How Should the EU Pull Their Weight? Designing and Implementing an Effective Delinked Pull Incentive for Antibiotics in the EU

ISPOR EUROPE 2022 PANEL SESSION

Moderated by
Adrian Towse
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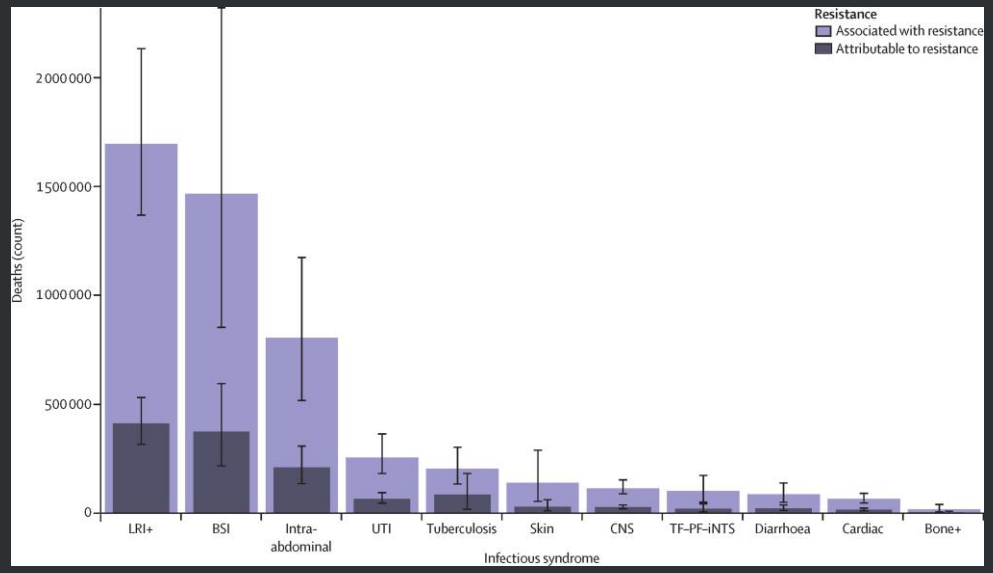
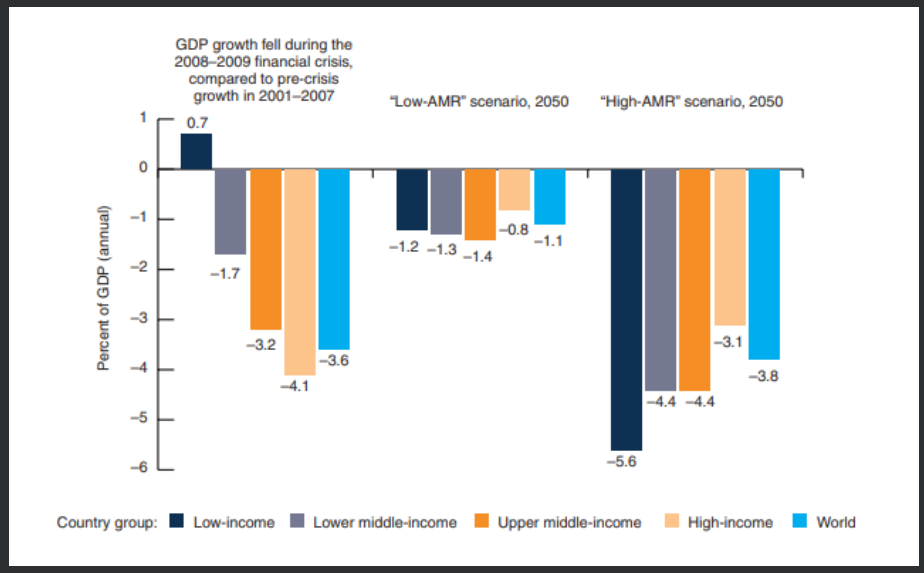
Antibiotic resistance is already having a significant impact on health and wealth globally.



