

Annex 2: Programme of Workshop on “Increasing Investments for AMR R&D”

Tuesday 28 May 2019, Domaine de Penthes, Geneva, Room: Espace Gallatin,

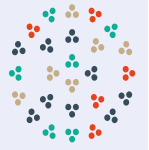
Time	Title	Speaker
8:30 – 9:00	Welcome Coffee and Registration opens	
9:00 – 9:10	Welcome and Opening remarks Vice-Chair of Global AMR R&D Hub	Bersabel Ephrem, Canada
9:10 – 9:20	Introductory Remarks, G20 Presidency - Japan	Chieko Ikeda – Senior Assistant Minister for Global Health
9:20 – 9:40	Keynote R&D in the Global Response to AMR	Dame Sally Davies – Chief Medical Officer, UK
	Plenary Session 1 – One Health	Chair: Larry Kerr – US Department of Health and Human Services
9:40 – 9:55	<u>Setting the Stage:</u> Progress to date regarding implementing incentives and funding mechanisms	Christine Årdal – Norwegian Institute of Public Health
9:55 – 10:10	Fostering investment in development of new antimicrobial treatments	Peter Beyer – WHO
10:10 – 10:25	Financing AMR from an EIB perspective	Felicitas Riedl – European Investment Bank
10:25 – 10:40	Investing in agriculture to reduce human health externalities: a LMIC perspective	Delia Randolph –International Livestock Research Institute
10:40 – 10:55	STAR-IDAZ International Research Consortium: A Platform for Global Coordination of Animal Disease Research	Alex Morrow – STAR-IDAZ
10:55 – 11:15	Coffee Break	
	Plenary Session 2 – One Health	Chair: Padmini Srikantiah – Bill & Melinda Gates Foundation
11:15 – 11:30	Animal Health R&D: Barriers, Trends and Opportunities	Carel du Marchie Sarvaas – HealthforAnimals
11:30 – 11:45	Vaccines for AMR: recommendations, challenges, and incentives	Elizabeth Klemm – Wellcome
11:45 – 12:00	Diagnostics: status of current and novel technologies to preserve and protect existing medications	Adam Zerda – Becton Dickinson
12:00 – 12:45	Panel Discussion: Food for thought for the breakout session, with speakers from plenary sessions 1 and 2 and Jeremy Knox (Wellcome)	Moderators: Larry Kerr and Padmini Srikantiah

12:45 – 13:45	Lunch	
	Plenary Session 3 – Country Perspectives	
13:45 – 13:55	Strengths and weaknesses of research priorities on AMR in Europe	Chair: Marie-Cecile Ploy – EU Joint Action Antimicrobial Resistance and Healthcare-Associated Infections
13:55 – 14:05	A reimbursement model for keeping antibiotics available in Sweden	Jenny Hellman – Public Health Agency of Sweden
14:05 – 14:15	Antibiotic research and prudent use: The Swiss perspective	Nora Kronig – Swiss Federal Office of Public Health
14:15 – 14:25	Overview of public AMR R&D investments – funding instruments for a One Health approach and LMIC	Laura Marin – Joint Programming Initiative on Antimicrobial Resistance
14:25 – 14:35	Incentivizing investments in R&D in LMICs	Katerina Galluzzo – Unitaid
14:35 – 14:45	Fostering innovations addressing AMR threat, from India for global	Anand Anandkumar – Bugworks
14:45 – 14:55	Africa's place in investment and financing of AMR	Almoustapha Maiga – African Association for Research and Control of Antimicrobial Resistance
14:55 – 16:15	Workshop: Breakout session for discussions in smaller groups	Session Leader
Room: Espace Gallatin	<u>Human sector:</u> Where do we need to attract more investment (from new investors)? Do we need new mechanisms? How do we attract additional investments? Also include vaccines.	Jean-Pierre Paccaud - Global Antibiotic Research and Development Partnership
Le Grenier	<u>Animal sector:</u> Are business models from the human sector applicable to the animal field? What is the current situation, what are the needs? Also include vaccines.	Delia Randolph – International Livestock Research Institute
Pavillon Fontana	<u>LMIC:</u> What market economic models work in this context? Are funds/incentives in HIC applicable to LMIC? Analyse and provide suggestions for what is required in LMIC, including barriers and opportunities.	David Kaslow – PATH
16:15 – 16:45	Coffee Break	
16:45 – 17:30	Report Session: To provide a brief summary of discussions of round tables, and areas for future consideration by the Global AMR R&D Hub.	Moderator: Secretariat Global AMR R&D Hub One speaker/table, 10 min + 5 min discussions
17:30 – 17:45	Closing Remarks	Andrea Spelberg – Federal Ministry of Education and Research, Germany
18:00 – 19:00	Networking Reception	



HM Government

GLOBAL
AMR R&D
HUB



IACG | Interagency Coordination Group on
Antimicrobial Resistance

R&D in the Global Response to AMR

Professor Dame Sally C. Davies
Chief Medical Officer For England
Co-convener of the UN Inter-Agency Coordination Group on AMR

Global AMR R&D Hub Workshop
WHA 2019

The IACG

The IACG Recommendations



A. Accelerate progress in countries



B. Innovate to secure the future



C. Collaborate for more effective action



D. Invest for a sustainable response



E. Strengthen accountability and global governance

The IACG Recommendations

D1: The IACG calls on governments; global, regional, national, bilateral and multilateral financing and development institutions and banks; and private investors to systematically apply standards to assess risks and impacts related to AMR (**an AMR lens**) when making investments

E2: The IACG recommends the urgent establishment of a **One Health Global Leadership Group** on AMR

E3: The IACG requests the Secretary-General, in close collaboration with the Tripartite, UNEP and other international organizations, **to convene an Independent Panel on Evidence for Action against AMR** in a One Health context



Innovate to secure the future



B1: The IACG calls on public, private and philanthropic donors and other funders to **increase investment and innovation** in quality-assured, new antimicrobials, novel compounds, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials for human, terrestrial and aquatic animal and plant health, as well as implementation and operational research.

B3: The IACG calls on public, private and philanthropic research funders and other stakeholders to **build upon current research and development efforts** for new antimicrobials, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials; and to strengthen implementation and operational research and research coordination and collaboration in a One Health context.

The UK Perspective

UK AMR R&D Funding



LONGITUDE PRIZE



**Global AMR
Innovation Fund
(GAMRIF)**

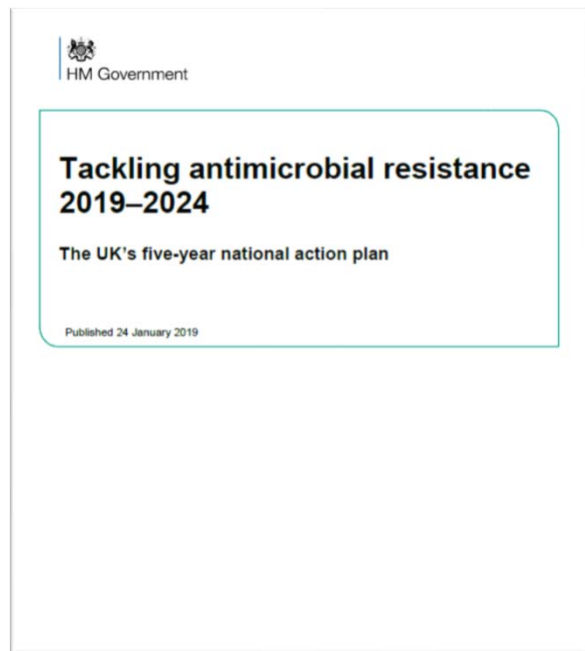
Data Re-use Prize

New data re-use prizes help unlock the value of research

The winners of our Wellcome Data Re-use Prizes have generated new insights in antimicrobial resistance and malaria research.



Pull Incentives: a UK perspective



‘We are leading the way in testing solutions that will address our global failure to incentivise the development of new antimicrobials and alternative treatments.

We will test innovative models that pay companies based primarily on a NICE led health technology assessment of their value to our National Health Service as opposed to the volumes used.’

Working Collaboratively





Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections



Co-funded by the
Health Programme
of the European Union

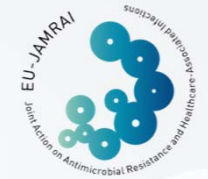
Setting the Stage: Progress to date regarding implementing incentives and funding mechanisms Global AMR R&D Hub Workshop

Work Package 9, Research & innovation
WP Leaders: Marie-Cécile Ploy and Christine Årdal
Date: May 28, 2019
Author: **Christine Årdal**, caa@fhi.no



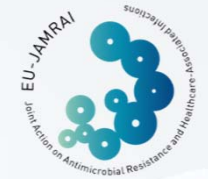
Norwegian Institute of Public Health

Mission of the EU-JAMRAI



EU-JAMRAI is a European Union Joint Action on Antimicrobial Resistance (AMR) and Healthcare-Associated Infections (HCAI) that brings together 44 partners from 28 countries and more than 30 stakeholders. Our mission is to **foster synergies** among EU Member States by **developing and implementing effective *One Health* policies** to fight the rising threat of AMR and to reduce HCAI.

WP9 – Research and innovation



1. To ensure that national processes for research and innovation priority-setting are grounded in a broad *One Health* approach and that both EU **Member States' research priorities and knowledge gaps** are addressed in the development of strategic research agendas
2. To explore and detail **European strategies to implement mechanisms to increase innovation** and other means to fight against AMR and HCAI
3. To ensure that national procedures are in place to **translate research findings into public health policies and practices** related to combating AMR and HCAI

Technologies and practices needed to combat AMR

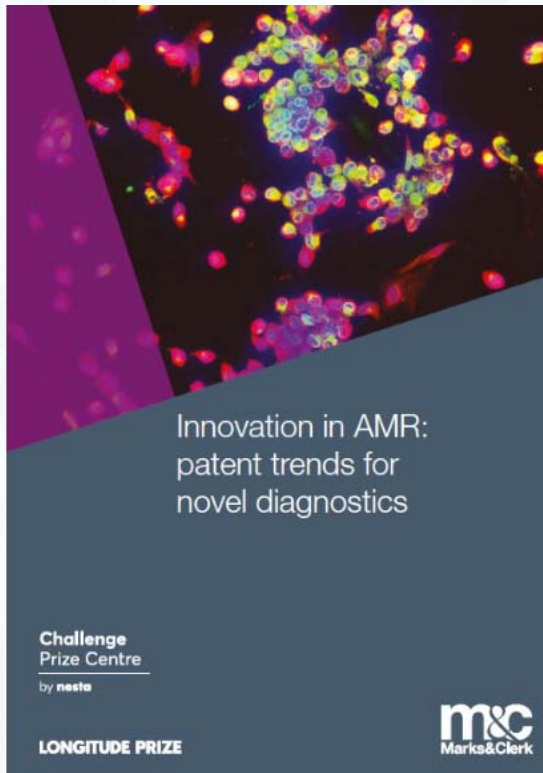


	Public awareness		Sanitation and hygiene
	Antibiotics in agriculture and the environment		Vaccines and alternatives
	Surveillance		Rapid diagnostics
	Human capital		Drugs
	Global Innovation Fund		International coalition for action

 Review on Antimicrobial Resistance

Source: AMR Review. 2016.

Status on diagnostic innovation



Longitude Prize, October 15, 2018:

Struggling to attract adequate funding because:

- Investors are concerned that price expectations are too low to assure return on investment
- Not convinced that financing will be available either from health systems or funders to help create this new market

Report recommendation:

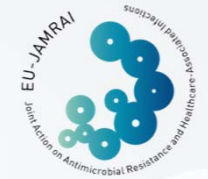
Purchase commitments

More coming from IMI's Value-Dx








Calls for incentives and funding mechanisms



Progress to date

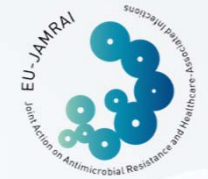


Significant push funding...

 Combating Antibiotic Resistant Bacteria			 Global Antibiotic Research & Development Partnership A joint effort of WHO and industry	 impact fund novo holdings	 
USD 502m (2016-21)	USD 960 m (2010-19)	€ 234m (2012-2024)	€ 270m (2017-23)	USD 165m (2018-23)	€ 700m (2014-20)
Novel therapeutics, diagnostics, preventatives, devices	Novel therapeutics, diagnostics, preventatives, devices	Novel therapeutics, diagnostics, surveillance, prevention, stewardship	Novel therapeutics, Optimize antibiotics, Develop combinations	Novel therapeutics, companion diagnostics	Novel therapeutics, diagnostics, economic models

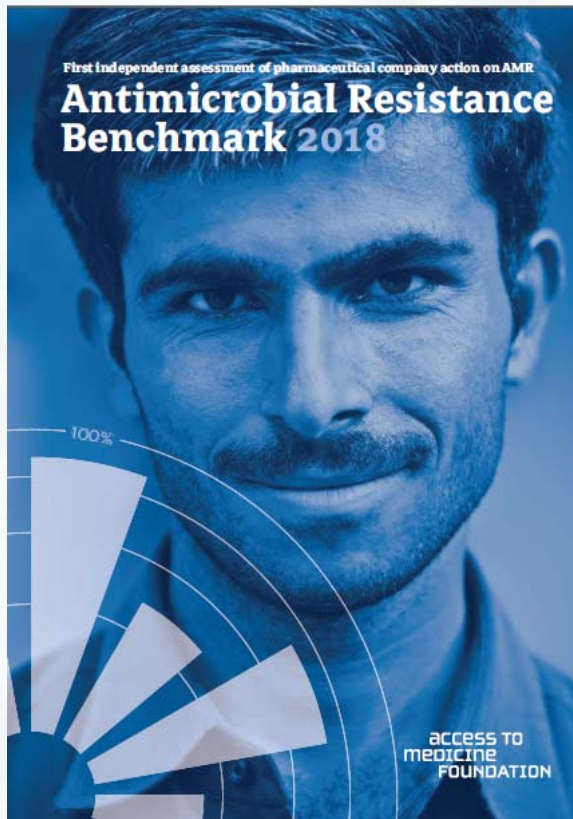
Source: K. Outterson, World AMR Congress 2018 and R. Bright, Forbes 2019.

Need for both “push” and “pull” incentives



- Push reduces the R&D costs and removes risk.
- Pull incentivizes the private sector to invest.
 - Public sector financing of antibiotic R&D = \$ 550 million per year (OECD, 2017)
 - Private sector financing = \$ 2 billion in 2016 (AMR Industry Alliance, 2018)
 - Pull pilots in Sweden and UK as well as GAIN Act in USA, so pull has not yet been implemented

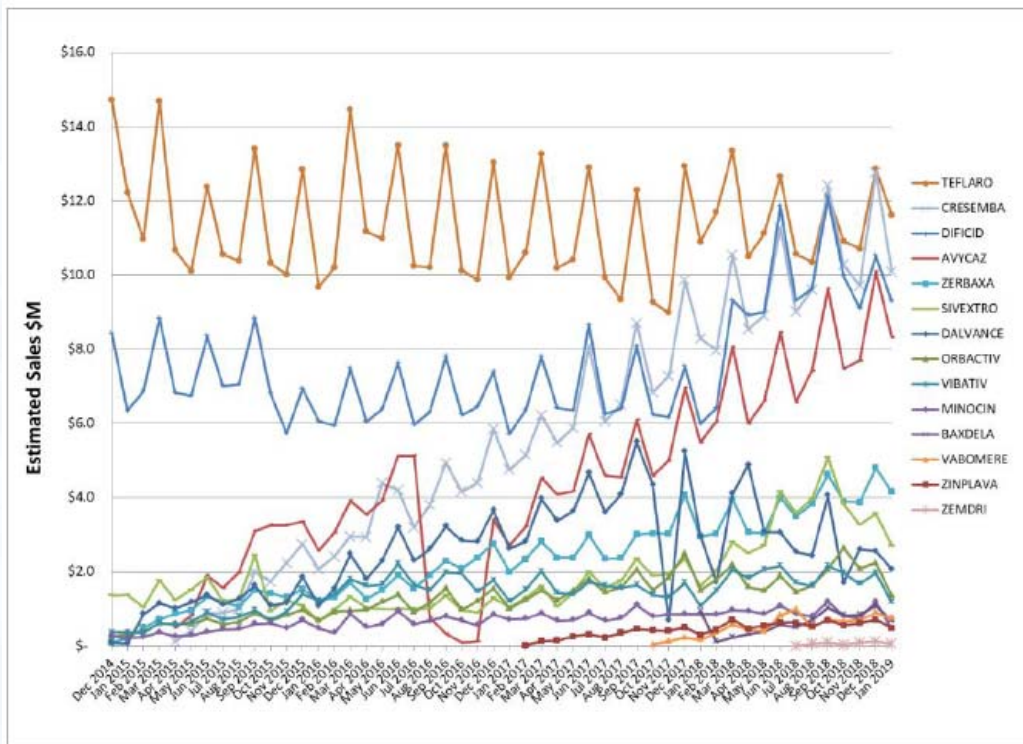
Disappearance of therapeutic innovators



Published in January 2018
and now:

- 5 of 29 (**17%**) antibiotic companies have left the market or dramatically downsized their activities, including...
 - 2 of 7 (**29%**) large pharmaceutical companies
 - 2 of 12 (**17%**) SMEs
 - 1 of 10 (**10%**) generic companies

Sales of newly launched antibiotics in US



Branded Antibiotic Sales Trajectories (3-month Moving Average; IQVIA Data through 1/31/19)

Source: Alan Carr, Needham & Co.

Impact of lack of pull incentives

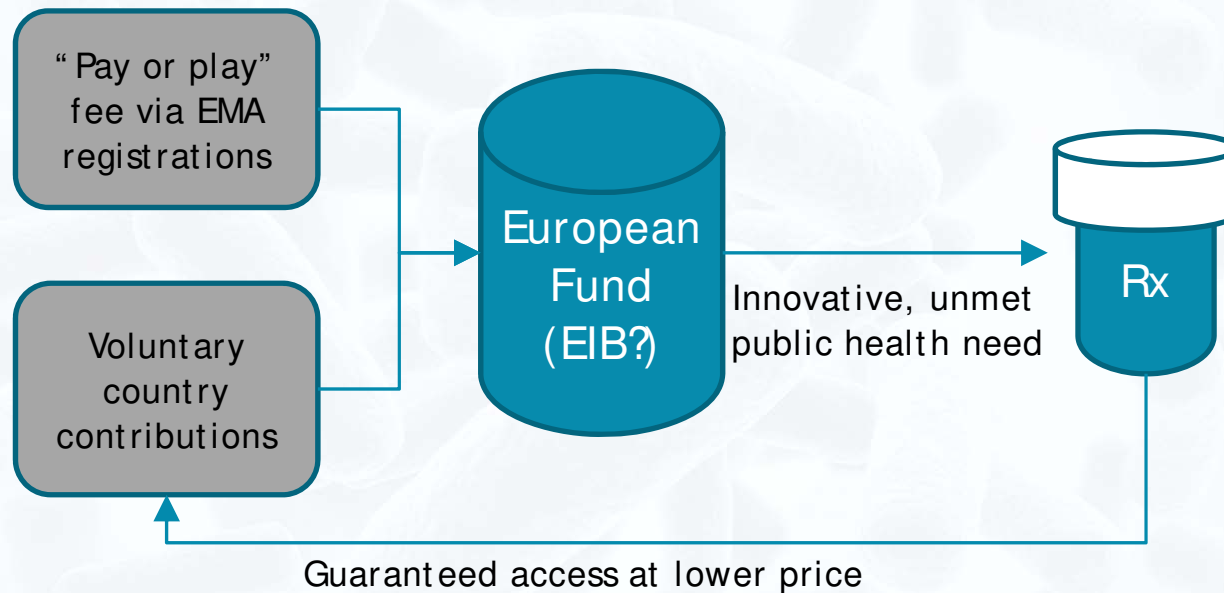


Achaogen:

- Raised USD 250 million in public and philanthropic funds and USD 200 million in private funds
- Initiated a Phase III clinical trial of plazomicin vs. colistin for CRE in 2014; 2,100 patients screened to enroll 37 over 2.5 years
- Launched plazomicin against CRE in USA in 2018; not registered or available in Europe
- Filed for bankruptcy April 2019

Sources: Economist 2019 and J. Rex Achaogen summary, 2019.

Assessing European appetite for a pull



At the same time, look at solutions to potentially ease innovators' costs (labeling, distribution, ...) while maintaining safety

How many essential antibiotics require support?









Meeting Report
*Antibiotic Shortages: Magnitude, Causes
and Possible Solutions*

“The experiences of several European countries indicate that **shortage of antimicrobial agents is common**, and the frequency of shortages seems to be **increasing**, despite Europe’s position as the second largest regional manufacturing center of antibiotics.”

Impact of no pull mechanism



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Source: K. Outtersson, World AMR Congress 2018 and R. Bright, Forbes 2019.

Thank you!

