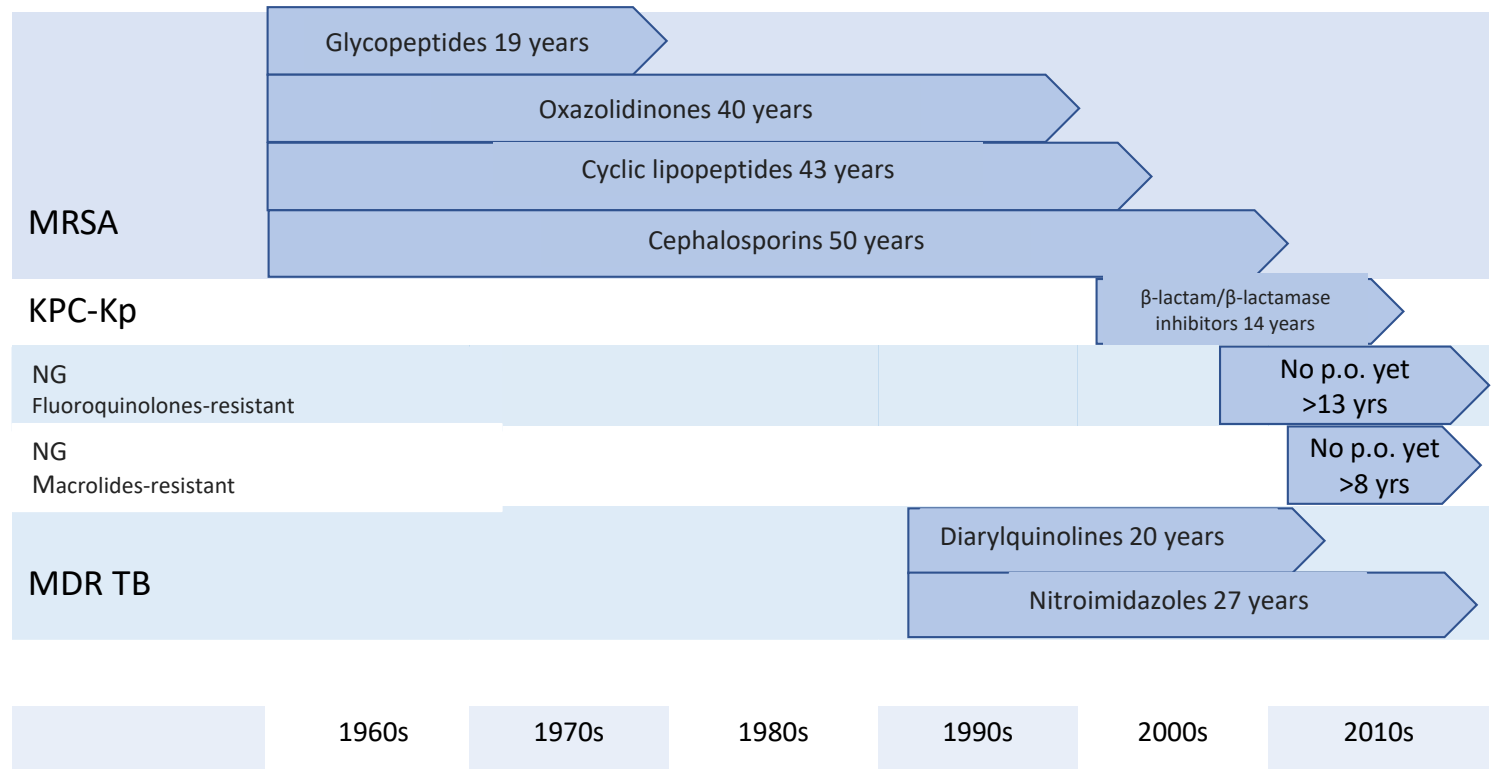
**How far in advance do we have to
plan?**

Push and Pull: How and How much?