"There were an estimated **4·95 million deaths** associated with bacterial AMR in 2019"[1]



"If AMR's current trajectory continues **global GDP will decline between 1.1 percent and 3.8** percent by 2050."[2,3]

1. Antimicrobial Resistance Collaborators, 2022: Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet

2. Milken Institute, 2022. Models for Financing Antibiotic Development to Address Antimicrobial Resistance
3. World Bank, 2017. Drug-resistant infections: A Threat to Our Economic Future

The England AMR pilot had three phases

ELIGIBILITY SCREEN
to select 2 antibiotics to participate in the pilot

2020

BROADER VALUE ASSESSMENT
to quantify the population-level benefit of each antibiotic

2020-2022

SETTING THE SUBSCRIPTION FEE
informed by the broader value assessment up to the £10 million/year cap

APRIL 2022

The antibiotic market is global and global solutions are needed

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USA

117TH CONGRESS
1ST SESSION

H. R. 3932

To establish a program to develop antimicrobial innovations targeting the most challenging pathogens and most threatening infections.

IN THE HOUSE OF REPRESENTATIVES

JUNE 16, 2021

Mr. MICHAEL F. DOYLE of Pennsylvania (for himself and Mr. FERGUSON) introduced the following bill; which was referred to the Committee on Energy and Commerce, and in addition to the Committees on Ways and Means, Veterans' Affairs, Armed Services, the Judiciary, and Homeland Security, for a period to be subsequently determined by the Speaker, in each case for consideration of such provisions as fall within the jurisdiction of the committee concerned

A BILL

To establish a program to develop antimicrobial innovations targeting the most challenging pathogens and most threatening infections.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Pioneering Antimicrobial Subscriptions To End Up surging Resistance Act of 2021" or the "PASTEUR Act of 2021".

EU

Clinical Infectious Diseases

VIEWPOINTS

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Financing Pull Mechanisms for Antibiotic-Related Innovation: Opportunities for Europe

Christine Årdal,[1] Yohann Lacotte,[2] and Marie-Cécile Ploy[2], on behalf of the European Union Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI)

How Should the EU Pull Their Weight? Designing and Implementing an Effective Delinked Pull Incentive for Antibiotics in the EU

1. What is the most appropriate mechanism for an EU pull incentive?
2. Which member states should be in- or excluded from payment?
3. How much should each member state pay?
4. How could the EU streamline value assessment methods?

Our panellists

Kevin Outterson will present the academic perspective on the panel. He will discuss the EU share of a global pull incentive needed to stimulate antibiotic development

James Anderson will cover the industry perspective in the panel and will discuss the importance of EU involvement in a pull incentive to generating a sustainable market for antibiotics

Christine Årdal will argue that European countries need to pay for predictable access, not consumption, to antibiotics that meet public health needs.

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Delinked Pull Incentives for Antibiotics in the EU

Christine Årdal, MBA, PhD
November 8, 2022

Antibiotic resistance symbol

Norwegian Institute of Public Health

Disclosures

Christine Årdal is a senior researcher at the Norwegian Institute of Public Health (NIPH) and previously the co-lead of the research and innovation work package of the EU Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI).

The views expressed in this presentation should not be considered to reflect the positions of NIPH, the Norwegian government or participating governments in EU-JAMRAI.

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Unavailability, a challenge for treating resistant infections

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Approval and commercial launch in fourteen high-income countries of NME antibacterials first approved by FDA, EMA, PMDA, or Health Canada, 2010-2019

INN	1st Approval	US	EMA*	UK	Sweden	France	Germany	Italy	Norway	Spain	Greece	Romania	Croatia	Denmark	Japan	Canada	Launches
cefiderocol	14-Nov-19	102	161	306	413												3
lascufloxacin	20-Sep-19														103		1
lefamulin	19-Aug-19	21	343														1
imipenem-cilastatin/ relabactam	16-Jul-19	321	212	382	382				290								4
omadacycline	2-Oct-18	122															1
sarecycline	1-Oct-18	92															1
eravacycline	27-Aug-18	35	24														1
plazomicin	25-Jun-18	6															1
meropenem/ vaborbactam	29-Aug-17	33	448	815	1037	1064											4
delafloxacin	19-Jun-17	196	910	1121													2
bezlotoxumab	21-Oct-16	115	89	174	131	1045	527	618	206	557					413		9
ceftazidime/ avibactam	25-Feb-15	35	484	748	827	1967	720	1049	310	999	980	933	1184	841			12
ceftolozane/ tazobactam	14-Dec-14	49	278	352	383	598	322	657	383	443	383	808	657	352	1630	291	14
oritavancin	6-Aug-14	56	224														1
tedizolid	20-Jun-14	10	276	315	438	577	276	1046	390	294	681	742		276	1432		12
dalbavancin	23-May-14	39	272	914	1279	1097	918	740		619	954	862	923				10
fidaxomicin	27-May-11	35	192	371	371	542	585	889	385	554	432	797	1711	371	2651	1648	14
ceftaroline	29-Oct-10	64	663	726	764	844	717	1007	755	1162	1315	795	2764	734			12
N approved or launched	18	17	14	11	10	8	7	7	7	7	6	6	5	5	5	2	0