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Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections



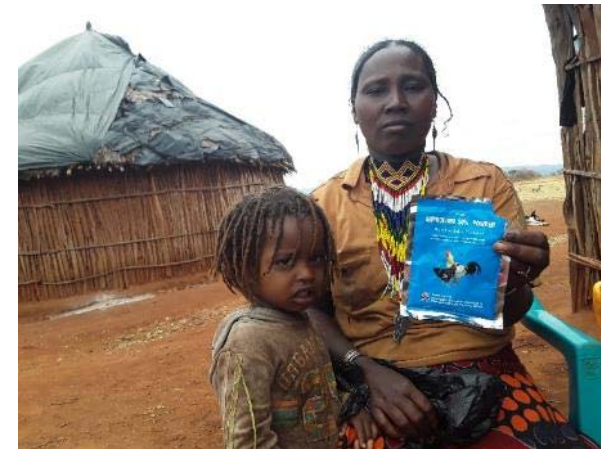
Co-funded by the
Health Programme
of the European Union

** This presentation arises from the Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), which has received funding from the European Union in the framework of the Health Program (2014-2020) under the Grant Agreement N° 761296. Sole responsibility lies with the author and the Consumers, Health, Agriculture and Food Executive Agency is not responsible for any use that may be made of in the information contained therein.*

Investing in agriculture to reduce human health externalities: a LMIC perspective

Delia Grace, Program Leader Animal and Human Health
INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE

Workshop on “Increasing Investments for AMR R&D”
Tuesday 28 May 2019, Domaine de Penthes, Geneva



ILRI
INTERNATIONAL
LIVESTOCK RESEARCH
INSTITUTE



CGIAR on the ground: 15 research centres | more than 70 countries



REDUCED POVERTY

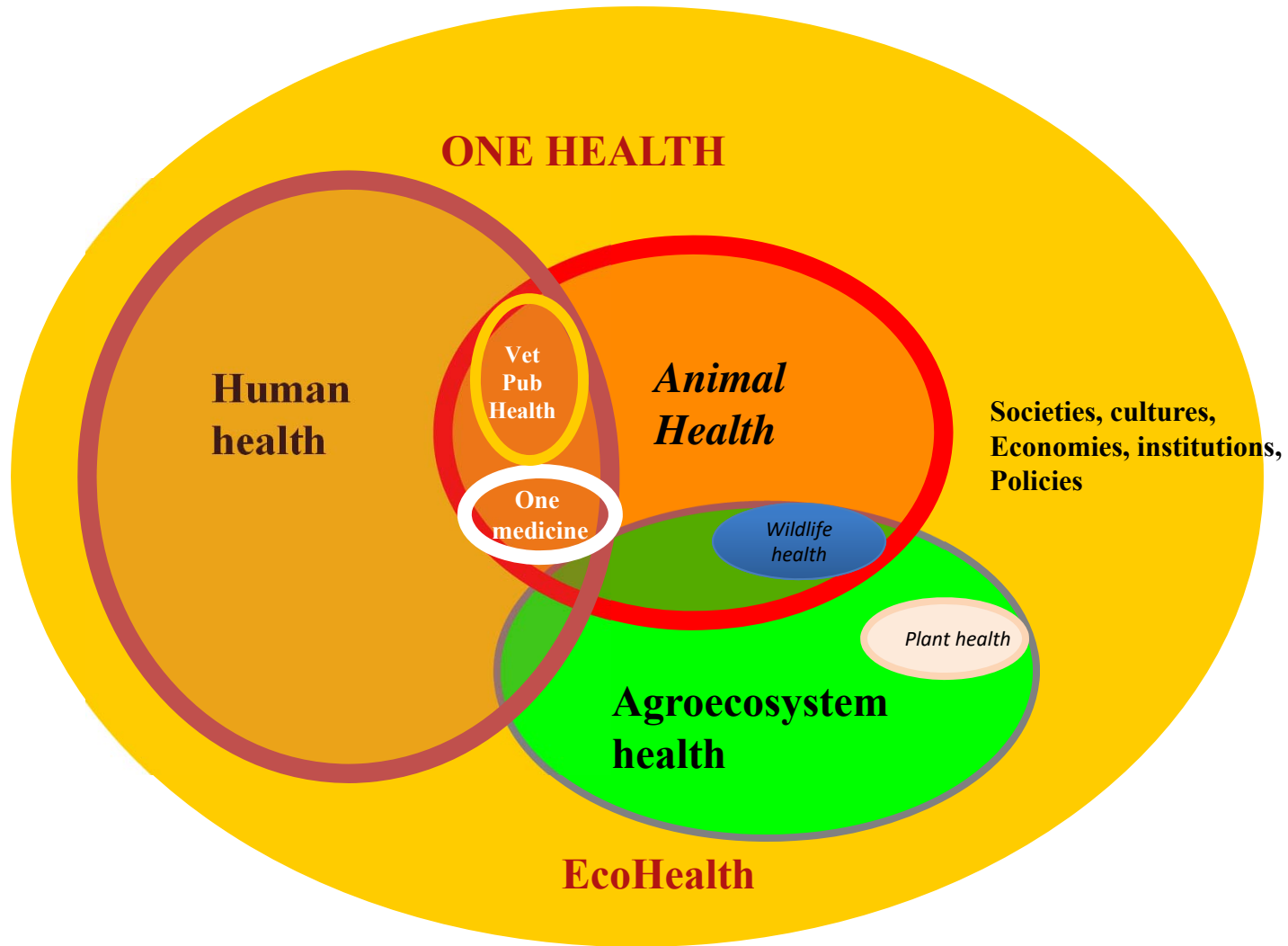
IMPROVED FOOD AND NUTRITION SECURITY FOR HEALTH

IMPROVED NATURAL RESOURCE SYSTEMS AND ECOSYSTEM SERVICES

More than 73% of all antimicrobials sold in the world are used in animals
Van Boeckel et al 2017
Around 80% of farmers rely on untrained health providers
Grace, 2015

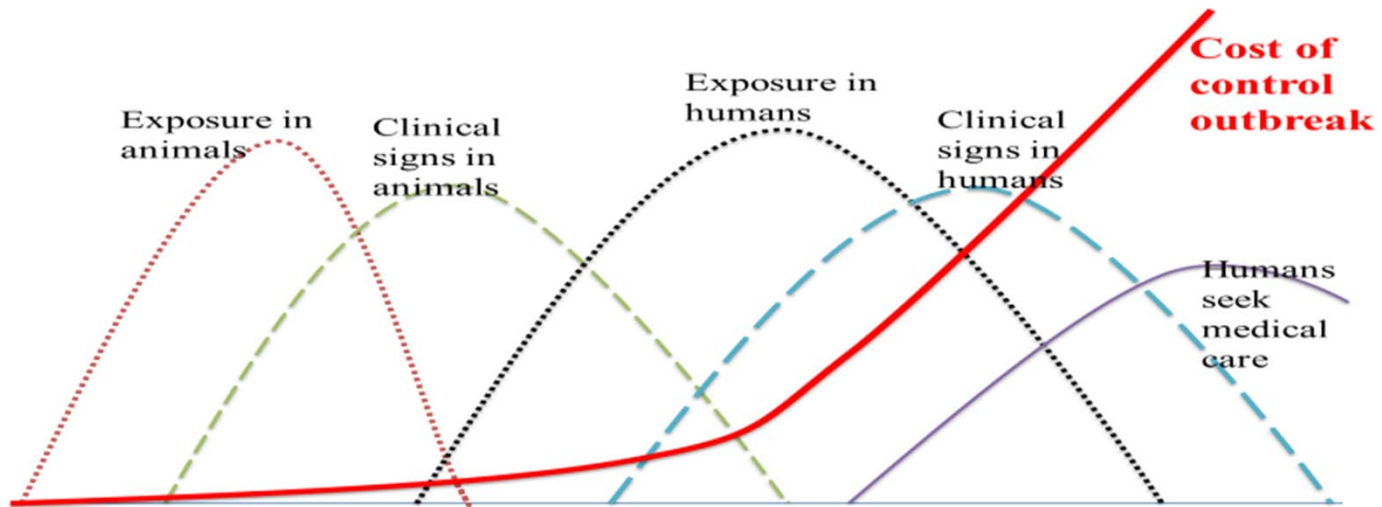


The One Health Argument



Better to control disease in the animal host than human victim

Surveillance and response in animal hosts can reduce costs by 90% (Grace, 2015)



Adapted from IOM 2009

Caveat: a problem of access as well as excess

- Animal disease is a key constraint:
Billions die each year from preventable & curable disease
- As livestock systems intensify in developing countries,
diseases may increase

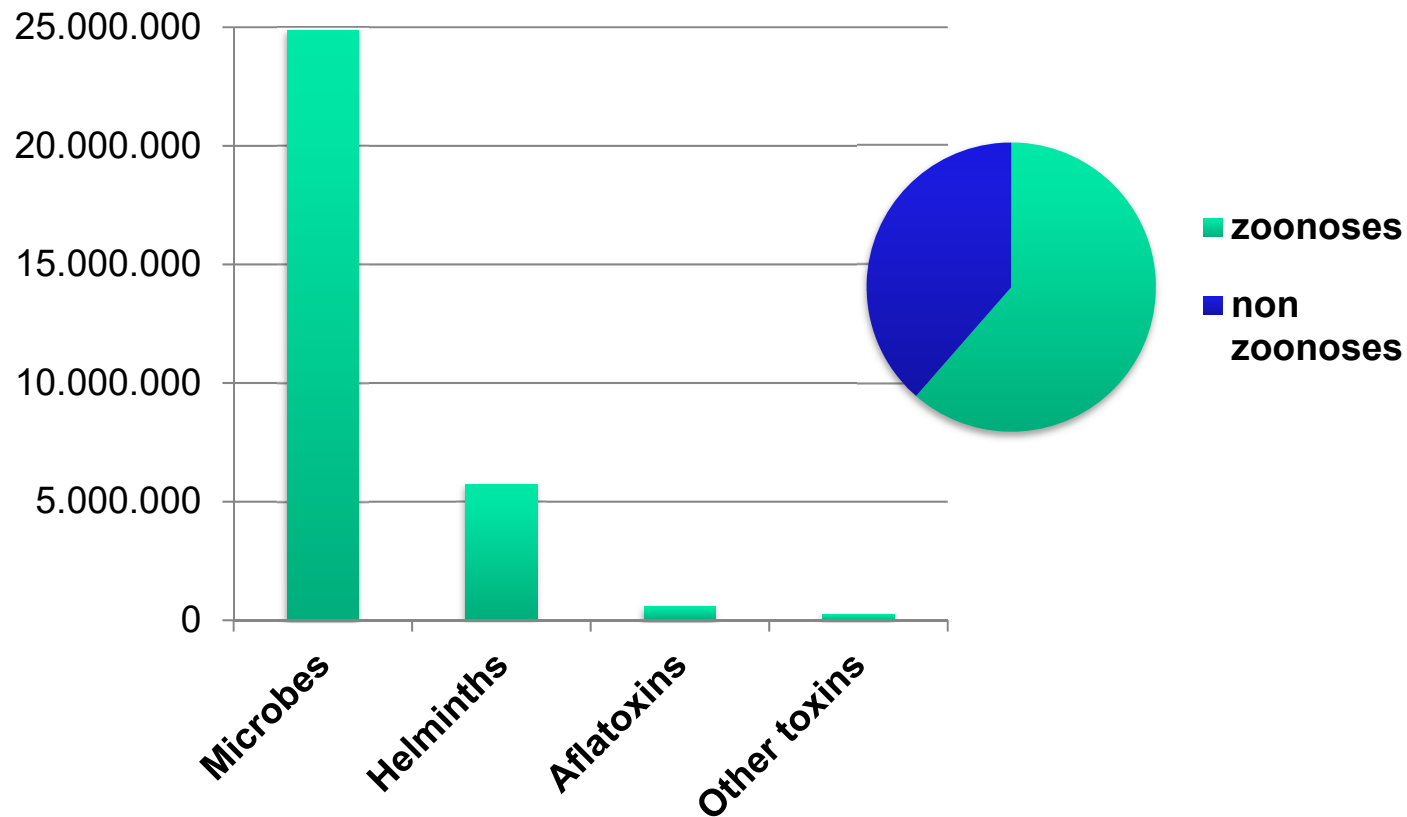


Annual mortality of African livestock
(Around half due to preventable or curable disease)

	Young	Adult
Cattle	22%	6%
Shoat	28%	11%
Poultry	70%	30%

*Otte & Chilonda,
IAEA*

Caveat: what human health externalities?



Health burden of foodborne disease in developing countries is comparable to that of HIV AIDS, TB or malaria

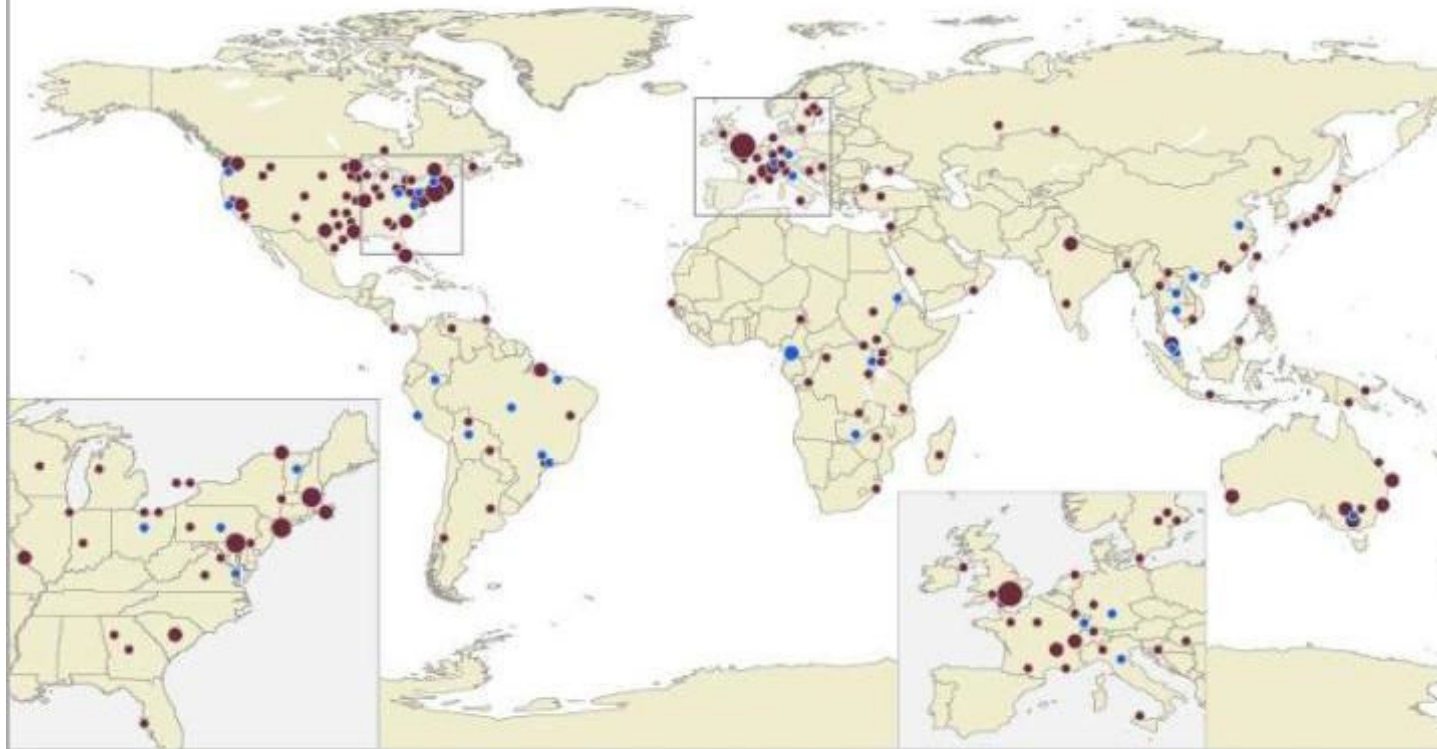
Havelaar et al., 2015

Emerging zoonotic disease events, 1940–2012

Potential Hotspots in US, Western Europe, Brazil, Southeast Asia

Most emerging human diseases come from animals. This map locates zoonotic events over the past 72 years, with recent events (identified by an ILRI-led study in 2012) in blue. Like earlier analyses, the study shows western Europe and western USA are hotspots; recent events, however, show an increasingly higher representation of developing countries.

- 1 EVENT
- 2-3 EVENTS
- 4-5 EVENTS
- 6 EVENTS
- EVENTS IDENTIFIED IN 2012 (recent emergence)



Map by IOZ, published in an ILRI report to DFID: *Mapping of Poverty and Likely Zoonoses Hotspots*, 2012.

Grace et al.,
2012

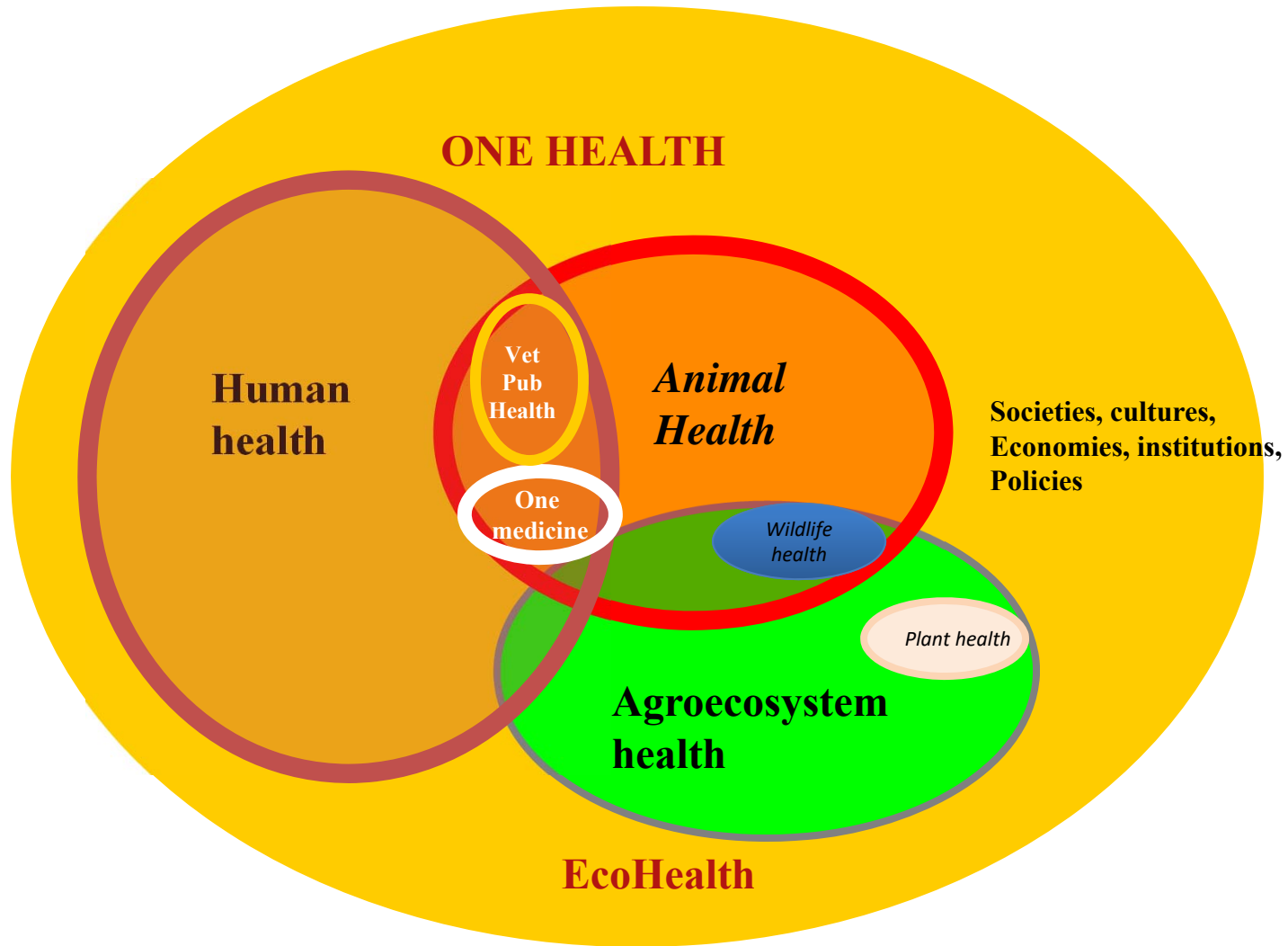
Investment case

- How much human AMR comes from agriculture?
- What interventions could reduce use in agriculture?
- What are the costs and benefits of these interventions?
What are the un-intended consequences?
Are interventions feasible?
- What effect does the intervention have on human AMR?
- What effect does the intervention have on human and animal well-being?

What we know

	HIC	LMIC
How much AMR from agriculture?	Certainly a little, maybe more	Don't know
Interventions shown to reduce AMU at scale	Yes	No
Interventions are affordable	Yes	Don't know
Interventions are feasible	Yes	Maybe not
Un-intended negative consequences	Likely small	May be large
Interventions appreciably reduce AMR in people	Don't know	Don't know
Effect on human and animal overall well-being	Don't know	Don't know

AMR is a One World challenge



Conclusions: 1

- Animal agriculture uses more AM than human health does and is rapidly trending up
- Most use and most growth in use is in LMIC
- Dual challenge: access as well as excess
- AMR is not the only externality of disease in LMIC and trade-offs need to be examined
- Evidence should under-pin a business case but is mostly lacking for LMIC
- Yet there is a strong rationale for One Health as the best approach for solving cross-sectoral challenges



Antimicrobial Resistance Hub

www.amr.cgiar.org

Launched during partner event, 21/22 February in Nairobi

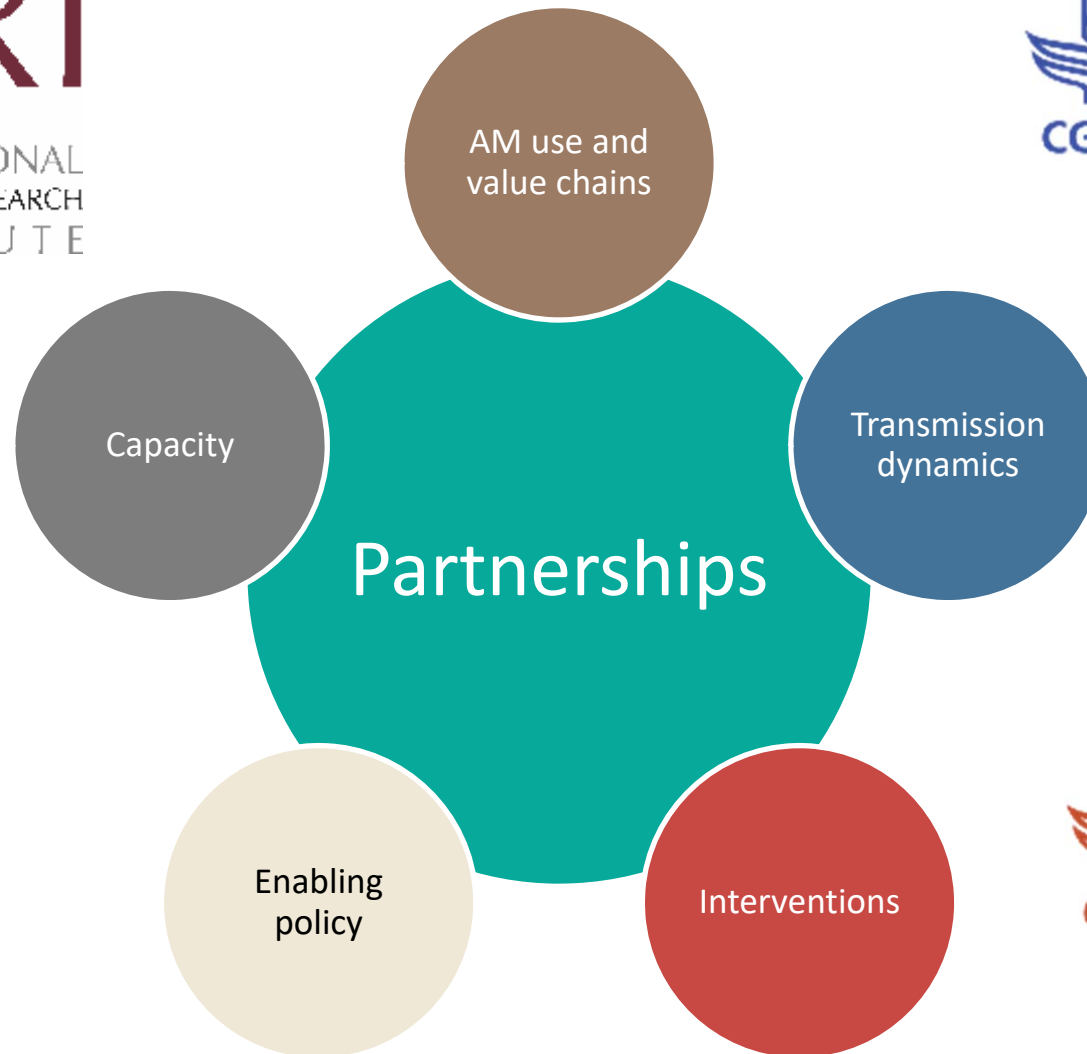
AMR in the CGIAR: Activity focus

ILRI

INTERNATIONAL
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RESEARCH
PROGRAM ON
Agriculture for
Nutrition
and Health



RESEARCH
PROGRAM ON
Livestock



RESEARCH
PROGRAM ON
Fish



For more information:
www.amr.cgiar.org

A global research and development partnership for reducing agriculture-associated antimicrobial



CAPACITY DEVELOPMENT

A key enabler in the fight against antimicrobial resistance is building greater local and national capacity in implementing one-health approaches that address this problem in smallholder aquaculture and livestock systems.

Our Approach

We conduct context-driven and systems-oriented research that combines social and biological sciences. With AMR research in agriculture and aquaculture and understanding linkages to public health outcomes, we can reap solutions emerging from our transdisciplinary approach.

We aim to reduce and refine AMU in agriculture and aquaculture and its impact on the environment, and to facilitate evidence-based communication around agriculture-associated AMR. This will help to mitigate AMR risks for people and contributes to improving the sustainability of global food and health systems. The implementation framework of our strategy is organized into five pillars.