From scratch? 10–20 years at least



Time from
discovery
to FDA
approval



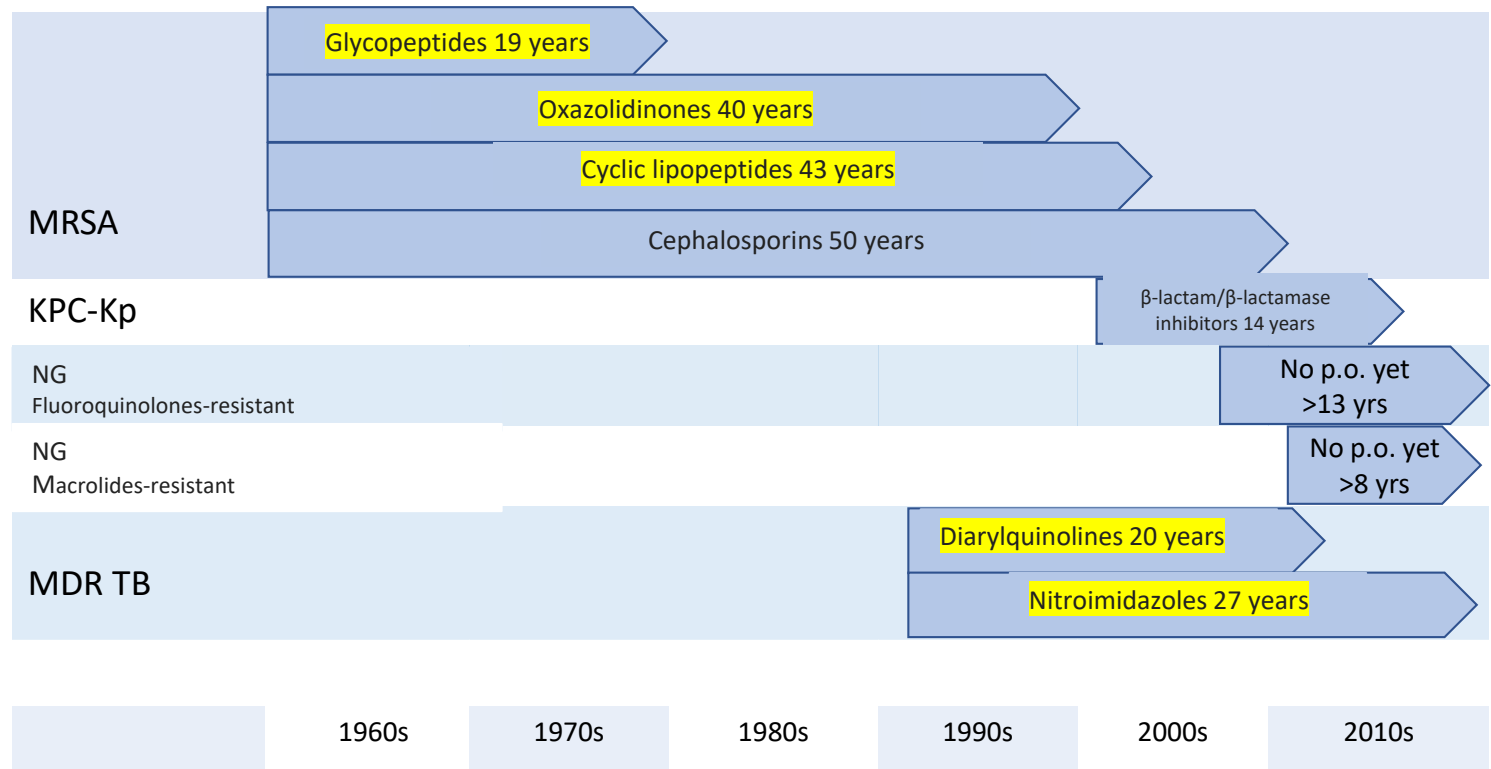
Sources: CDC AR Threats 2019, at 35; MRSA 1960 (Jevons MP 1961. BMJ); KPC-Kp 2001 (Vigitt H, et al. AAC 2001); NG-CR 2007 (CDC, MMWR 2007); NG-AR 2012 (Soge OO, et al. STD 2012); MDR-TB 1992 (Vallarino ME, et al., Pub H Rep 1992). Drug approvals: Vancomycin approved 1958, but US usage did not grow until 1979 (Kirst HA 1998. AAC). Other approvals from [Drugs@FDA.gov](https://www.fda.gov/drugs). For emergence of MRSA resistant to ceftaroline prior to its FDA approval, see Kelley WL et al., AAC 2015.

From scratch? 10–20 years at least

And, completely new classes are higher risk and slower



Time from
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Sources: CDC AR Threats 2019, at 35; MRSA 1960 (Jevons MP 1961. BMJ); KPC-Kp 2001 (Vigitt H, et al. AAC 2001); NG-CR 2007 (CDC, MMWR 2007); NG-AR 2012 (Soge OO, et al. STD 2012); MDR-TB 1992 (Vallarino ME, et al., Pub H Rep 1992). Drug approvals: Vancomycin approved 1958, but US usage did not grow until 1979 (Kirst HA 1998. AAC). Other approvals from Drugs@FDA.gov. For emergence of MRSA resistant to ceftaroline prior to its FDA approval, see Kelley WL et al., AAC 2015.



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Push and Pull: How and How much?

Antibiotic paradox

- If you invent a bad antibiotic, use will be limited
- If you invent a good antibiotic, use will be *very* limited*
- In both cases, prices will be low by modern standards

*And should be ... see next slide!

Rational stewardship limits sales ... *and this is a good thing!*

- Usage-based income will not cover costs^{1,2}
 - New antibiotics often have \leq \$25m/year in sales
- Running costs of a drug in its first 10 years: \$350m³
 - \$100m in post-approval commitments: pediatrics, etc.
 - \$25m/year to run the plant that makes your drug, surveillance, pharmacovigilance
- And to repay the investors who got you here?
 - Average cost to approval = \$1.3b (Wouters, JAMA 2020)⁴
 - With the \$350m in running costs, zero hope of repaying everybody even if your sales hit \$50m/year
- *Investing in antibiotics is madness!*

Push and Pull are both needed

- Push is well underway:
 - \$750m: Discovery to Phase 1: CARB-X, Novo REPAIR, etc.
 - \$1b: Phase 2-3: AMR Action Fund
- Pull is now needed: The UK pilot as a benchmark
 - GBP 10m/yr x 10 years = GBP 100m
 - The UK is 3% of the G20: 100m x 33 = GBP 3.3b \approx \$4b
- This is right on target! *Strong work, Team UK!*
- So, how do we engage and extend?
 - Wealthy countries need to contribute their fair share
 - Targets must be fair and consistently available
 - So far, the only sizeable further effort is in the US

Summary

- The problem is now well-defined
 - After 10 years of effort, we really understand the issues
- The solutions are equally clear
 - Push funding is familiar and is having an effect
 - The big mental shift is in Pull: We must think differently about antibiotics
- Antibiotics are the Fire Extinguishers of Medicine
 - Like other infrastructure, we must buy them in advance

#FireExtinguishersOfMedicine