All data as of 12/31/20

Notes: INN = international nonproprietary name; Empty cell = not commercially launched, except in the EMA column where empty cell = not approved by EMA; Number = lag from first approval to commercial launch, in days, except in the EMA column where number = lag from first approval to EMA approval, in days. The US was the country for all first approvals and first commercial launches, with the exception of lascufloxacin, approved and launched only in Japan. Color key: green = lowest lag in days; red = highest lag in days; yellow = 50th percentile lag in days.

Source: Outterson K, Orubu ESF, Rex J, Årdal C, Zaman MH. Clin Infect Dis 2021.

Need to pay for predictable access not consumption.

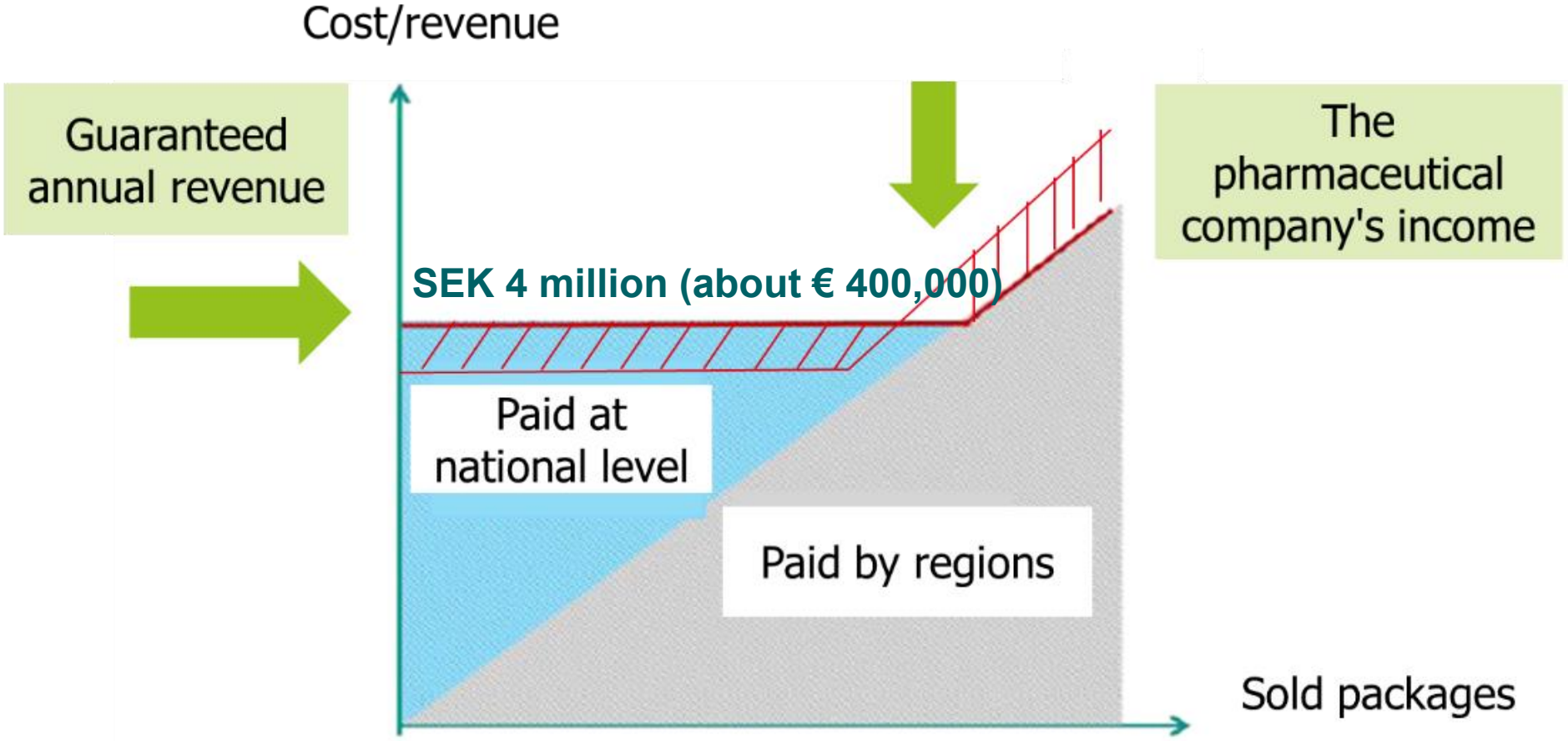
Pull incentive – transferable exclusivity voucher