STAR-IDAZ International Research Consortium: A Platform for Global Coordination of Animal Disease Research

Alex Morrow

Overview



- Background to STAR-IDAZ
- International Research Consortium (IRC)
 - Objectives and deliverables
 - Partners
 - Structure
- Topics and Working Groups
- Research Roadmaps
- International Research Call – ICRAD ERA-Net Co-fund



Background

STAR-IDAZ (Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses)

The overall aim:- to improve coordination of research activities on the major infectious diseases of livestock and zoonoses so as to hasten the delivery of improved control methods.

International Research Consortium on Animal Health - STAR-IDAZ IRC



Higher level of commitment for coordinated research activities through the STAR-IDAZ International Research Consortium for Animal Health (IRC)

- Agree minimum level of investment in research on priorities over a five year period (threshold \$US 10 million; group funding commitment possible)
- Agree delivery targets
- Agree to coordinate/align funding to deliver these targets (members' own funding procedures, unless agreed otherwise; governance document & policy guidelines)
- Agree to share research results (as much as necessary, without jeopardising IPR)
- 26 Partners from 17 countries including one international research organisation (ILRI), one charity (BMGF), the European Commission and three industry have signed the Letter of Intent to participate.
- Total combined five-year research budget of \$US 2.5+ billion

IRC Objectives and Deliverables



The overall objective of STAR-IDAZ IRC is to coordinate research at international level to contribute to new and improved animal health strategies for at least 30 priority diseases/infections/issues

The deliverables include:

- Candidate vaccines
- Diagnostics
- Therapeutics
- Other animal health products and procedures
- Key scientific information/tools to support risk analysis and disease control

IRC Launch





STAR-IDAZ

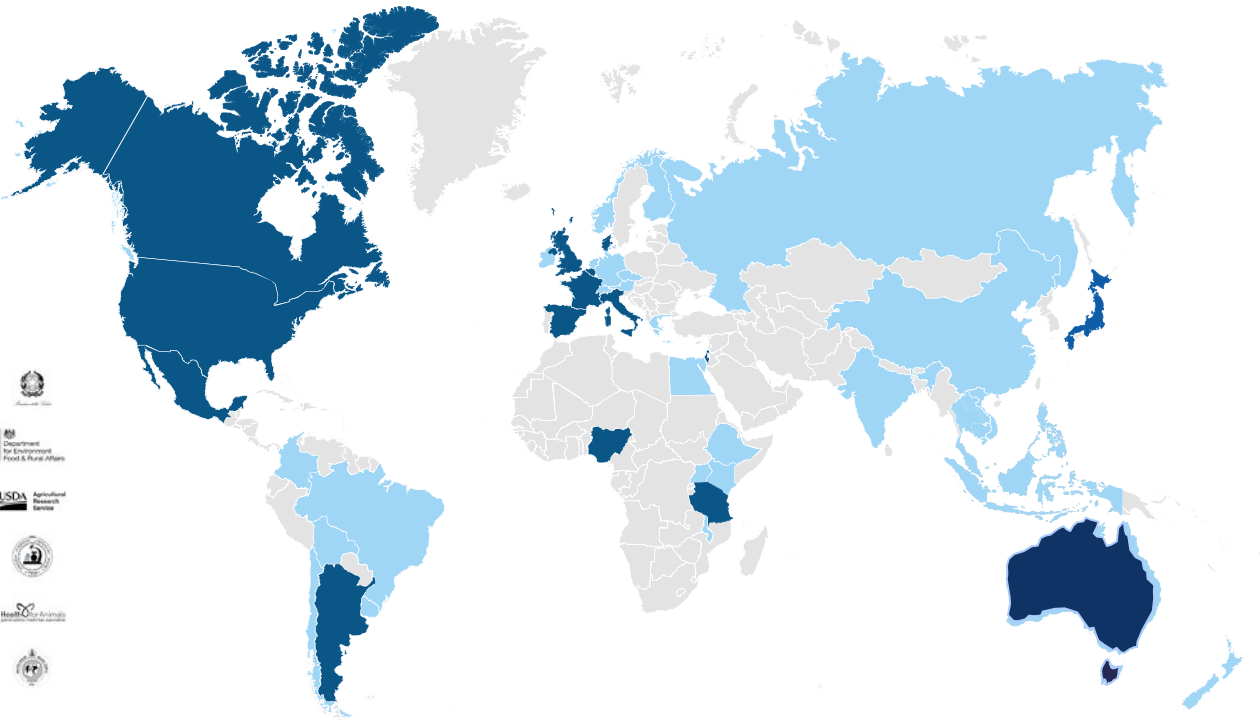
International Research Consortium on Animal Health

26 Partner organizations

17 Member countries

50 Associated countries

\$2.5B Research investment



IRC Executive Committee Partners



1. Danish National Veterinary Institute (DTU Vet), Denmark
2. National Institute of Agricultural Research (INRA), France
3. The French Agency for Food, Environmental and Occupational Health & Safety (ANSES), France
4. Ministry of Health, Italy
5. Ministry of Agriculture, Nature and Food Quality (LNV), The Netherlands
6. National Institute for Agriculture and Food Research and Technology (INIA), Spain
7. Department for the Environment, Food and Rural Affairs (Defra), UK
8. Biotechnology and Biological Science Research Council (BBSRC), UK
9. Regional Consortium; Universiteit Gent (Ghent University), Université de Liège, the Federal Public Service Health, Food Chain Safety and Environment (unit Contractual Research) and CODA-CERVA (Veterinary and Agrochemical Research centre)
10. Kimron Veterinary Institute, Israel
11. International Livestock Research Institute (ILRI), Kenya
12. Tanzania Veterinary Laboratory Agency (TVLA), Tanzania
13. National Institute of Animal Health, National Agriculture and Food Research Organisation (NIAH), Japan
14. Agriculture Research services, United States Department of Agriculture (USDA ARS), US
15. National Institute of Agriculture Technology (INTA), Argentina
16. Ministry of Science, Technology and Productive Innovation (MINCYT), Argentina
17. Canadian Food Inspection Agency (CFIA), Canada
18. World Organisation for Animal Health (OIE)
19. Zoetis
20. Bill and Melinda Gates Foundation (BMGF)
21. HealthforAnimals (Global Animal Medicines Association)
22. Diagnostics for Animals (Veterinary Diagnostics Manufacturers) (formerly EMVD)
23. European Commission
24. Regional Consortium; Nigerian Animal Health Research Network led by National Veterinary Research Institute Vom
25. National Advisory Council on Animal Health (CONASA) and the National Autonomous University of Mexico (UNAM), Faculty of Veterinary Medicine and Zootechnics (FVMZ)
26. CSIRO Australian Animal Health Laboratory (AAHL), Australia

European One Health Action Plan against Antimicrobial Resistance (AMR)



DEVELOPING A GLOBAL RESEARCH AGENDA

The Commission will:

foster international research collaboration on AMR in the animal health sector in the STARIDAZ International Research Consortium.

Governance Structure



SIRCAH (Secretariat)

Scientific Committee

Working Groups

Immunology Vaccinology	Diagnostics	Influenza	AMR and the Dev. of Innovative Alternatives
ASF	Vector-borne diseases	Brucellosis	Bovine Tuberculosis
FMD	Emerging Issues	One Health	Coronaviruses
Mastitis	Animal genetics/genomics	Foresight	Epidemiology
Helminths	Porcine Respiratory Disease Complex	PRRSV	????

Secretariat for the International Research Consortium on Animal Health (SIRCAH)



- **Establish working groups** for priority diseases and crosscutting issues - assisting with the organisation of meetings, including helping to pull together the **gap analysis** and **mapping funding activities** against identified research needs.
- **Produce and publish gap analysis and roadmap reports from working groups.**
- Advise the Scientific Committee (SC) and ExC on **how research programmes could be aligned** and make funding recommendations based on the gap analysis, roadmap reports and current funding activities.
- **Maps funding activities** against identified research needs, and **helps mobilise resources** to address them
- Facilitating **knowledge transfer** to bring innovation to the market

Working Groups

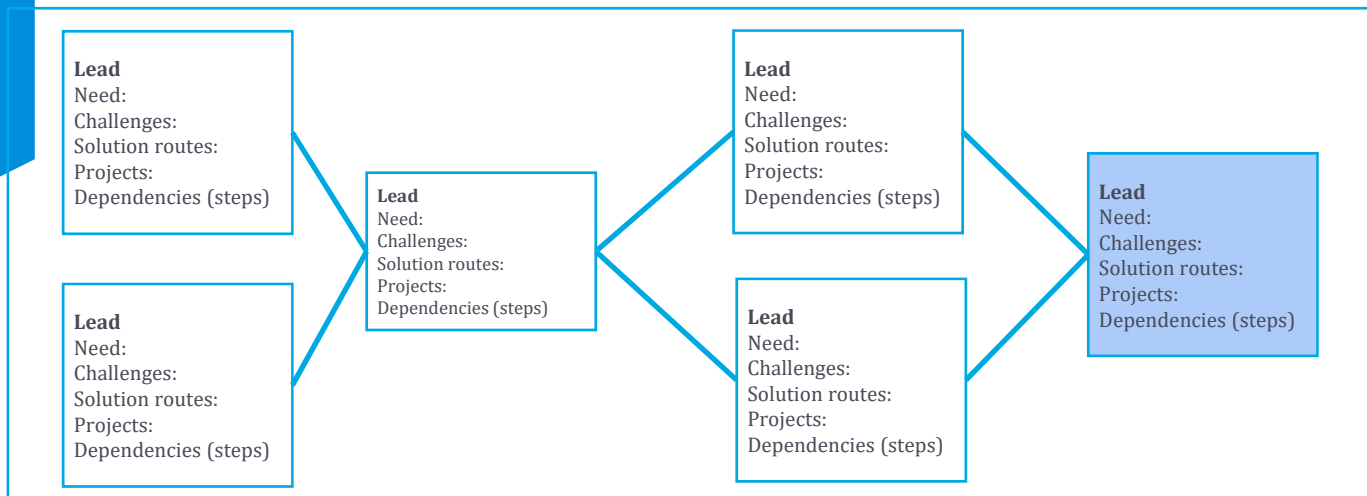


- Porcine Reproductive and Respiratory Syndrome
- Influenza
- **Bovine tuberculosis**
- **Foot and Mouth Disease**
- Brucellosis
- African Swine Fever
- **Vector-borne diseases**
- **Corona viruses**
- Mastitis
- Helminths including anthelmintic resistance
- Porcine respiratory disease
- Pox virus infections
- Others to come

- **Vaccinology**
- Emerging issues
- One Health (including food-borne pathogens)
- Animal genetics/genomics for animal health
- Epidemiology
- Diagnostics (tools and technologies)
- **AMR and the Development of Innovative Alternatives**

Lead Roadmap

Roadmap can be plotted by showing all the leads that are dependencies

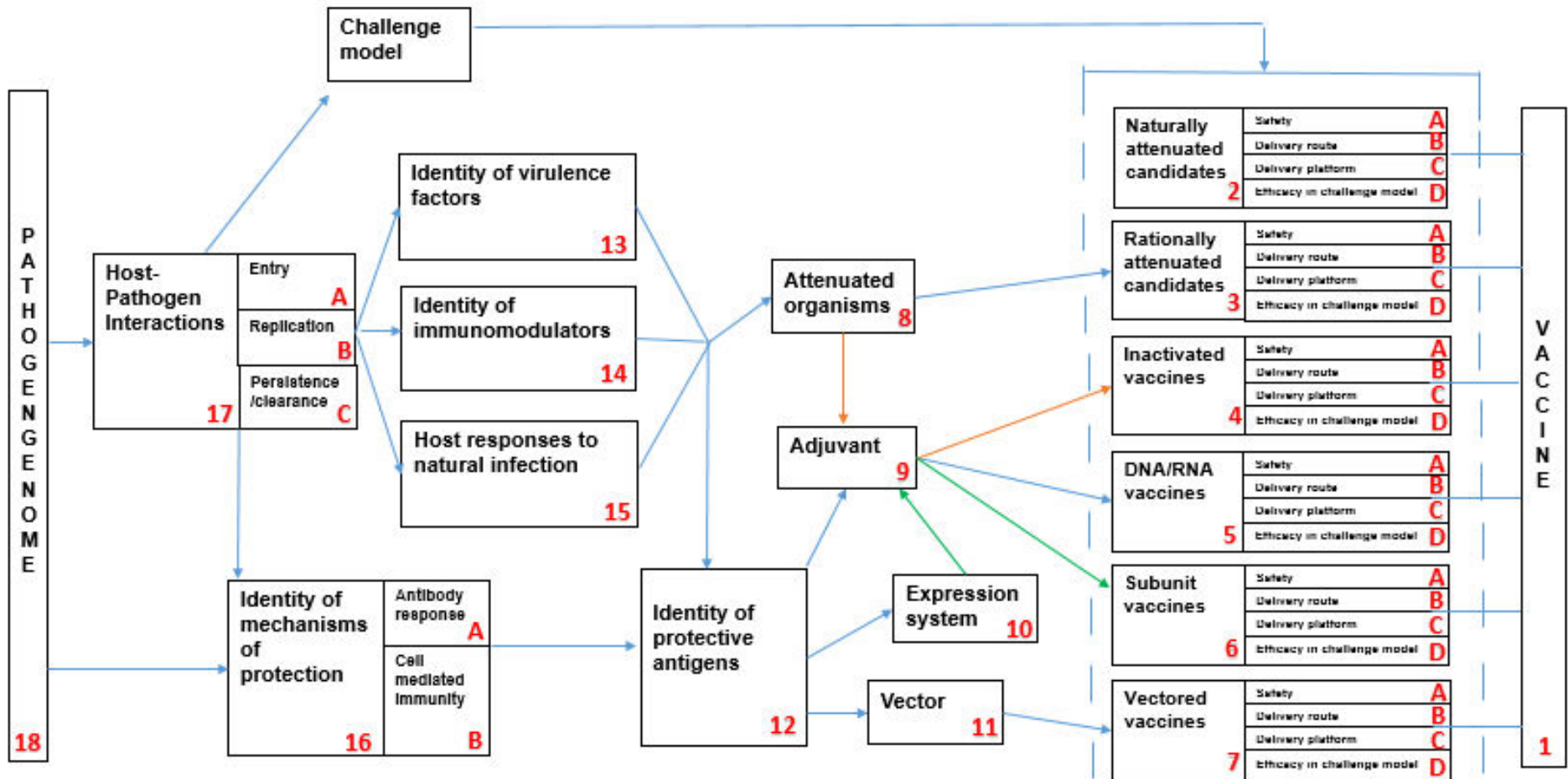


Roadmaps



- Way of visualizing a complex problem showing the gaps and helping to decide what projects need to be developed to create workable solutions.
- Available online providing a valuable tool for the research community including funders.
- The interactive vaccine candidate roadmaps have been launched
 - Diagnostics, therapeutics and epidemiology and control to follow
- Current research projects from IRC partners are being mapped onto the roadmaps and linked to the challenges associated with each lead allowing users to assess the extent to which the challenges are being addressed and identifying areas requiring further attention.

Research Roadmap for Vaccine Development



Lead Summaries



Title:

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

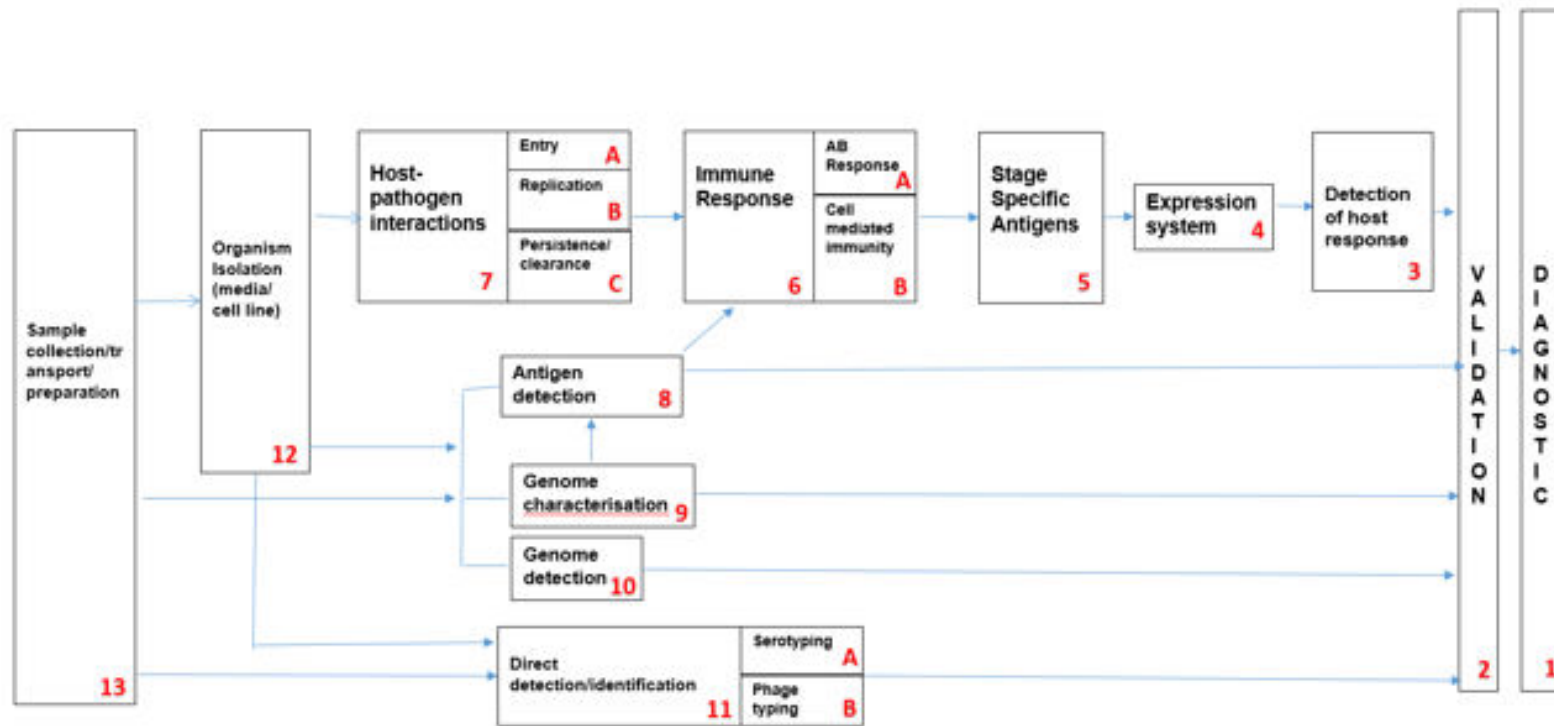
State of the Art

Existing knowledge including successes and failures

Projects

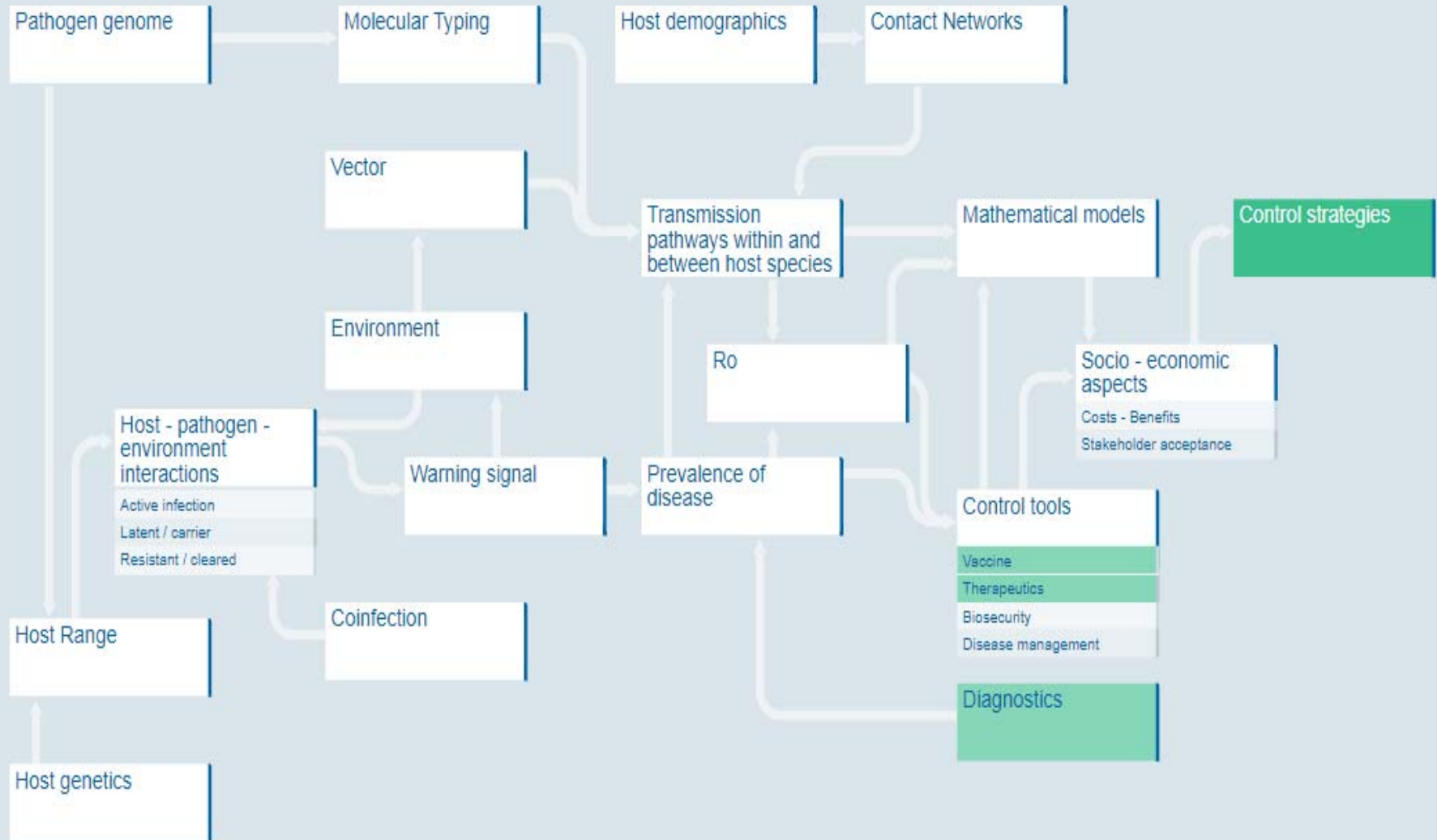
What activities are planned or underway?

Diagnostic Test Development Roadmap



Epidemiology and development of disease control strategies

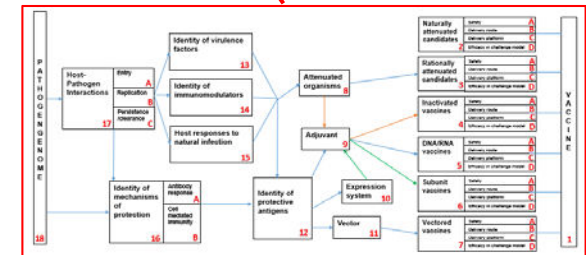
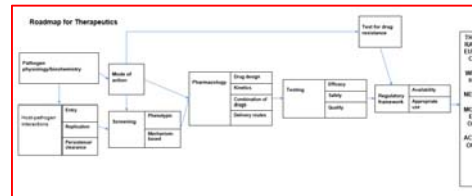
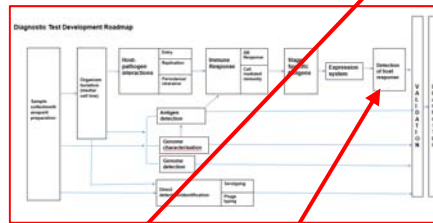
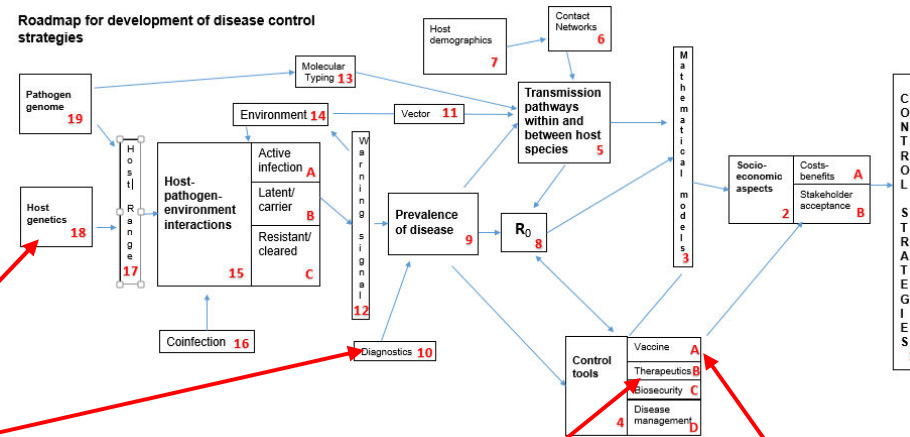
Overarching Roadmap



Research roadmaps for focused gap analysis



Roadmap for development of disease control strategies



Each lead/box is underpinned by...

1. Research question
2. Challenges
3. Solution routes
4. Dependencies
5. State of the art
6. Projects

Projects mapped onto gaps

- Overview
- Objectives and deliverables
- Outputs
- Progress

Research projects



Project Title

Funding organisation

Research organisation

Animal and pathogen

Project objectives

(Expected) deliverables with (expected) delivery dates and links to outputs (reports and data)

AMR and the Development of Innovative Alternatives



Alternatives to Antibiotics and their mode of action

The microbiome

Immunomodulation

How growth promoters work

– compartmentalisation of resources

RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE



Recommendation B3: The IACG calls on public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts for new antimicrobials, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials; and to strengthen implementation and operational research and research coordination and collaboration in a One Health context by:

- a. Supporting, facilitating and strengthening coordinated global mapping of research and development activities and funding to address antimicrobial resistance;
- b. Establishing and maintaining platforms for sharing information on research and products in development in both ongoing and completed research and development activities;
- c. Promoting synergies and opportunities for collaboration among funders, researchers and research platforms in human, animal and plant health, and the environment; and
- d. Promoting openness and transparency in data from all research, monitoring and surveillance sources, including overcoming data protection provisions that restrict such data sharing.

International Coordination of Research on Infectious Animal Diseases (ICRAD) ERAnet.

Purpose:

To support multi-disciplinary research to improve animal health and welfare, addressing some of the key endemic and (re)-emerging threats e.g. African Swine Fever and Animal Influenza, and developing novel detection and intervention strategies (including vaccines).

How:

Establish and operate a joint funding mechanism for animal health research on an international basis.

Reduced duplication of effort, better alignment of science, access to a wider knowledge base, collective action against global threats and challenges.

Previous ERAnets in Animal Health

EMIDA (Animal Health Research):

- 25 funding organisations
- €45m invested
- 26 projects funded (collaborative international networks)

ANIHWA (Animal Health and Welfare Research)

- €30m invested
- 33 projects funded

bTB, BTV, FMD, Campylobacter, Mastitis, TSEs, etc...



**European Animal Health
& Welfare Research**
COLLABORATIVE WORKING GROUP

ICRAD ERAnet (progress)

- Proposal moving to contract negotiations with European Commission
- Currently 26 funding organisations committed to support (Europe)
- Additional expressions of interest and commitments from other international funding bodies (Americas, Asia, Africa)
- EU will also contribute funds toward the joint call
- Approximately €20m for the first research call



**European Animal Health
& Welfare Research**
COLLABORATIVE WORKING GROUP

Themes of ICRAD research call

1. Improved understanding of endemic and emerging infectious animal diseases
 - ASF, Animal Influenzas and other priority diseases
 - Host/pathogen interactions, Epidemiology, Host immunology
2. Generic technology platforms for producing novel and/or improved vaccines
 - Including in relation to reduced use of anti-microbials
3. Rapid, accurate and easy to use in-field diagnostics technology

Alignment of European research investment with other international initiatives

- Opportunity to align investments (currently €20m committed)
- Potential for better co-ordination of research efforts
- Shorten the innovation pathway
- Lead to delivery of research output that has an impact
 - Disease control
 - AMR
 - Food security

Contact us



For further information on:

- STAR-IDAZ IRC visit www.star-idaz.net.

STAR-IDAZ IRC Project Office:

Alex Morrow or Luke Dalton

Defra, Area 5B, Nobel House, 17 Smith Square,

London SW1P 3JR

Alex.Morrow@Defra.gov.uk , Luke.Dalton@Defra.gov.uk

Stefano Messori (OIE)

s.messori@oie.int

Thank You For Your Attention

<http://www.star-idaz.net/>



Increasing investments for AMR R&D

Barriers, trends and opportunities in the animal health world

Global AMR R&D Hub Workshop

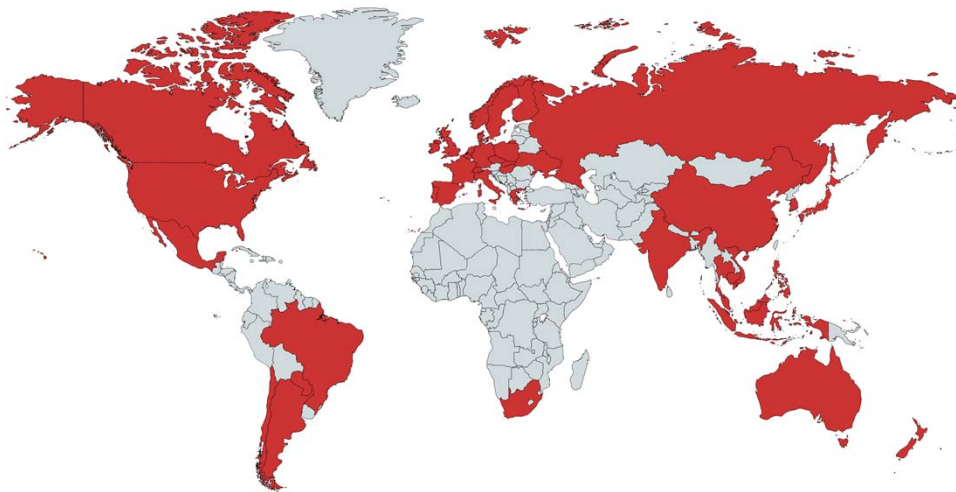
Geneva, 28 May 2019

HealthforAnimals Executive Director

Carel du Marchie Sarvaas



29 Regional & National Associations



vaccines, antibiotics, parasiticides,
nutrition and other products

85% of global animal medicines sector

Ten Largest Animal Health Companies Working in 100+ countries

zoetis

Elanco

Boehringer
Ingelheim

vetoquinol
ACHIEVE MORE TOGETHER

ceva

MERCK
Animal Health

B
A
Y
E
R

Virbac

Phibro
ANIMAL HEALTH CORPORATION

ZENOAQ

- 1. Animal and human health: differences/similarities**
- 2. Animal health trends**
- 3. Fighting AMR: myths and successes**
- 4. AMR R&D in animal health**
- 5. Policy recommendations**

Differences human and animal health

Animal health: smaller market, multiple species, different diseases

- fraction of the human medicines market
- one product does not work for entire patient base



Additional regulatory requirements

- products for food-producing animals require additional investment to verify food + environmental safety

Paying for medicine

- no public healthcare systems for animals
- animal owners pay the full cost of medicines
- no distorting economic effects



Disease control and prevention

- animal sector does not collect all its sick patients in one place...
- in animal health, biosecurity allows optimal prevention/control systems
- animal sector can implement mass and mandated vaccination
- animal sector can implement welfare + economic endpoints (euthanasia)⁴

Similarities human and animal health

In both sectors:

- same stringent (and costly) regulatory processes
- fewer active large players in antibiotic R&D
- long review times in smaller markets that reduce the likelihood of wide authorizations and availability of all medicines
- similar business model challenges:
 - How to develop an antibiotic which will likely be limited in usage?
 - How to get a ROI in a market that allows easy access to, and use of, cheap generic antibiotics?



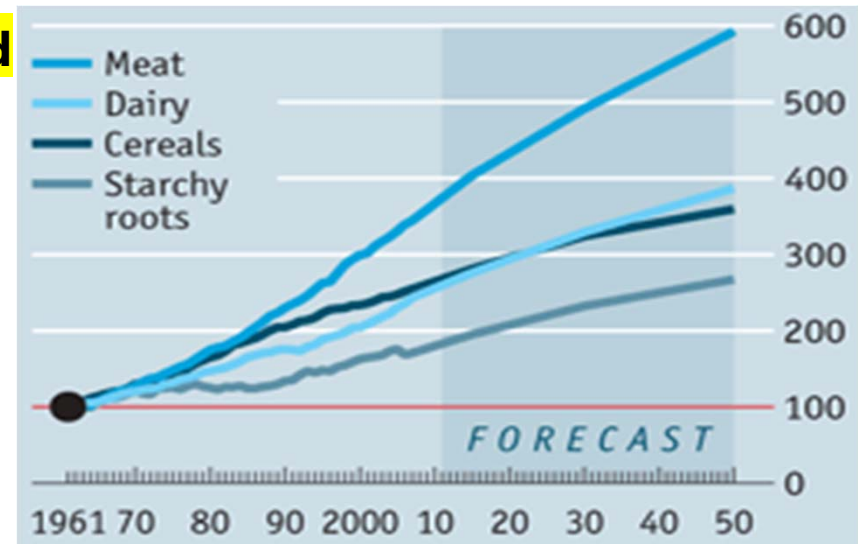
Five market trends influencing AMR R&D (1)

1. More people, money, protein demand and animals

- Demand for animal protein skyrocketing especially in LMI countries
- 5 out of 6 most valuable commodities: animal-source (milk, eggs, poultry, swine, beef)
- Demand for the full gamut of existing AH available products

2. More trade, travel, diseases, disease spread

- 4 billion airline passengers each year
- Food trade ↑ (poultry trade 520% in 20y)
- (Re) emerging and production diseases
- 13 zoonoses = 2.4b cases of human illness + 2.2m deaths a year
- Temperatures ↑ = vector borne diseases ↑



3. The rise of pets

- Explosive growth of pets in many markets
- Life expectancy ↑, euthanasia ↓, quality of life ↑
- Humanization and premiumization
- Comparatively lucrative market
- 60% AHC income U.S. from pets, 40% livestock

Five market trends influencing AMR R&D (2)

4. Increased percentage of revenues from biologicals

- Share of vaccines + other products up in many markets
- Antibiotics use down in high income countries
 - USA: 33% decline in AB sales '16 to '17
 - UK: AB sales fell 40% from 2013
 - Significant reductions in AT, BE, FR, DE, HU, IT, NL, others
 - Europe: AB share of revenues '14 to '17 (19% → 13%)
 - Global decline of new ABs. No new registrations since 2011



5. Changing animal health offering and business

- More integrated: genetics, diagnostics, surveillance, treatment, prevention, OTC Health, parasiticides, herd management, nutrition, prediction, etc.
- More IT/data: 'Big data', smartphones, satellite data, smart tags, wearable devices, remote monitoring, telemedicine, E-prescription, etc.
- Better science: biotech, enzymes, vaccine technologies, genomics, etc.
- More outward looking: R&D externalization, cross-over from biotech, human health

CONCLUSION
none of the trends favour increased investment into new antibiotics

Fighting AMR: three myths

MYTH: Antibiotic residues are often found in food.

- **Not true:** national residue survey results in areas like U.S./EU find rates of no/negligible levels
- Livestock products have statutory withdrawal period stating minimum amount of time after treatment, before meat, milk or eggs from that animal can enter the food chain

MYTH: Critically important antibiotics are routinely used in livestock.

- **Not true:** all new AB classes introduced for human use in the last 30 years do not have registrations for use in animals
- By far most uses of AB in animals are in tetracyclines, sulfonamides and penicillin classes - these are not critically important antibiotics (CIA) as defined by the WHO

MYTH: Farm animals are the major source of human-resistant infections.

The experts say otherwise...

"The major cause of AMR in humans remains the use of antibiotics in human medicine." (ECDC)

"...most deaths related to AMR occur from drug-resistant infections picked up in healthcare settings, such as hospitals and nursing homes." (CDC)

"...clinical issues with AMR in human medicine are primarily the result of antibiotic use in people rather than the use of antibiotics in animals." (UK Dep. of Health)

Fighting AMR (1)

What has been happening?

- Close planning and cooperation between stakeholders (farmers, food chain, vets, industry) in many countries
- Responsible use campaigns and measures across many countries highly effective – see EU, US and other countries' antibiotic use data
- No AB growth promotion uses / indications in EU, US, and many countries
- Rapid shifts of private producer investments to prevention and biosecurity

Measurement

- Globally, animal health world (OIE) has successfully collected antibiotic use data for years



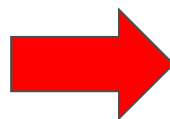
- AMR data from many countries shows no/low AMRB levels in most species

Fighting AMR (2): Industry Commitment



An industry wide Commitment

- Supported by organizations representing 200+ animal health companies and 700,000 veterinarians
- Underpinned by **concrete actions**
 - Responsible use partnerships
 - New vaccine and diagnostic R&D
 - Research and monitoring
 - Veterinary support
- Reporting on results summer 2019



**View full Commitment
and 'Principles in Action' at
HealthforAnimals.org/OurCommitment**

Five Core Principles



Principle 1: Protect animal health and welfare in a unified One Health approach.



Principle 2: Use antibiotics judiciously and responsibly.



Principle 3: Promote disease prevention and increased access to products and expertise.



Principle 4: Invest in development of products for prevention and treatment.



Principle 5: Increase knowledge, transparency and communication.

AMR R&D in animal health (1)

1. Antibiotic "*low hanging fruits*" plucked a long time ago.....
2. Divergence: human health R&D focused on different diseases, pathogens
3. Antibiotic volume restrictions discourage investment. The focus on use reporting creates pressure for reducing volumes
4. Animal antibiotics investment jeopardized by uptake in human use (e.g. pleuromutilins)
5. Additional hurdles for veterinary antibiotics
 - ROI in a much smaller market
 - Not be on a list of AB classes reserved for human-only use
 - Have Codex food/consumer safety standards set for trade
6. No therapeutic crisis in animal health, yet....



AMR R&D in animal health (2)

7. Contradictory to invest in new antibiotics and hold for last resort use
8. Non-science based measures (Article 118 in the EU) create trade barriers that undermine investment in new antibiotics
9. Societal + retail pressures re antibiotics are a business risk for companies
10. Future markets will be more generic, meaning with reduced value

CONCLUSIONS

1. Antibiotic R&D funds diverted to:

- prevention and non-AB products
- companion animals
- maintaining existing products (“defensive” R&D)
- others (pet antiparasitic, anti-inflammatories, generics, cardiac, skin/dental care, nutritionals)

2. AH industry continues to invest in R&D for animal-only antibiotics, BUT like the human health sector, such R&D is performed by only a few companies and investments very carefully scrutinized internally.

Reducing the need to use antibiotics

Animal health sector is investing in products/approaches to reduce the **need to use medically important antibiotics**

Anti-bacterial products

- **New antibacterials**, with a lower footprint for human health
- **Susceptibility enhancing products**, virulence modifiers or adjuvant to maximize benefit of antimicrobial therapy or minimize risk of resistance development

Infection prevention products

- **Vaccines**
- **Supportive products** that make animals less susceptible to getting a bacterial infection or make it better able to cope with an infection

Infection prevention approaches

- bio-security, husbandry, stress mitigation, teat sealants, reduced disease susceptibility, etc



Nine policy recommendations (1)

1) Make the most sensible use of what we have

- Preferential encouragement of classes which have low relevance to human medicine
- Willingness to downgrade importance rankings in accordance with medical utility
- Too easy for regulators to say "*they are all important*" - a reasonable number of antibiotics must be available in animal health to avoid overdependence

2) Increase the odds of a reasonable ROI

- Using the traditional ROI approach, there is likely no market sufficiently large or interesting enough to warrant a full new antibiotic program in animal health
- Reverse the hollowing-out of Codex standards, allow equivalency agreements to supplant positive list requirements

3) Improve the regulatory environment and expand global regulatory convergence

- Cost of generating regulatory data is upwards of 70% of cost of bringing to market
- Need to streamline burden that disincentivizes, delays or restricts progress
- Reduce review times and adopt specific response time goals
- Develop and /or maintain clear scientific criteria for decision making

Nine policy recommendations (2)



4) More support for animal vaccination

- Vaccines development is not easy - financial incentives
- Increased regulatory incentives will help drive investment

5) Support 'alternative' approaches, but weed out non-viable ones

- Have a panel (including private sector) assessing which merit public support
- Financial incentives that lower barriers to bring these to market
- Expedited regulatory assessment



6) Improve data protection

- When generics come to market, AB use increases - opposite of what's wanted
- Solution: increase patent periods/ data protection for antibiotics and 'alternatives'

7) Define better policy performance metrics

- Discipline of defining what improvement is expected in human health is lacking
- Set policy performance metrics to reflect anticipated benefit to human medicine
- Unintended consequences: f.e. experience shows that if a use limit is set on weight, large reductions are achieved by switching to more potent products (often CIAs)

Nine policy recommendations (3)

8) Smarter financial incentives

What doesn't work:

- Financing AH companies to develop new antibiotics – undesirable and unrealistic
- Guaranteeing prices/volumes politically difficult (maybe ok on human side)
- Prizes don't incentivize large companies as finance isn't the issue (but ok for SMEs)

What could work:

- Invest in regulatory convergence to share burden
- Fund promotion of benefits of vaccination
- Finance promising SME/academic R&D
- Organize research in consortia
- Use tax tools to ease investment
- Research into diagnostics (cheap, reliable, pen/bedside diagnostic)



9) Stronger (and smarter) political leadership

- Need directional messages how new veterinary antibiotics will be viewed
- Ensure AMR decisions are based on science
- Increase public investment in animal health and reinforce public veterinary services

The last and best slide

HealthforAnimals is finalizing two detailed reports:

Roadmap to Reducing the Need for Antibiotics

- 49 detailed case studies of actions being undertaken
- Release: summer 2019

Animal Vaccination: Hurdles and Solutions

- Hurdles: economic, societal, political, trade, technical, regulatory
- 60+ specific solutions for policymakers, industry, farmers, vets
- Release in summer 2019

Want a free copy?

carel@healthforanimals.org or alex@healthforanimals.org

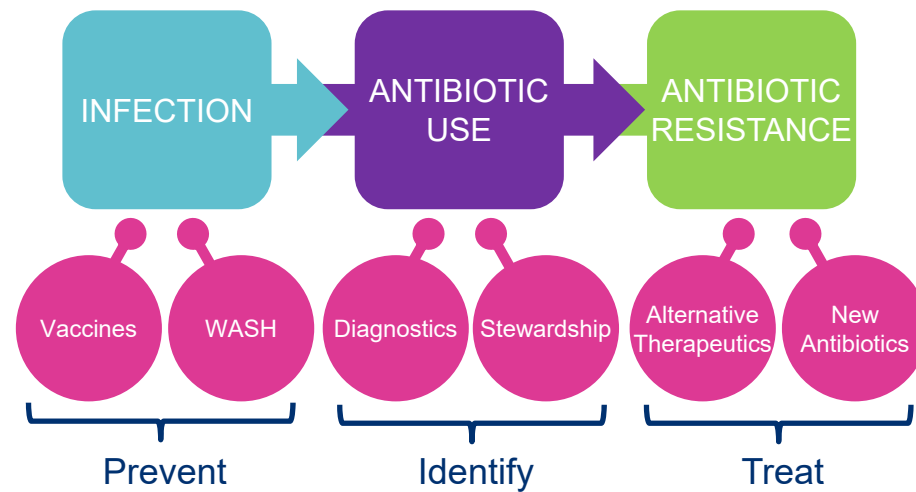
www.AnimalHealthMatters.org
www.healthforanimals.org



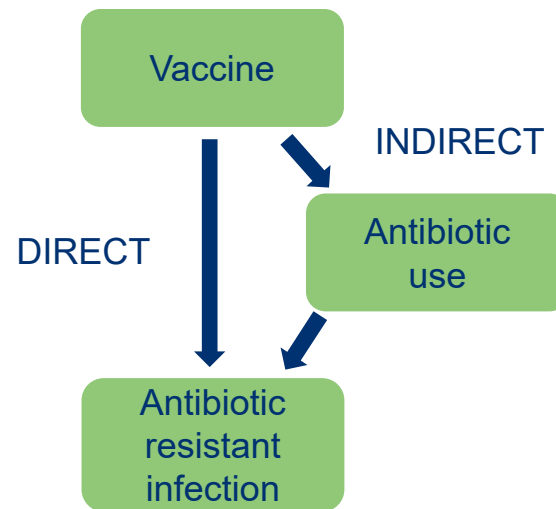
Vaccines to tackle drug resistant infections

AMR R&D hub workshop
28 May 2019

Tackling AMR requires a multi-faceted approach



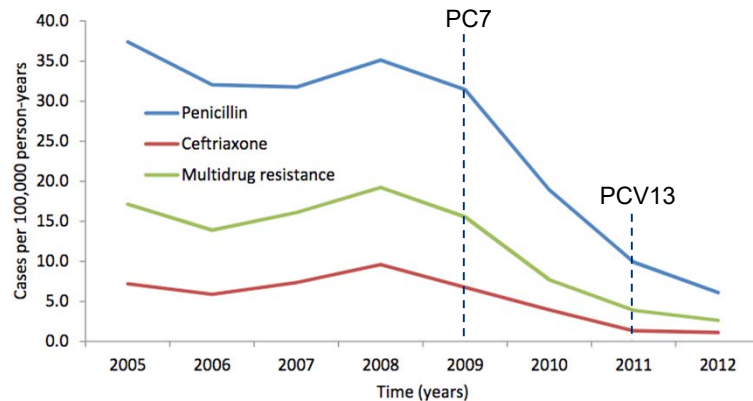
Vaccines combat AMR in two ways



1. Prevent infection, carriage and spread of resistant organisms (direct)
2. Reduce antibiotic use and therefore selective pressure (indirect)

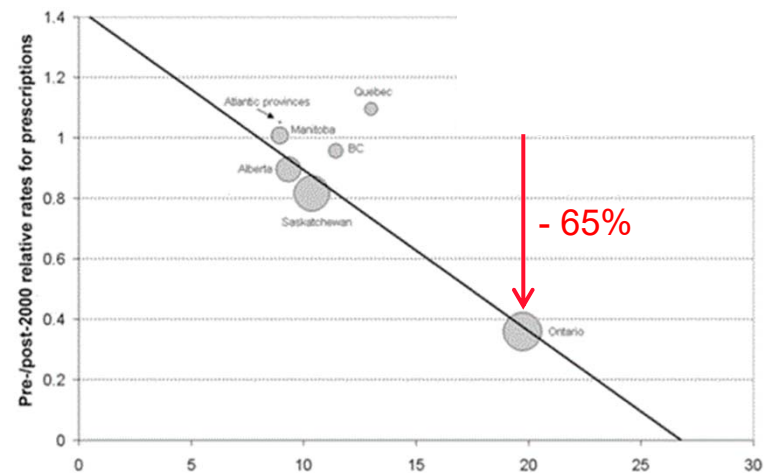
Vaccines combat AMR in two ways: examples