Would likely stimulate antibiotic innovation, but…

- At a great cost (estimated at least 5x the cost of other incentives), paid by Member States
- Prolonging high prices of non-related medicines, most likely those treating small patient populations
- No access commitment for the antibiotic
- No legal precedent
- Significant opportunities for gaming

Sources: Årdal, Lacotte, Ploy, 2020. https://doi.org/10.1093/cid/ciaa153
IQVIA, 2021. https://www.iqvia.com/insights/the-iqvia-institute/reports/the-global-use-of-medicines-2022

Sweden's annual revenue guarantee



- MSD - ceftolozan-tazobactam
- MSD - imipenem-cilastatin-relebactam
- Shionogi - cefiderocol
- Pharmaprim - meropenem-vaborbactam
- Unimedic Pharma - fosfomycin

Sources: Questions and answers about procurement in pilot study for new remuneration model. Public Health Agency of Sweden: https://www.folkhalsomyndigheten.se/contentassets/92ec9ceb2f2f428cb683add24b4f785b/faq-upphandling-pilotstudie.pdf

Potential European annual revenue guarantee

EC / EMA

Marketing authorization holder

Commit to access & stewardship reqs

Opt in

New antibiotics matching public health needs

List of eligible antibiotics

European Commission

Joint tender description for revenue guarantee

Signed contracts for revenue guarantees

Guarantee payment

Normal national procurement and reimbursement processes

Guarantee amount owed

Opt in (a set minimum number)

Important antibiotics with vulnerable supply

National governments

Sources: Årdal, Lacotte, Edwards, Ploy. 2021, https://doi.org/10.3390/antibiotics10060749
Slovenian Presidency, https://www.jazmp.si/en/slovenian-presidency-of-the-council-of-the-eu-2021/

Why an annual revenue guarantee?

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1. It **ensures access** to the selected antibiotics, while operating **independently** from national HTA, pricing, and procurement models.

   "11 of 13 countries would prefer a common, multinational incentive, so long as it is independent from national medicine pricing, procurement, and reimbursement processes."

2. It rewards **success**.

   Between 2014-20 five antibiotics were approved for "critical" drug/bug combinations, ten were discontinued. Innovative antibacterials have higher scientific failure rates.

3. It can ensure **profitability** for innovators and suppliers of **both old and new** antibiotics.

The revenue guarantee amount is flexible, tailored to the attributes of the antibiotic.

Sources: Årdal, Lacotte, Edwards, Ploy. 2021, https://doi.org/10.3390/antibiotics10060749
Pew Trusts, 2019. https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2019/five-year-analysis-shows-continued-deficiencies-in-antibiotic-development

- Europe needs to test new incentives to secure access to important antibiotics, both old and new.
- Designed well, this incentive will also stimulate innovation.
- An annual revenue guarantee seems the most promising, aligned with Member States' expectations, with the ability to adjust over time based upon lessons learned.

Thank you to Marie-Cécile Ploy and Yohann Lacotte for their feedback on these slides.