Direct:
Decrease in drug resistant infections
Pneumococcal vaccine



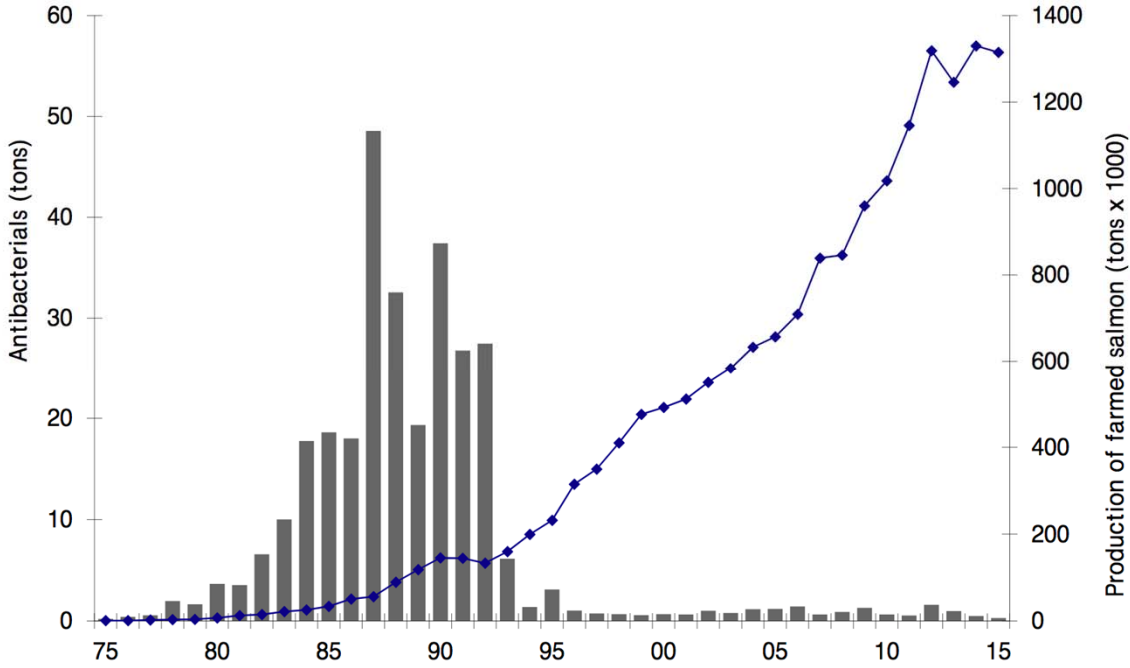
von Gottberg *et. al.* NEJM 2014

Indirect:
Decrease in antibiotic prescriptions
Influenza vaccine

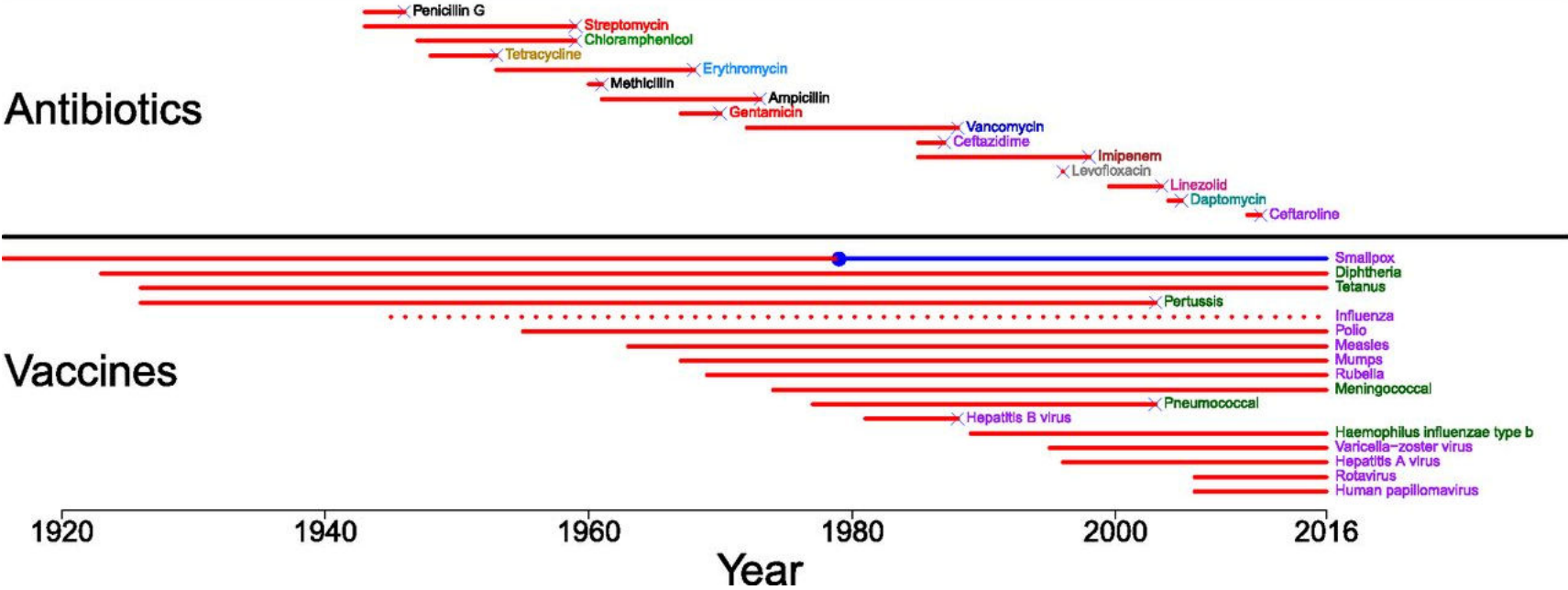


Kwong *et. al.* CID 2009

Use of vaccine in salmon farming decreased antibiotic usage



Vaccines offer a long-term approach



Kennedy and Read, PNAS 2018



Vaccines and antibiotics are complementary approaches

	Antibiotics	Vaccines
Administration	Treatment	Prevention
Hesitancy	Low	Concerning
Evolution of resistance	Rapid	Rare
Access considerations	Rational stewardship required	Broad access encouraged
Commercial attractiveness	Poor- market incentives needed	Variable
R&D Pipeline	Poor	Healthy
Target specificity	Wide range	Narrow range
Damage to microbiome	High	Low

How can we use vaccines to
their full potential?

Which vaccines would reduce AMR?

- 1- Vaccines for pathogens that are becoming more difficult to treat with antibiotics**
- 2- Vaccines for pathogens that cause symptoms that drive antibiotic use**

The WHO and CDC have developed lists of pathogens requiring development of new antibiotics

More information is needed for vaccines



VaccinesforAMR.org



Vaccines to tackle drug
resistant infections
An evaluation of R&D opportunities



Enable evidence-based decision-making for vaccine development to address AMR

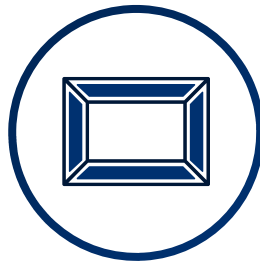
Consolidate information



Sources:

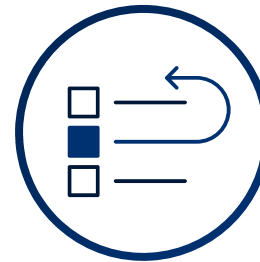
- Expert interviews
- Databases
- Scientific literature

Analyse data



Develop scorecard framework for pathogen assessment

Side-by-side comparison



Enable prioritisation by researchers, funders, and policy-makers aligned with varied individual and institutional focus

Identify action items



Encourage targeted attention and investment to fill knowledge gaps and promote vaccine development and uptake

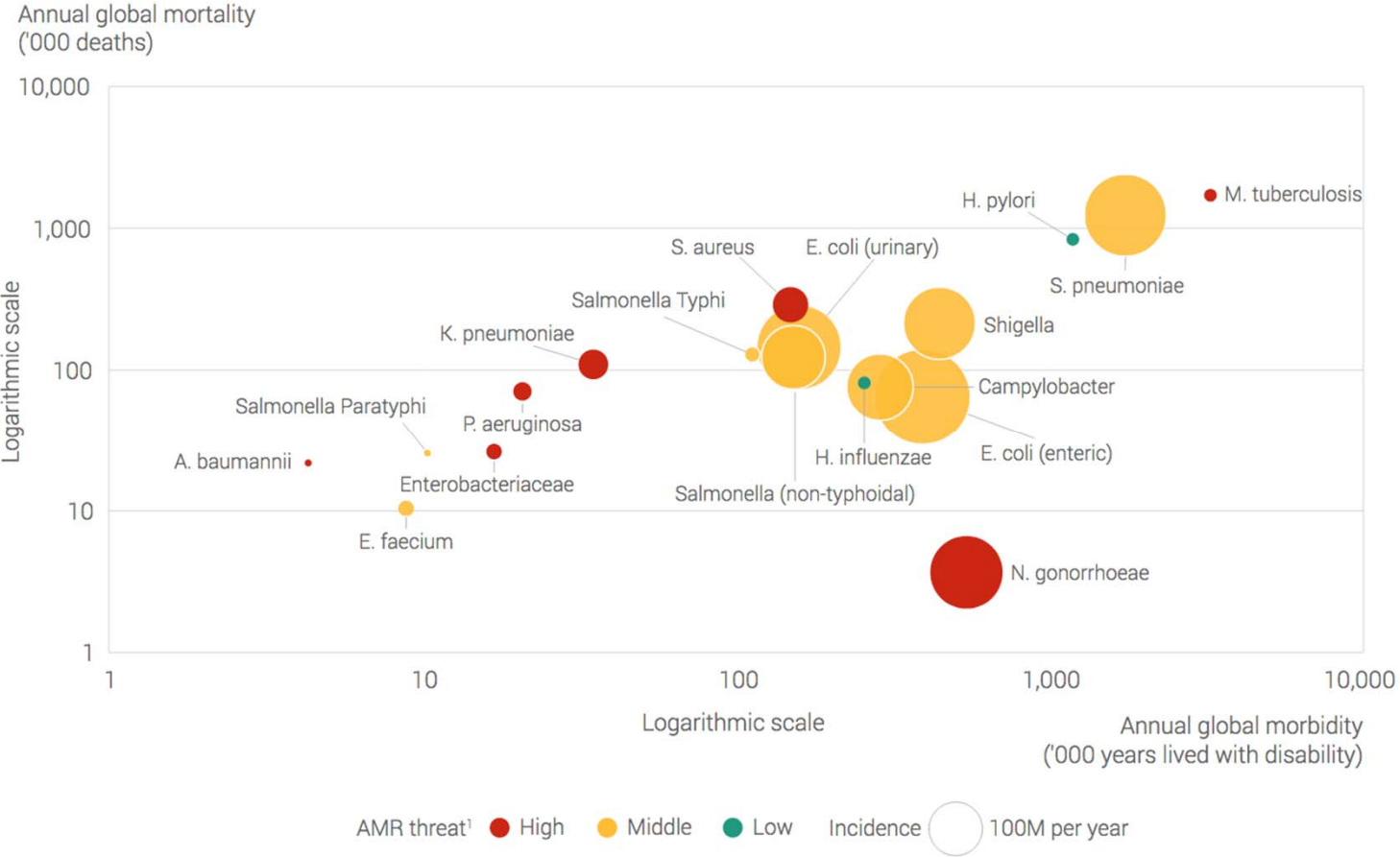
Scorecard for pathogen assessment

Health Impact
Mortality and Morbidity
Urgency of AMR threat & Attributable antibiotic use

Probability of R&D Success
Pipeline robustness
Pathogen biology
Ease of pre-clinical and clinical R&D

Probability of Uptake
Expected policy stance
Payer, government and Gavi support
Barriers to uptake
Commercial attractiveness

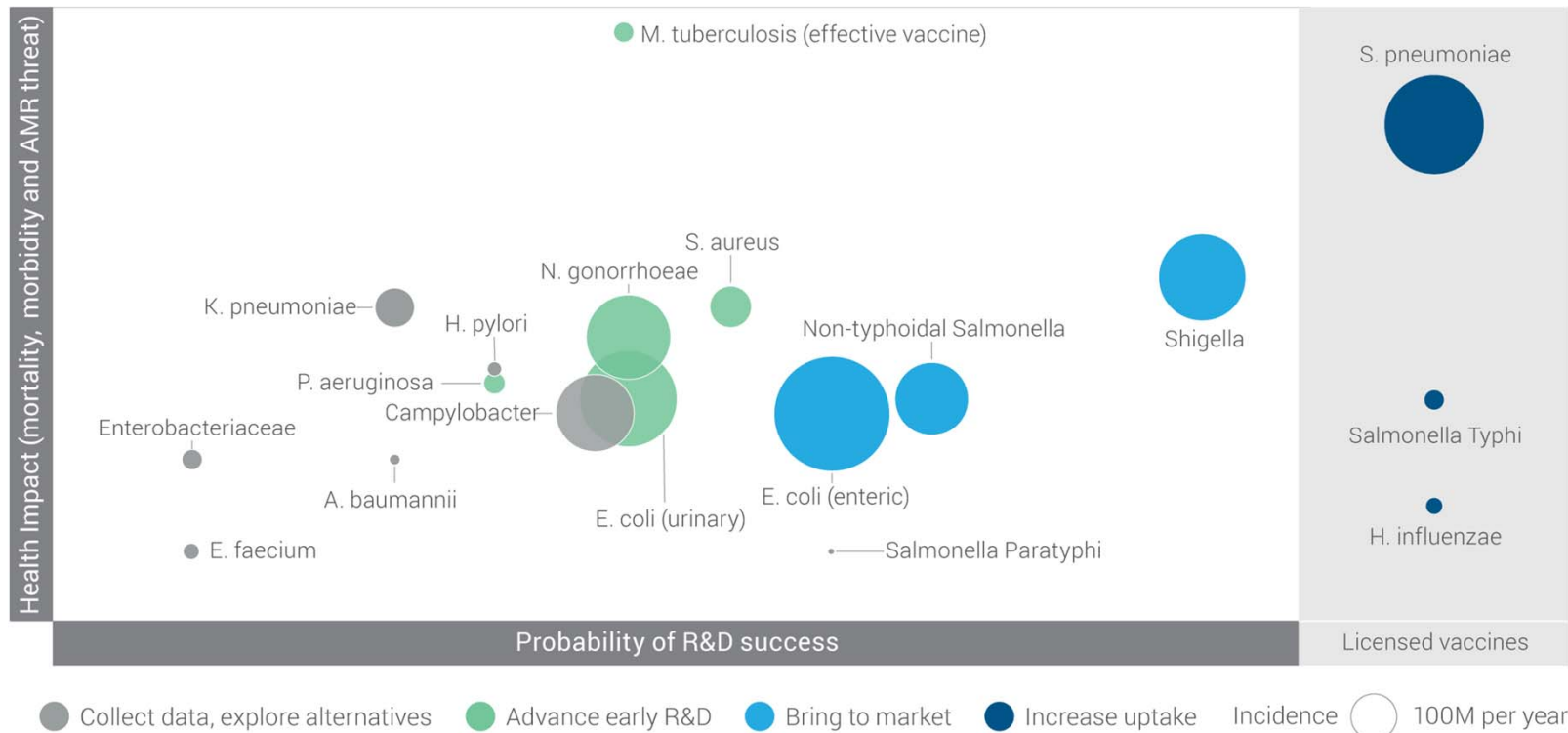
Health Impact



Vaccine R&D pipeline robustness

	Pre-clinical	Phase I	Phase II	Phase III	Marketed	Score
<i>H. influenzae</i>	8	1	2	3	46	2
<i>S. pneumoniae</i>	31	7	8	3	7	2
<i>S. Typhi</i>	6	2	2	2	20	2
<i>Shigella</i>	15	2	2			1.5
<i>M. tuberculosis</i>	25	4	8	2	13	0.5
<i>S. aureus</i>	23	3	2			0.5
<i>E. coli</i> (enteric)	11	2	3	1	1	0.5
Non-typhoidal <i>Salmonella</i>	5					0.5
<i>S. Paratyphi</i>	2	1		1		0.5
<i>N. gonorrhoeae</i>	4					0.5
<i>E. coli</i> (urinary)	1	1	1			0.5
<i>H. pylori</i>	9	1				0
<i>P. aeruginosa</i>	4					0
<i>E. faecium</i>	4					0
<i>Campylobacter</i>	3	1				0
<i>Klebsiella</i>	3					0
<i>Enterobacteriaceae</i>						0
<i>A. baumannii</i>						0

Pathogen clusters for prioritised action



Weighting used for chart

Health Impact – Mortality (50%), Morbidity (20%), AMR (30%).

Prob. of R&D success – Pathogen biology (30%), Pre-clinical and clinical R&D (30%), Pipeline robustness (40%).

1

Increase uptake and access for existing, effective vaccines

H. influenzae



S. pneumoniae

S. Typhi

2

Bring to market new vaccines where the pathogen is better understood by accelerating clinical development

E.coli (enteric)



Non-typhoidal *Salmonella*

Shigella spp.

3

Advance early R&D for high impact pathogens with unclear R&D feasibility, by investing in early stage research



[*M. tuberculosis*
N. gonorrhoeae



[*E. coli* (urinary)
P. aeruginosa
S. aureus

4

Collect data and explore alternatives for pathogens currently less well-suited to vaccine development



S. Paratyphi



[*Campylobacter*
H. pylori
K. pneumoniae



[*A. baumannii*
Enterobacteriaceae
E. faecium

The path forward

- Increase global coverage for existing vaccines
- Drive development of new vaccines
- Address market issues for certain vaccines
- Consider pathogens that drive antibiotic use
- Collect data to quantify impact of vaccines on AMR
- Incorporate AMR into vaccine decision-making
- Incorporate vaccines into AMR national action plans







Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections

GLOBAL
AMR R&D
HUB



Co-funded by the
Health Programme
of the European Union

Strengths and weaknesses of research priorities on AMR in Europe

May 28, 2019 - Global AMR R&D Hub Workshop on “Increasing Investments for AMR R&D”

**Yohann Lacotte,
Christine Årdal,
Marie-Cécile Ploy**

**UMR Inserm 1092
University of Limoges
EU-JAMRAI Coordinator**

EU-JAMRAI: The place to be to tackle AMR!



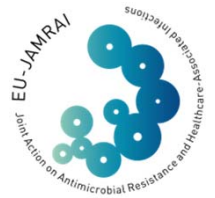
www.eu-jamrai.eu

Europe fostering synergies to keep antibiotics working

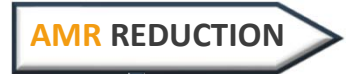


www.eu-jamrai.eu

EU-JAMRAI objectives



Mapping of research priorities in European Member States



1- Decrease consumption of antibiotics in humans and animals



2- Test wide implementation of programs to prevent HCAI



3- Analyse gaps in national action plans



4- Propose incentives for the development of antibiotics and diagnostic tools



5- Improve surveillance in human and animal



6- Increase awareness on AMR

How to map research priorities within Europe?



7 voluntary countries extracted research priorities from their national research programs on AMR

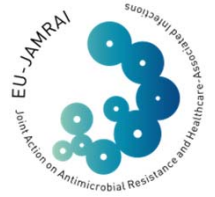


38 research priorities extracted

14 different research areas

		France	Greece	Netherlands	Norway	Slovenia	Spain	UK
Development of new tools	Development of new antibiotic molecules							
	Development of new alternatives to antibiotics (vaccine, phages, antibodies, peptides ...)							
	Development of new diagnostic tools							
Fundamental research	Research on the bacterial mechanisms involved in resistance							
	Research on the causes and consequences of the appearance and dissemination of AMR							
	Other specific research unrelated to animals nor environment	<i>Clostridium difficile</i>		membrane biogenesis, microbial ecology	continued carriage, microbial ecology			microbiome
Animal sector	Investigating new technologies to help developing antimicrobial molecules or diagnostic tools	artificial intelligence		synthetic biology				genomic technologies
	Research on the interaction of AMR with the veterinary sector (transfer of resistances between animals and humans, dissemination of resistances, ...)							
	Research of new antibiotics for use in veterinary medicine							
	Improve understanding of the critical factors that lead to a high consumption of antibiotics in farms							
	Evaluate the impact of food additives used in animal feeds (copper, zinc, coccidiostats, ...) on the AMR							
Environmental sector	Implementation, testing and evaluation of diverse IPC measures in the veterinary sector							
	Research on the interaction of AMR with the environment (transfer of resistances between the environmental bacteria and human pathogens, dissemination of resistances, ...)							
	Explore the effect of different drivers of resistance (disinfectants, biocides and heavy metals, ...) in nature							
	Explore the impact of fertilizers, especially manure, on the spread of AMR							
	Investigate the cost-effectiveness of cleansing environment measures							
Implementation, testing and evaluation of diverse IPC measures in the environmental sector								

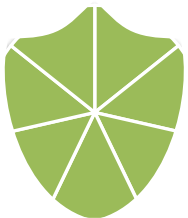
European strengths (1)



All participating countries consider **fundamental research** on AMR as a priority (bacterial mechanisms involved, causes and consequences of the appearance and spread of resistance,...)



All participating countries consider **strengthening surveillance** as a priority



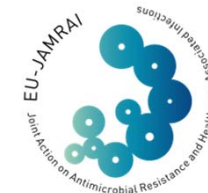
All participating countries consider **implementation of IPC programs** as a priority



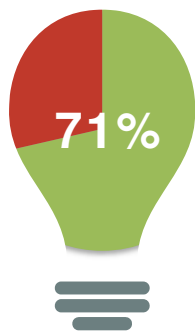
Most interventions are still not sufficiently evidence based

→ more research needed

European strengths (2)

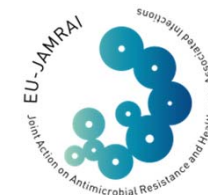


participating countries consider assessment of **best practices and strategies for antibiotic stewardship** as a priority



participating countries consider development of **antibiotics, alternatives to antibiotics or diagnostics** as a priority

European strengths (3)



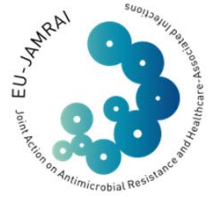
European steadiness to **structure and improve research networks**



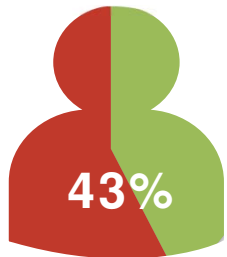
71% of the participating countries see **International/ European research collaborations** as a priority

58% of the participating countries have developed a “**national steering committee**” to structure and coordinate research regarding AMR

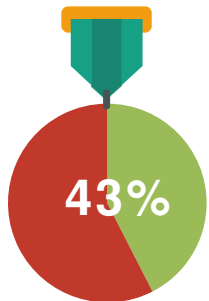
Europe could do better...



participating countries consider research on the **interaction of AMR with the veterinary sector** (transfer of resistances between animals and humans, dissemination of resistances, ...) as a priority

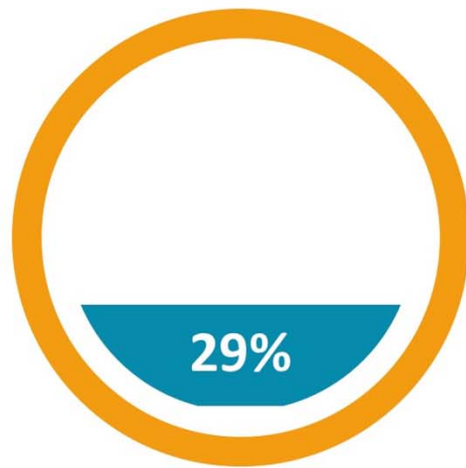
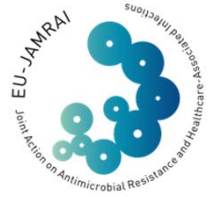


participating countries consider **involvement of socio-economic science** to improve knowledge of the critical aspects that lead to inappropriate use of antibiotics as a priority



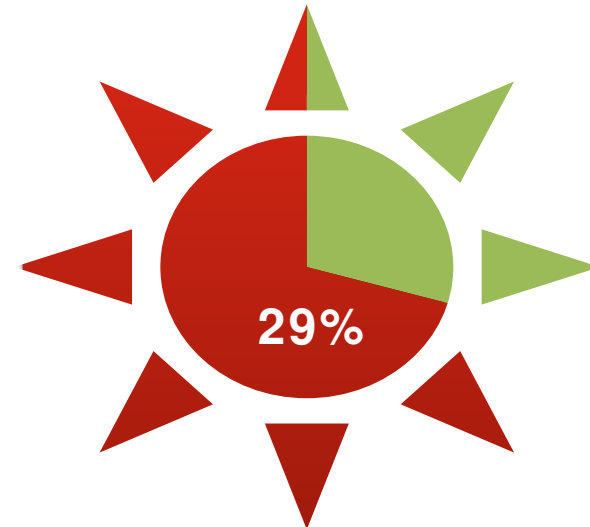
participating countries consider research on **new economic incentives** to foster innovation as a priority

Gaps (1)



Participating countries with research on cleansing measures or how to implement IPC programmes in the environment

Environmental field
----- STILL -----
left **BEHIND**



Participating countries with research on the drivers of resistance (disinfectants, biocides, manure, heavy metals...) in the environment

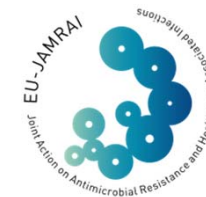
**We are looking at research priorities stated in national research programmes*

Gaps (2)

Only **1** out of **7**
--- countries ---
reports research on
CLINICAL TRIALS
--- efficiency ---

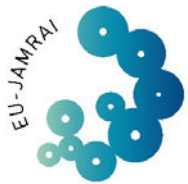


Laconic research
-- on the **SPREAD** --
of **resistance genes**
-- through **FOOD** --
or **IPC measures** in
-- the **FOOD CHAIN** --

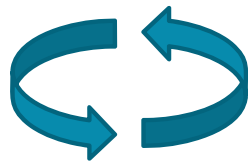


**We are looking at research priorities stated in national research programmes*

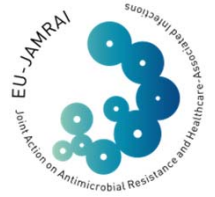
Work in synergy with other initiatives



Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections



HCAI & IPC research priorities



Impact of IPC programmes

IPC guidelines evaluation and implementation

Training

Surveillance and monitoring

Impact of patient environment on HCAI and AMR reduction

Behavioral science

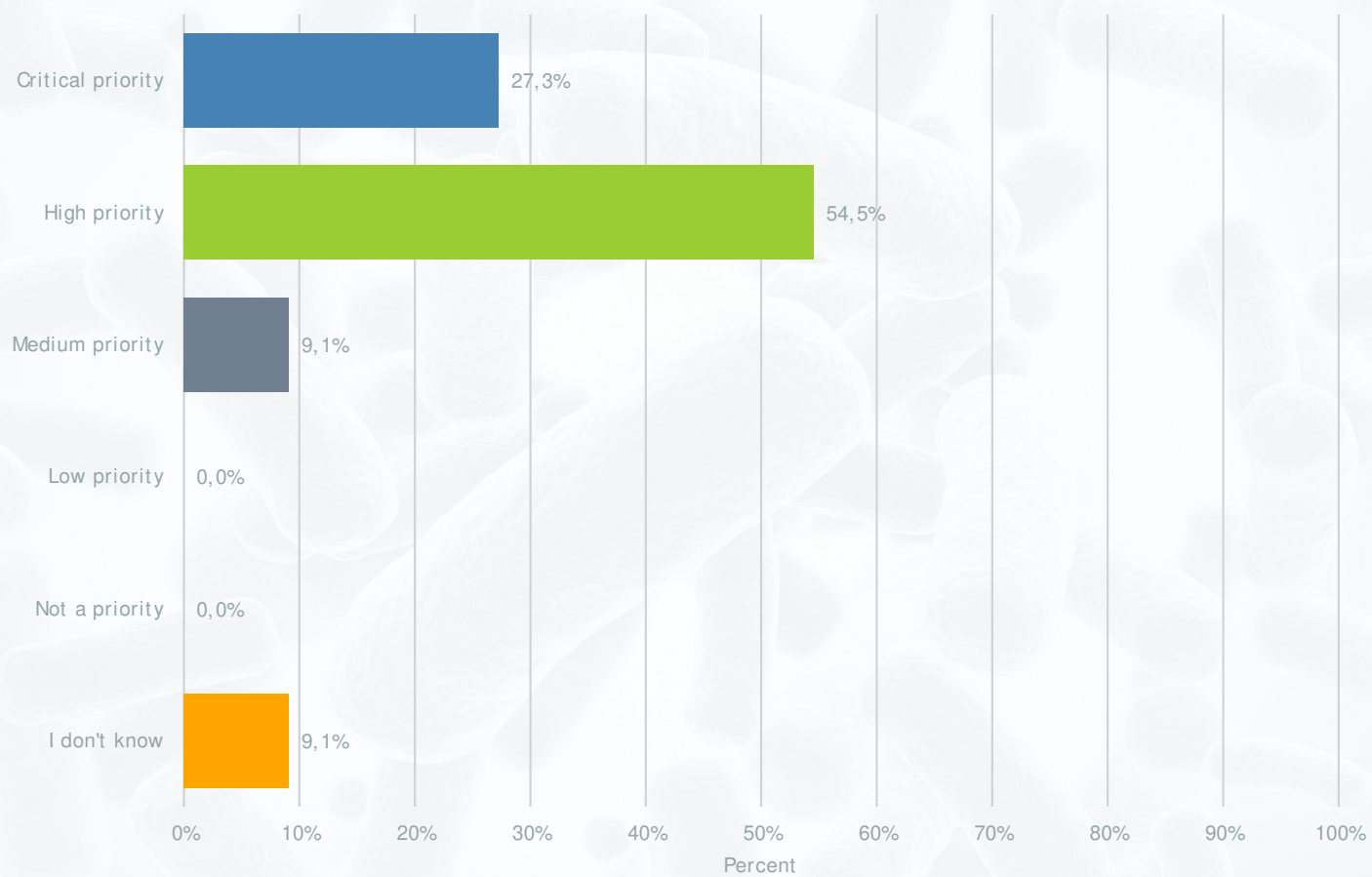
One Health

Research is needed to assess the impact of IPC measures in different operational contexts including small farms, industrial farms, feedlots, slaughterhouses, fish farms, and more.

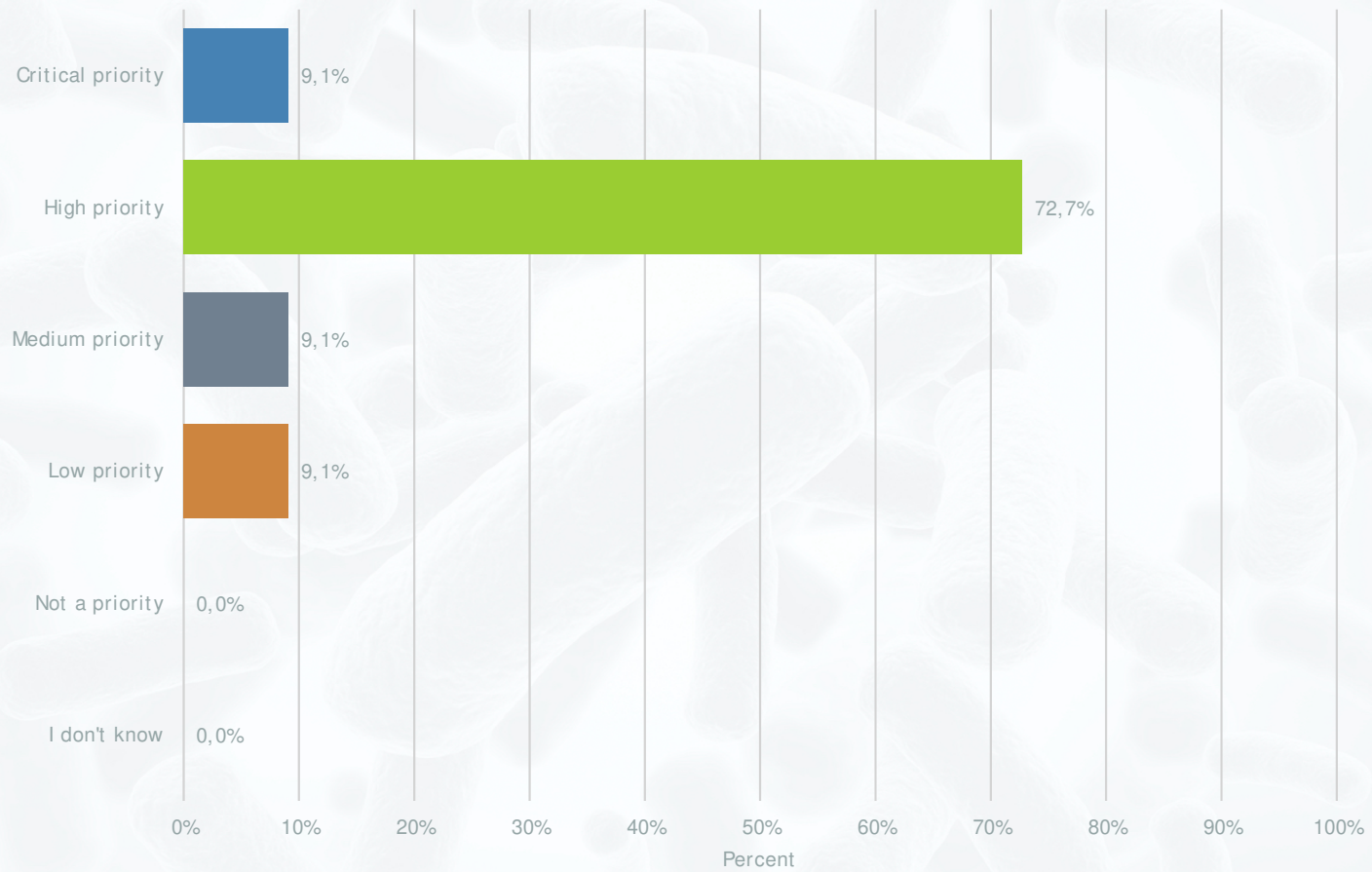
18 IPC experts in 12 countries



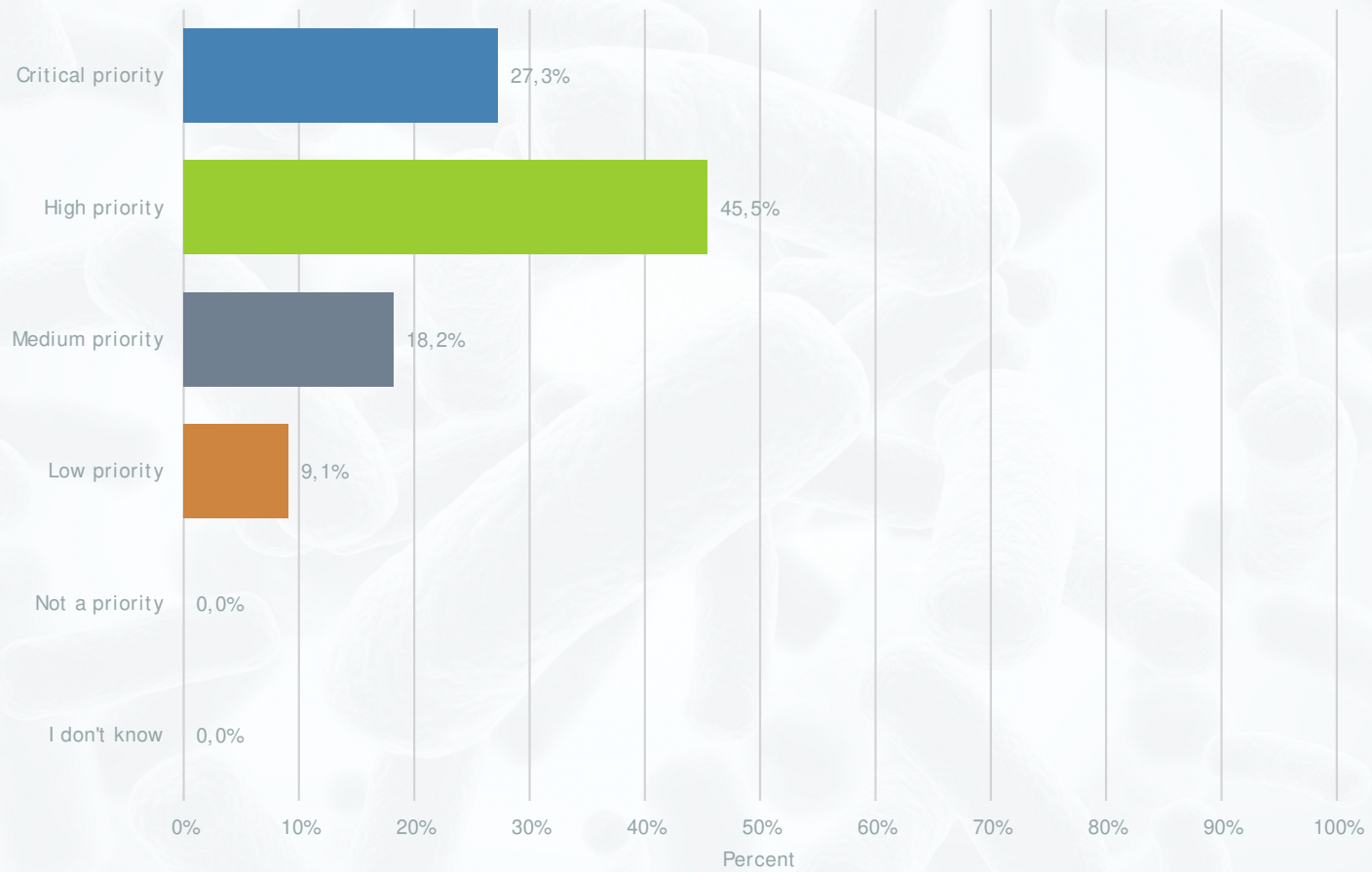
Impact and cost-effectiveness of hospital-based IPC programmes



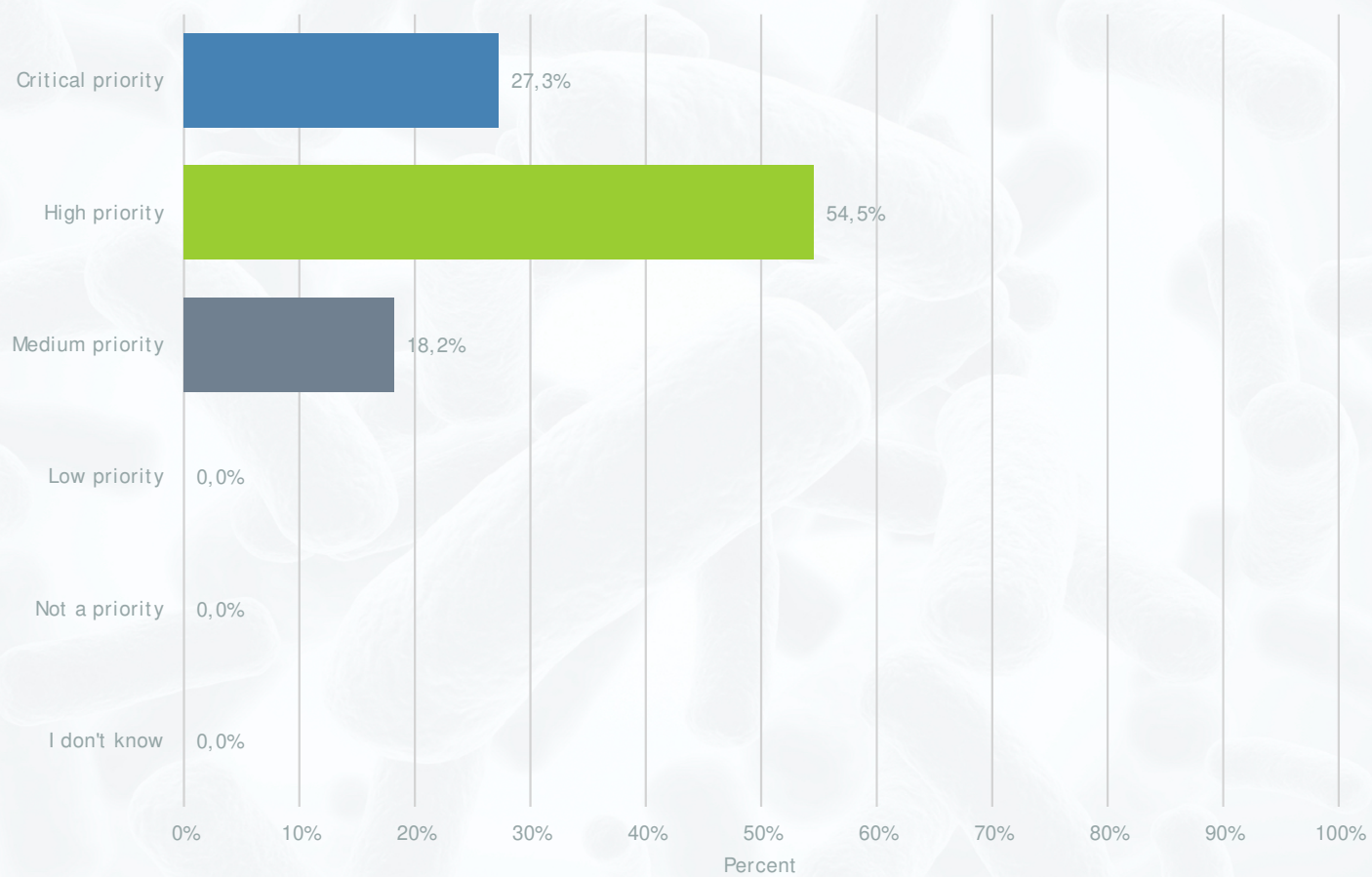
Additional tools are needed to evaluate IPC training programmes and implement them.



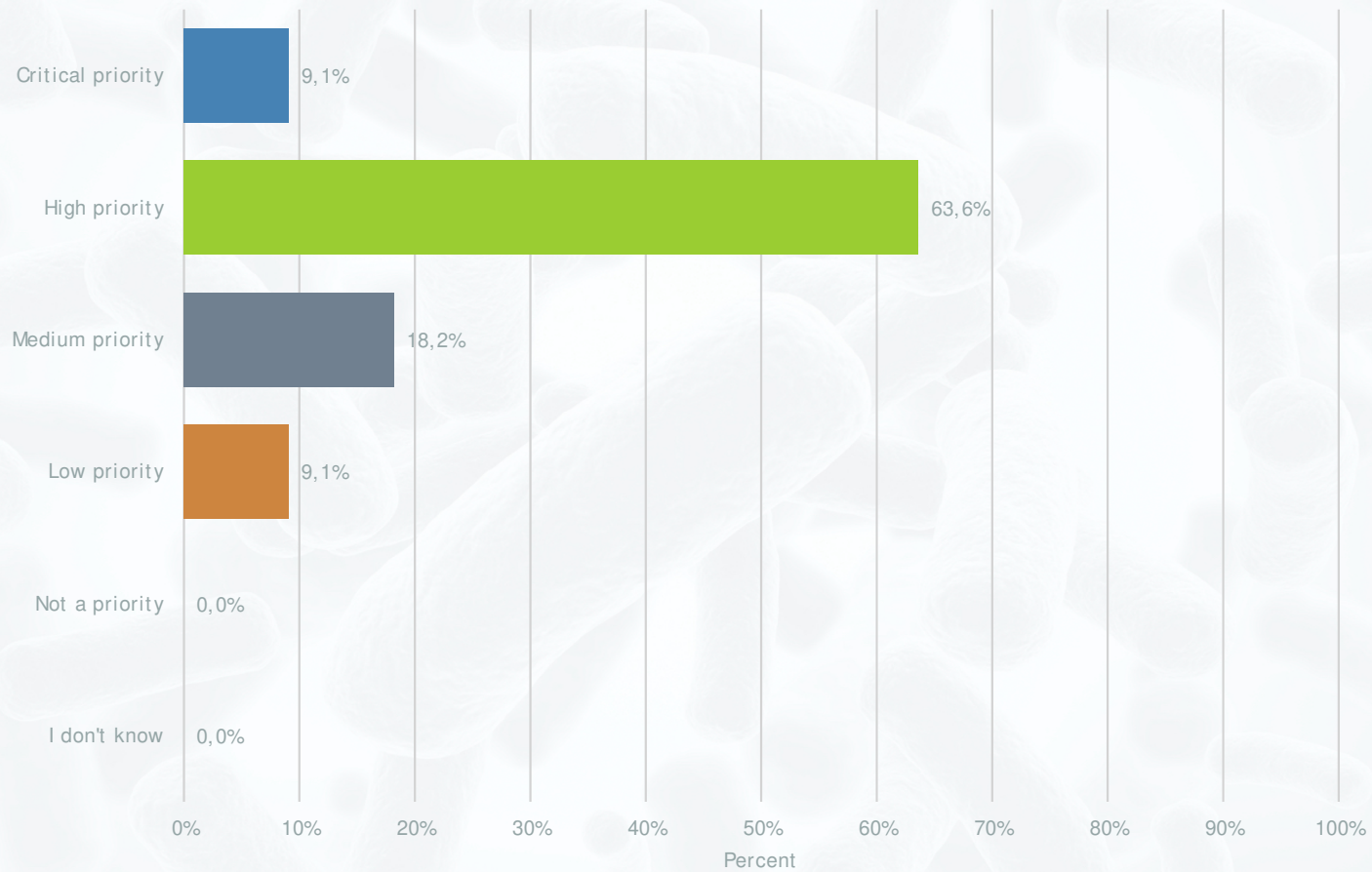
Innovative tools for training (Simulation, AI, e-learning, ..): impact on practice change



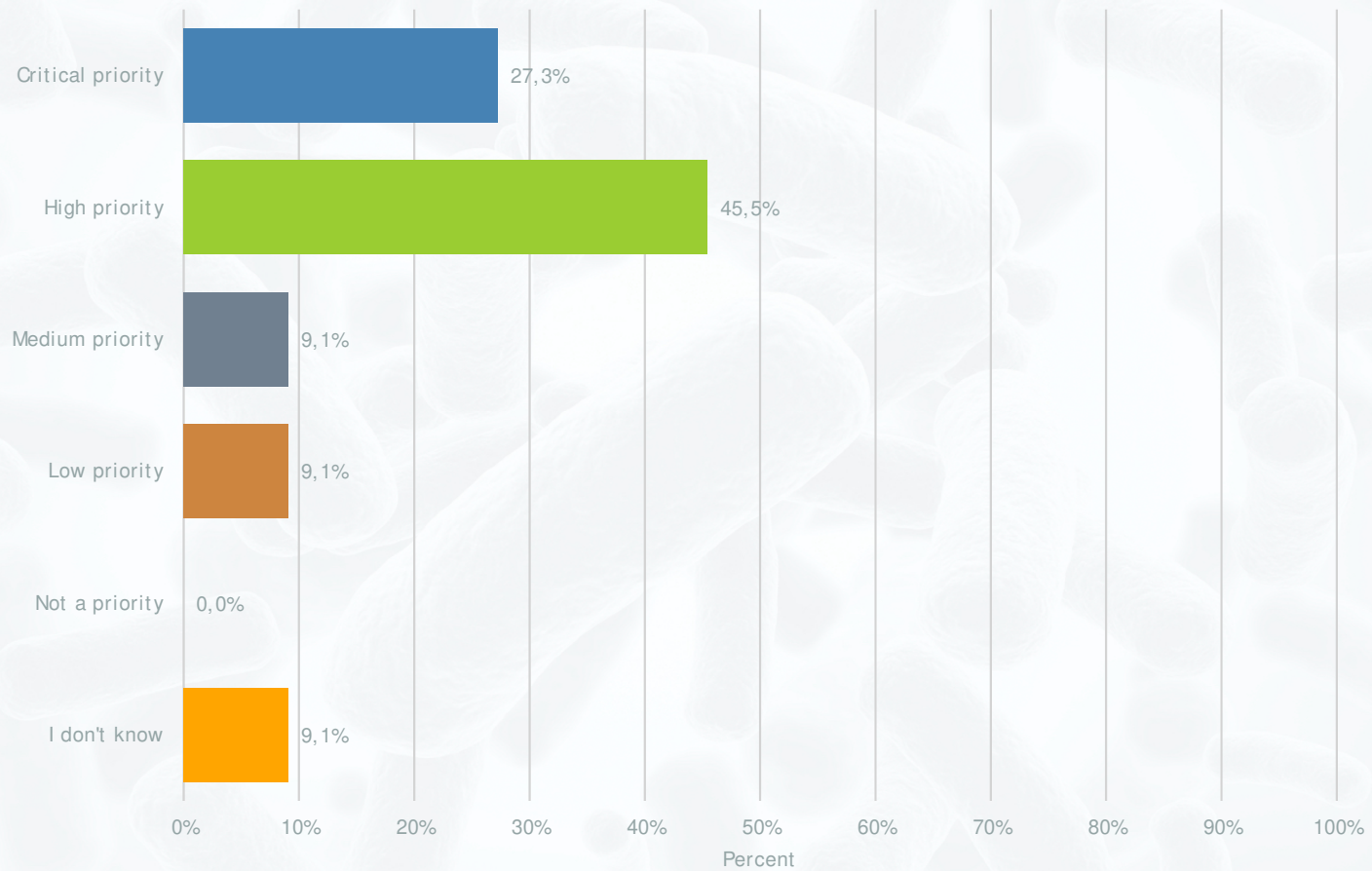
Develop standards to monitor IPC measures beyond hand hygiene (catheter-related BSI, VAP, UTI)



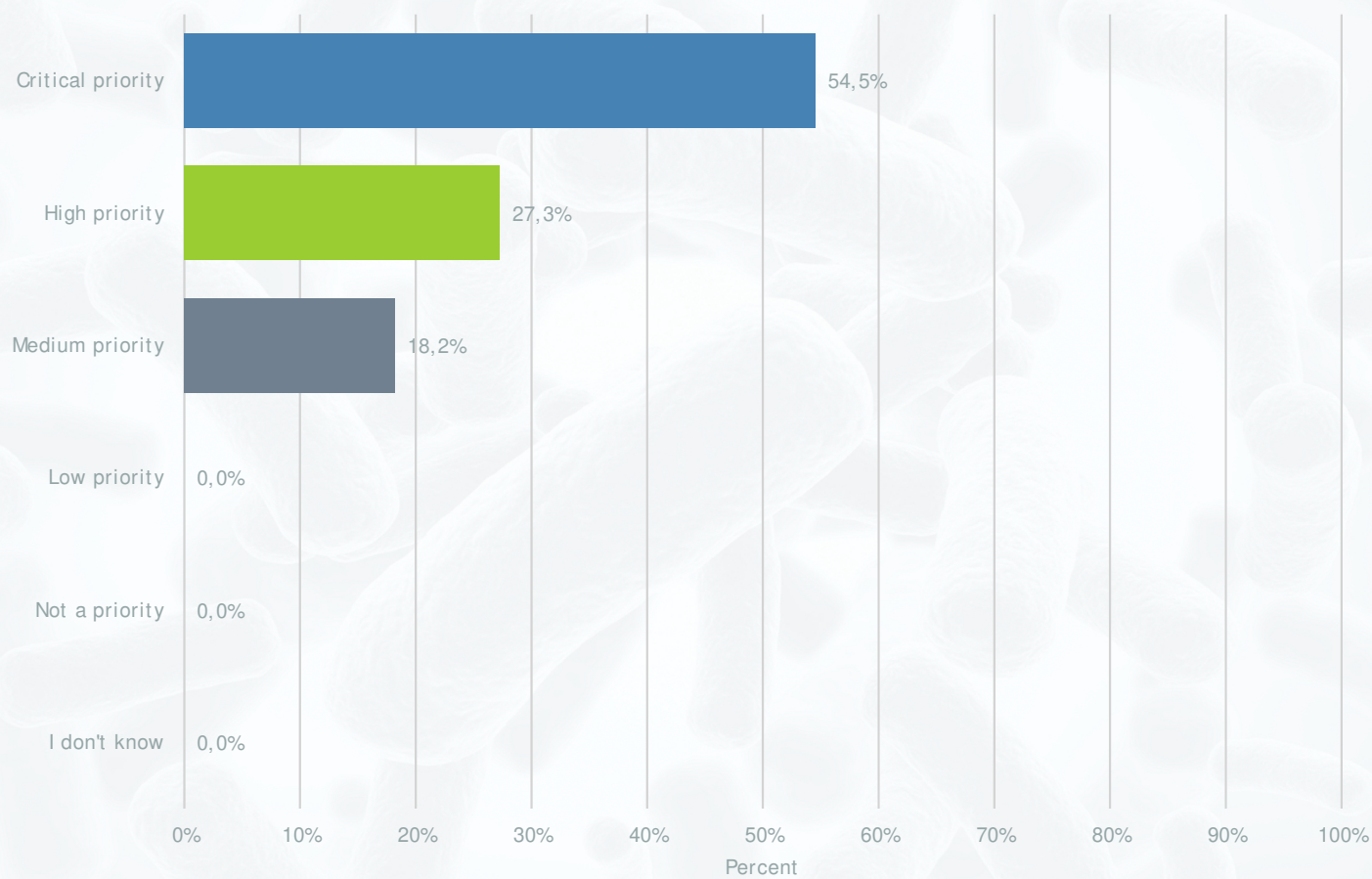
There are a number of innovative, new methods to monitor compliance to IPC practices, including electronic and infrared approaches for example. These need to be tested in multiple settings to assess their value for IPC programmes.



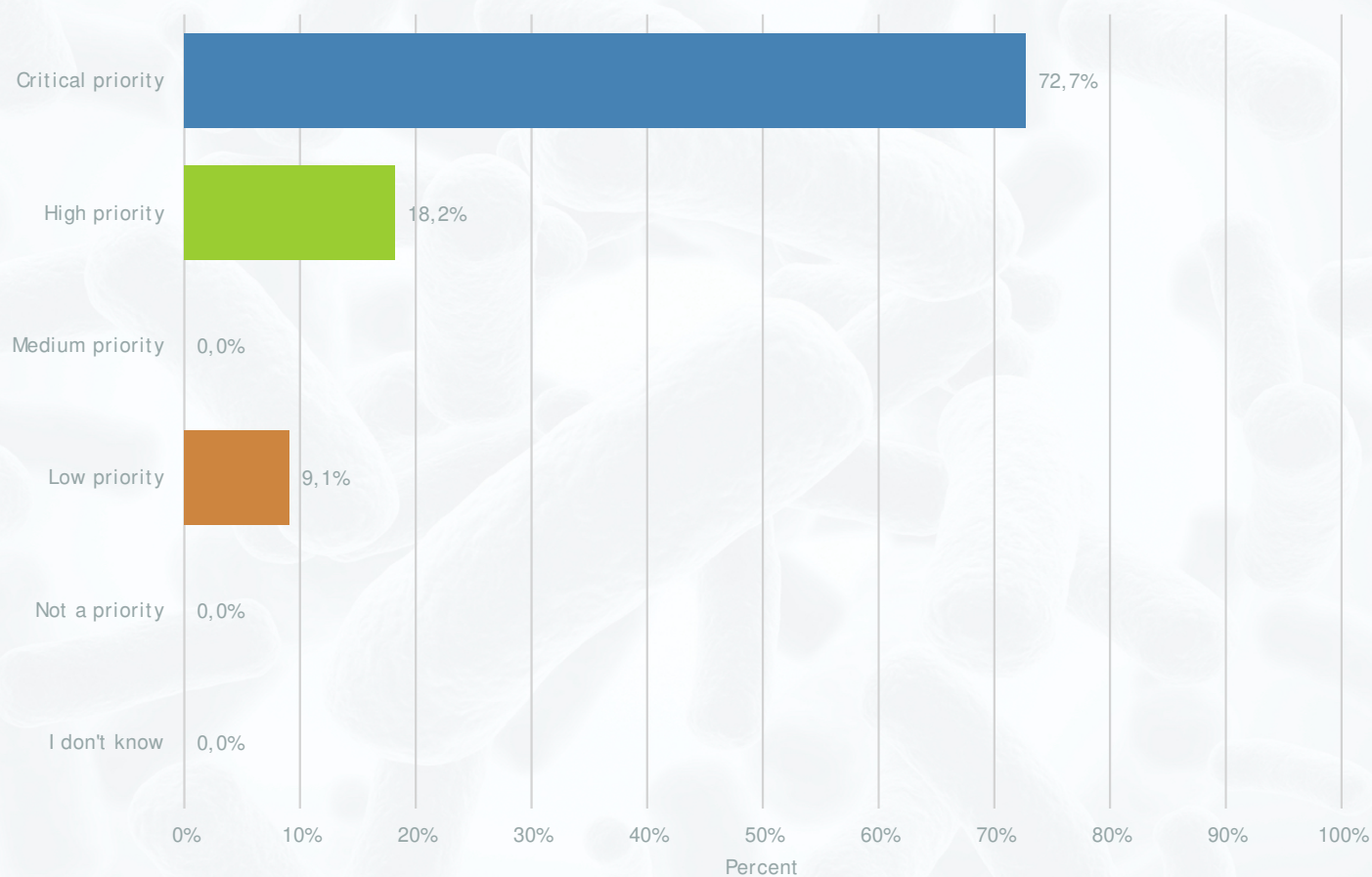
Insufficient data are available on the impact of infrastructural changes at the facility level on the reduction of HCAI and AMR (accessibility to specific equipment, density of hand washing points, single room, facilitation of care circuits, and more).



Research is needed to explore the impact of patient-to-bed ratio on the spread of HCAI and AMR, (staff workload, available staffing bed occupancy, and visitor frequency).



Studies are needed to assess the demographic, organizational, economic, sociological, and behavioral factors facilitating success but also the barriers and challenges to implement effective IPC programmes.



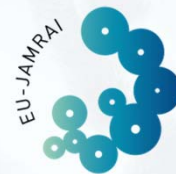
Thank you

marie-cecile.ploy@unilim.fr

**Inserm, University of Limoges
France**

www.eu-jamrai.eu

 @EUjamrai  EUjamrai  EUjamrai



Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections



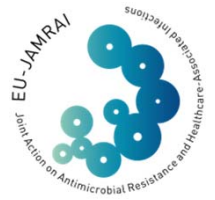
Co-funded by the
Health Programme
of the European Union



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** This presentation arises from the Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), which has received funding from the European Union, under the framework of the Health Program (2014-2020) under the Grant Agreement N° 761296. Sole responsibility lies with the author and the Consumers, Health, Agriculture and Food Executive Agency is not responsible for any use that may be made of the information contained herein.*

To summarize



European research priorities	High priority	<ul style="list-style-type: none">• Improving fundamental knowledge on AMR• Strengthening surveillance systems• Implementing IPC measures (but more research needed)• Developing innovative drugs or diagnostic tools• Evaluating stewardship interventions• Structuring research networks
	Medium priority	<ul style="list-style-type: none">• AMR in the animal field• Involvement of socio-economic science• Development of new economic tools to support R&D
	Low priority	<ul style="list-style-type: none">• AMR in the environment• AMR in the food chain• Improvement of clinical trials

Small amount of participating countries

but good diversity :

- Various incomes
- Various levels of antibiotic consumption
- Various processes in the implementation of their NAP on AMR...



Folkhälsomyndigheten

A reimbursement model for keeping antibiotics available in Sweden

Workshop on Increasing Investments for
AMR R&D

Jenny Hellman, Public Health Agency of
Sweden



Risk of insufficient availability of some antibiotics in Sweden

- Small market.
- Low resistance rates.
- Restrictive use.

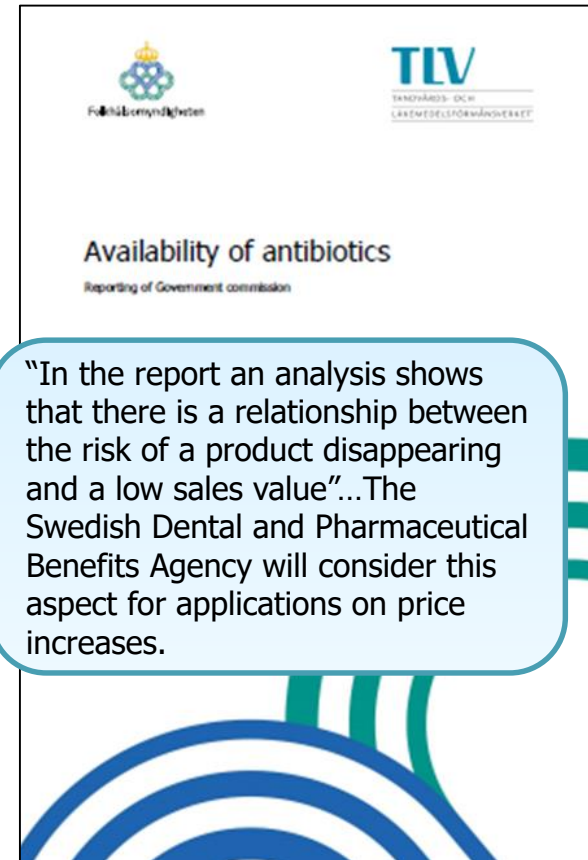
Some products face such low demand that there is a risk that pharmaceutical companies choose not to have them available on the Swedish market.

Governmental commissions: Making antibiotics available

- 2014-2015: preparatory studies and commission within the National Pharmaceutical Strategy.
- 2016-2017: to propose one or several models for ensuring availability of existing antibiotics of special medical value available.
 - Including aspects of responsible use.
 - Not a model for incentives for research and development of new antibiotics.

Recommendations

- Pilot an alternative reimbursement model.
 - requisition antibiotics highly prioritized in terms of medical value (“new ab”).
- Regional procurement to include commitments of volumes and security stocks.
 - antibiotics without market protection.
- Special considerations for price increase applications.
 - prescription antibiotics without market protection.
- No new models for responsible use.



Working model for identifying antibiotics

- Low sales
- Few MHA

Risk of insufficient national availability?

No →

Yes ↓

- Activity against identified high-risk resistance types,
- Ecologic profile
- Role treatment guidelines

Special medical value?

No →

Yes ↓

**Categories
antibiotic products for
specific models**

- New requisition antibiotics
- Antibiotics without market protection



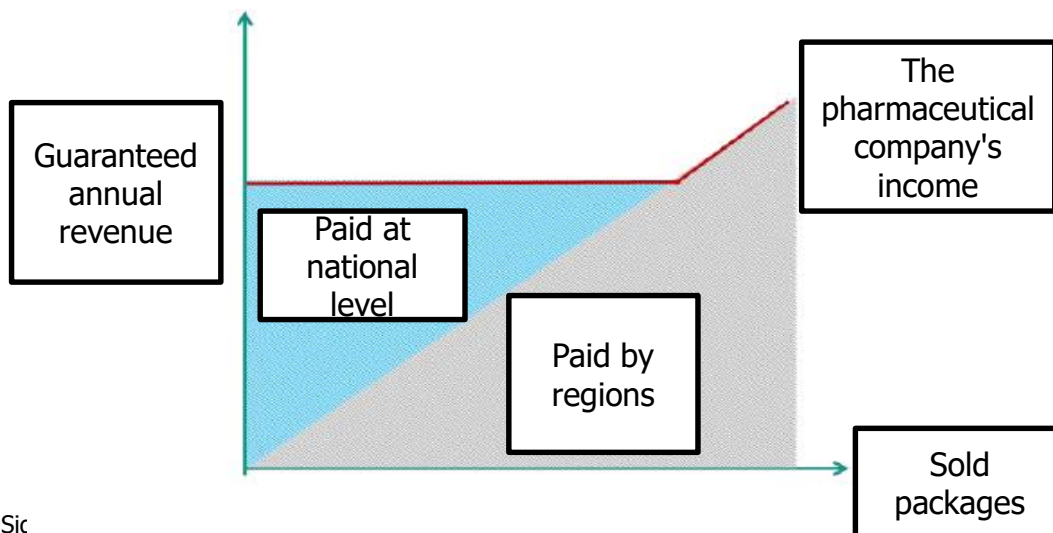
Ongoing governmental commission

- 2018-2022: Pilot study of proposed reimbursement model.
 - Testing of contracting process and legal aspects.
 - Evaluation of effects on availability.

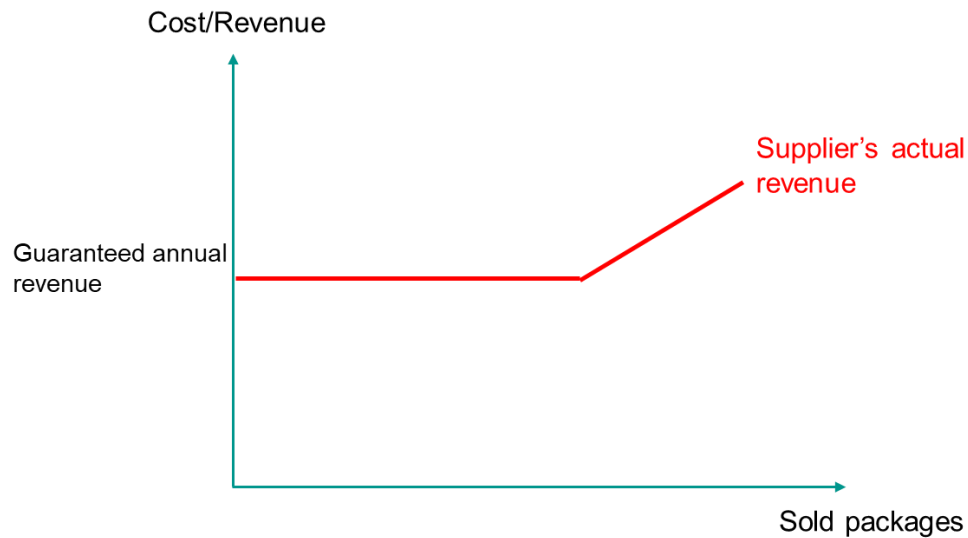
Goal: To give the government a recommendation if, and in what way, the model should be extended.

Suggested model for the pilot

- New antibiotics with low expected sales.
- Guaranteed annual revenue → In return the company delivers a certain amount in specified time limits.
- Regions continue to pay for their usage.
- If the revenue of companies from regions is lower than the guaranteed level, the difference will be paid nationally and yearly.



How to set the *guaranteed annual revenue*?



- VBP?
- Fixed cost?
- Based on estimations of the volume that needs to be available? "Medical worst case scenario"

Changes of Revenue Streams

- The total revenue over the contract years will be higher.
- Revenues come earlier.
- Revenues are less uncertain.

Why do we believe in our model?

– If contract → access is guaranteed.



"Netflix-style subscription model" (*Economist*)

Other benefits:

- Not increase the use.
- Not buy stocks.
- The total revenue will be higher
- Adaptable to other countries?



July 2018-May 2019- Planning phase

- Identified and start discussions with relevant partners.
- Procurement strategy.
 - Competition aspects.
 - Decentralized health care system.
 - National procurement.
- Legal aspects.
 - EU state aid rules.
 - Pilot funded nationally – options for potential extension?
- Sweden 's Innovation Agency (Vinnova) intended funder for the pilot.
- Monitoring and evaluation.



Folkhälsomyndigheten

Thank you!

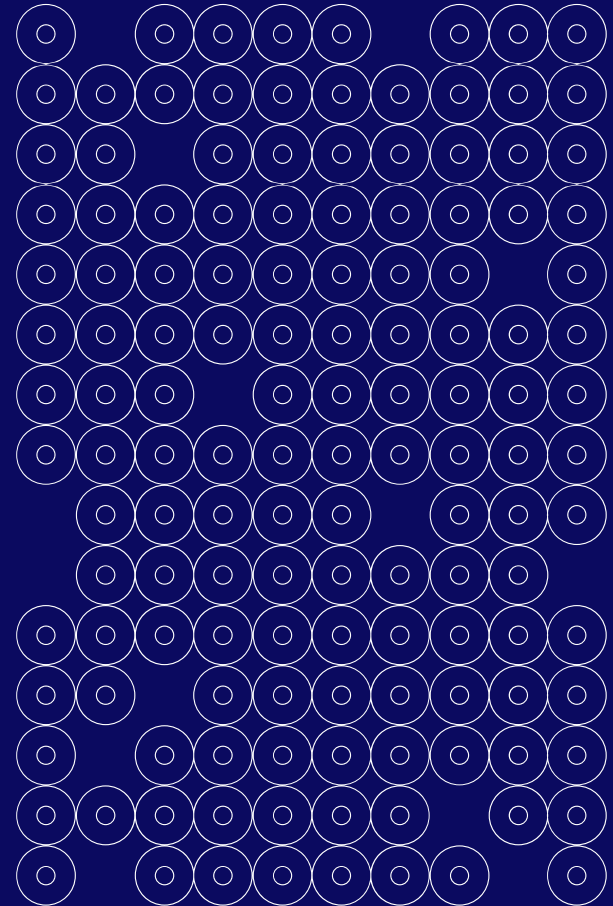
jenny.hellman@folkhalsomyndigheten.se



Overview of public AMR R&D investments – funding instruments for a One Health approach

Laura Marin
JPIAMR Head of Secretariat

Geneva, 28 May 2019





Joint Programming Initiative on Antimicrobial Resistance

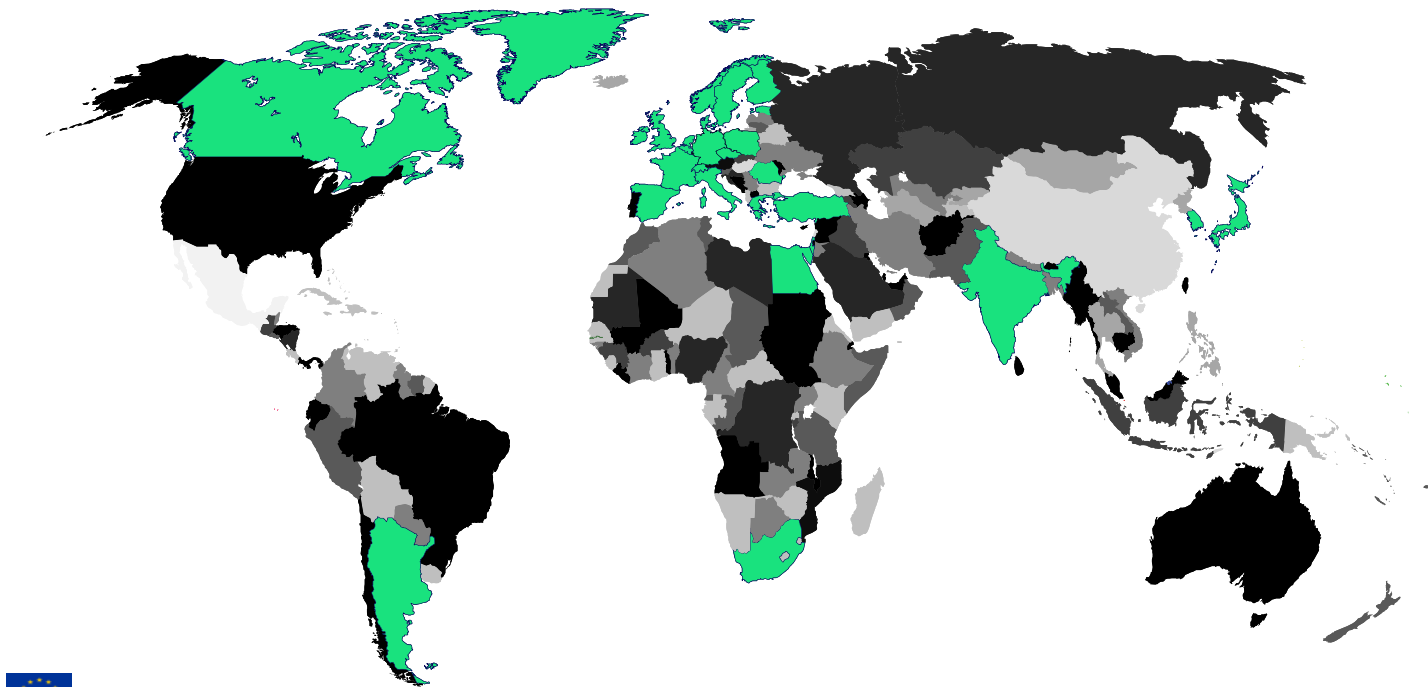
Mission: To join forces across nations by leading the alignment, coordination, and support to Antimicrobial Resistance One Health collaborative research and global policy activities

International collaborative platform that:

- aligns national research funding
- coordinates AMR research and funding on a global scale
- supports collaborative action for filling knowledge gaps on AMR with a One Health perspective

JPIAMR: A Global Organisation

Uniting 27 countries to address AMR



The European Commission (DG Research) is a full non voting member

 JPIAMR member states



Research Prioritisation: The Strategic Research and Innovation Agenda



Research Prioritisation: The Strategic Research and Innovation Agenda

Priority topic Focus

Therapeutics Discovery of new antibiotics and therapeutic alternatives, and the improvement of current antibiotics and treatment regimens

Research and innovation objectives

- Find new antibiotics and targets
- Develop new chemical entities and scaffolds
- Improve pharmacokinetics and pharmacodynamics of antibiotics, including neglected antibiotics
- Use personalised medicine and artificial intelligence to improve therapies
- Develop alternatives for antibiotics
- Develop treatment protocols based on



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58% of the total investment
is in Therapeutics



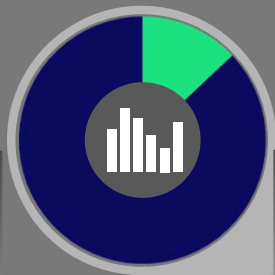
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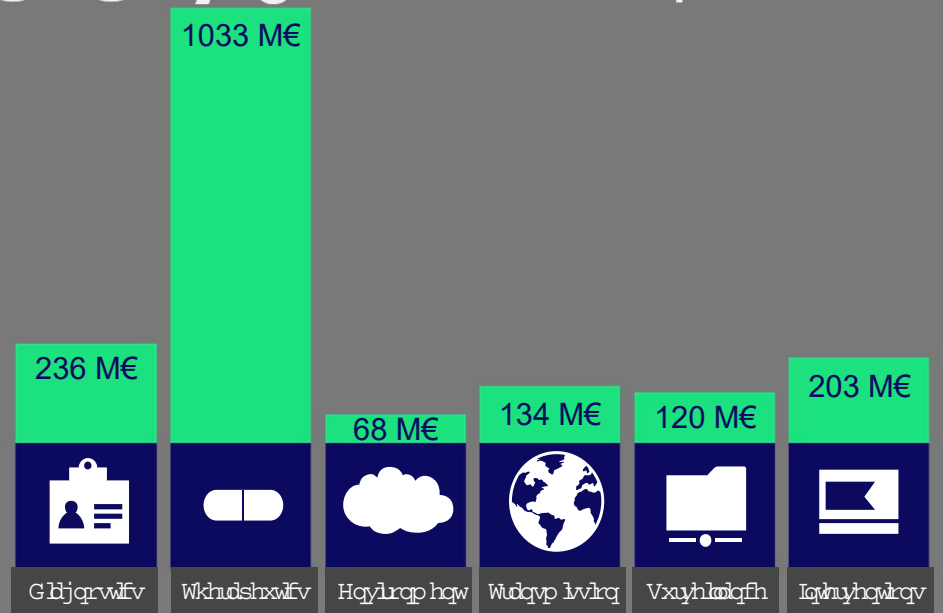
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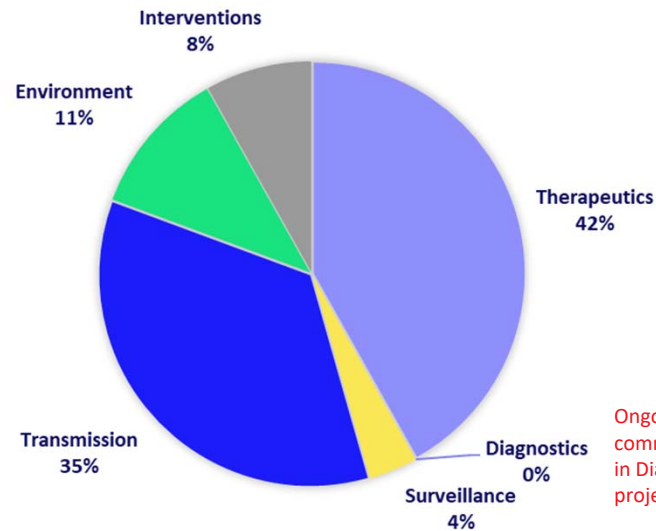
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JPIAMR: Global AMR Research Funder

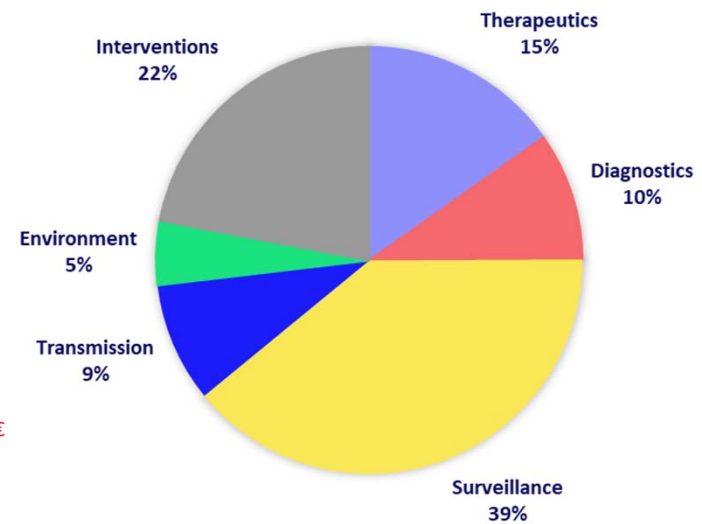
- Basic, pre-clinical and phase 1 clinical trials
- To date 49 projects, 31 networks in AMR research have received over 85 M€

PROPORTION OF RESEARCH PROJECTS PER PRIORITY RESEARCH AREA



Ongoing call in 2019 has committed to investment of 20 M€ in Diagnostics and Surveillance projects

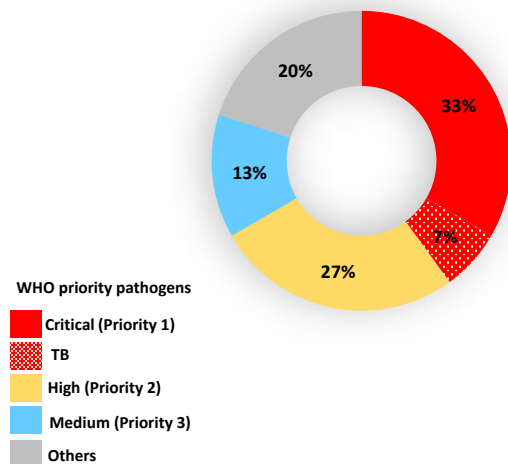
PROPORTION OF NETWORKS PER PRIORITY RESEARCH AREA



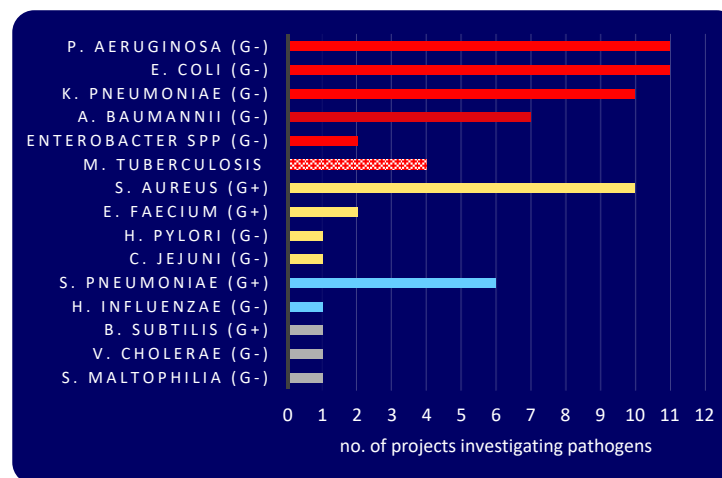
JPIAMR funded 20 projects in Therapeutics research

- 100 partners in 17 countries
- 25M Euros invested






JPIAMR supported research projects addressing pathogens categorised under WHO Priority Pathogens List



Distribution of JPIAMR funded projects on the basis of pathogens studied

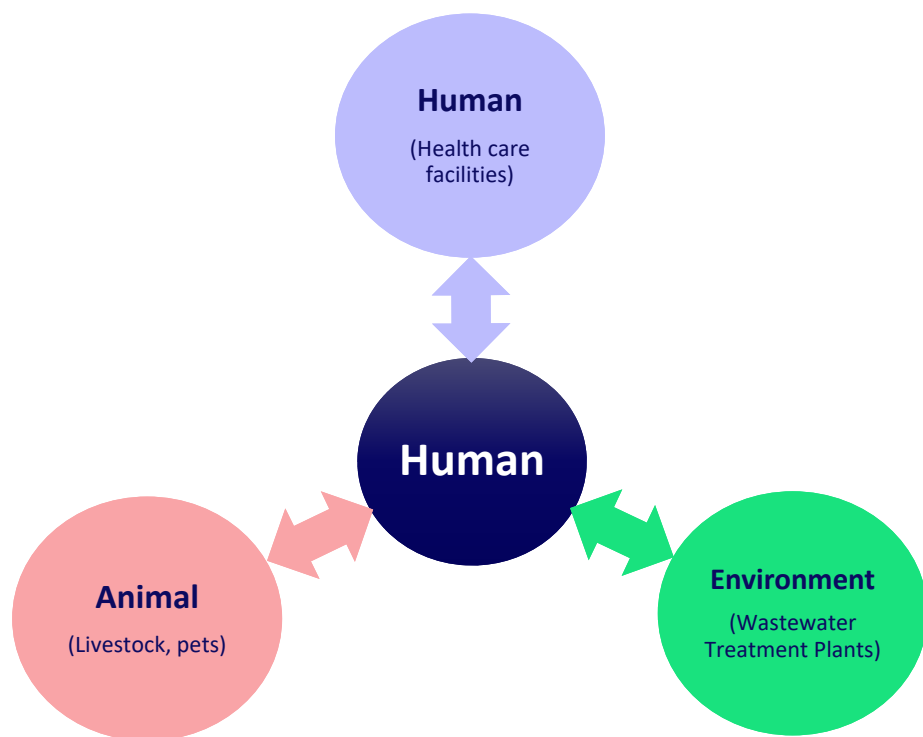


Coordination International AMR drug development funders

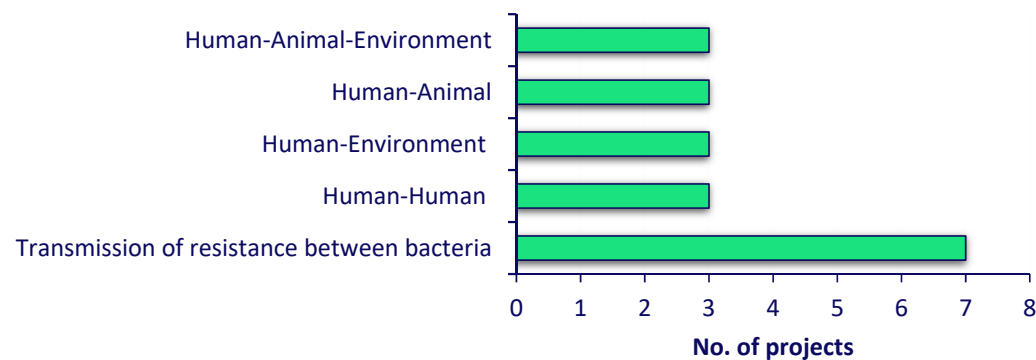
					
Products	Novel therapeutics, diagnostics, preventatives, devices	Novel therapeutics, diagnostics, surveillance, prevention, stewardship	Novel therapeutics, Optimize antibiotics, Develop combinations	Novel therapeutics, companion diagnostics	Novel therapeutics, diagnostics, economic models
Pathogens	High priority defined by WHO and CDC, largely Gram-negatives	WHO priority pathogens Member state national priorities	WHO priority pathogen list, especially Gram-negatives	High priority defined by WHO and CDC	<i>Priority pathogens including pathogens on WHO priority list</i>
Stages of development	Hit-to-lead through end of Phase 1	Discovery research	Any stage of development to patient access	Lead optimization through end of Phase 1	Whole value chain
Geography	Global	Global	Global	Europe & U.S.	Global
Funding instruments	Non-dilutive funding and expert support	Research project grants, Networks, Virtual research institute	Sponsor role (preclinical studies & clinical trials)	Convertible loans and royalty-based	Financial, in-kind and expertise support
Funding allotments	Flexible, with milestones; >30% cost share	Direct funding 1m to 5m x project	Direct funding and flexible partnerships	USD 1m to 15m	Direct funding, grants of € 4.4 to 211m (50 percent in kind contribution)
Conditions	Stewardship and market access requirements		Stewardship and access. Consider in/out licencing	Stewardship and access requirements (<i>in progress</i>)	Limited compensation when value generated

JPIAMR funded 19 projects in Transmission research

- 118 partners in 17 countries
- 30M Euros invested



Distribution of JPIAMR supported projects on Transmission



Joint Transnational Research Call 2019

Diagnostics and Surveillance of Antimicrobial Resistance

Funding research projects addressing the development of diagnostic and surveillance tools, technologies and methods to detect AMR. Projects should address the diagnosis of AMR infections in clinical and veterinary settings or the surveillance of AMR in humans, animals and the environment.

Promoting projects with impact in LMIC settings in Asia and Africa.

Publication of call:
Dec. 5, 2018

Deadline pre-proposals:
Feb. 15, 2019

Deadline full proposals:
June 14, 2019

No. of participating countries:
16

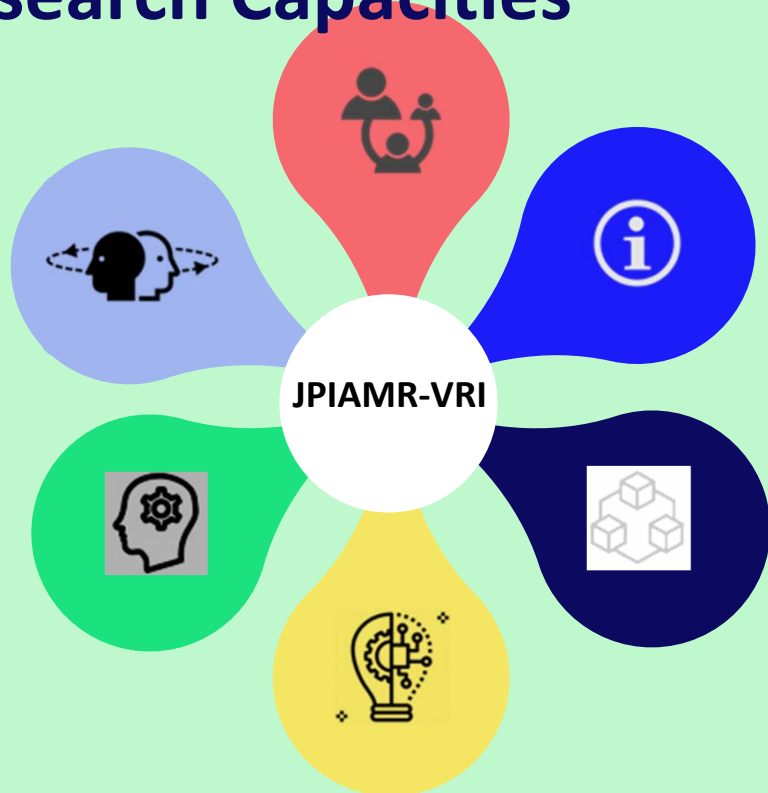
Budget:
21 million Euro

Funding start:
Dec 2019/
early 2020

Achieving research collaboration with LMICs

- Applications: 71 consortia 344 partners in total
- Partners from 53 countries applying.
- Strong participation from China (8 projects) and India (9 projects)
- 36 projects have LMIC from Africa. 37 projects include Asian partners funded by Canada. Only 7 projects lack participation from Africa or Asia.
- 2 coordinators from Tanzania, 2 from Uganda, 1 from Ethiopia, 2 from South Africa, 1 from India, 2 from China and 1 from Bangladesh
- Non-Europeans 15% of all coordinators.

JPIAMR-Virtual Research Institute Research Capacities



Connecting

Bridging Partnerships, Collaborations, Forums, Forum, Workshops, Webinars.



Access

Enabling Global Access, Mappings, Frameworks, Blueprints, Expertise, Knowledge Transfers, Blueprints, Structuring.



Data Sharing

Online Sharing Platforms, Libraries, Catalogues.



Scientific Innovation

Building Evidence in all domains of AMR, including human and animal health and the environment.



Capacity Building

Training, Virtual Education, Train the Trainers, Exchange Programs.



Awareness

Developing and Sharing research results, Promoting AMR in the Global Agenda

Funding Roadmaps

Next funding opportunities:

2020 New Round of grants JPIAMR-Virtual Research Institute

Networks plus call.

2020 Aquatic Pollutants – supporting AMR Water research

To fill existing key knowledge gaps regarding the environmental behaviour of new and emerging pollutants as well as pathogens in inland waters and the marine environment, and their impacts on ecosystems and human health.

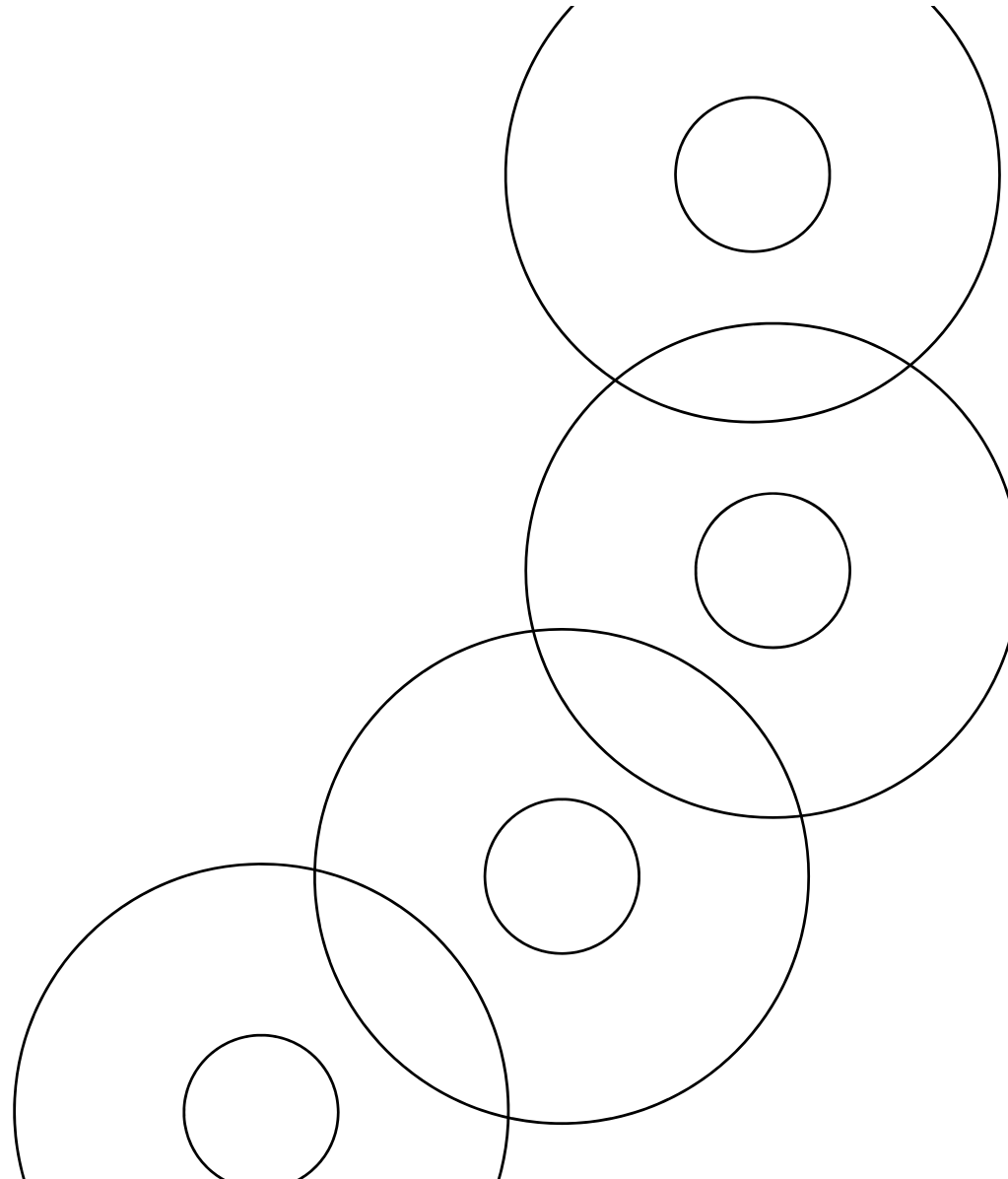
2021: One Health interventions to prevent or reduce the development and transmission of AMR

Thank you

www.jpiamr.eu
twitter.com/JPIAMR
facebook.com/JPIAMR

Acknowledgments: Shawon Lahiri

www.jpiamr.eu twitter.com/JPIAMR facebook.com/JPIAMR



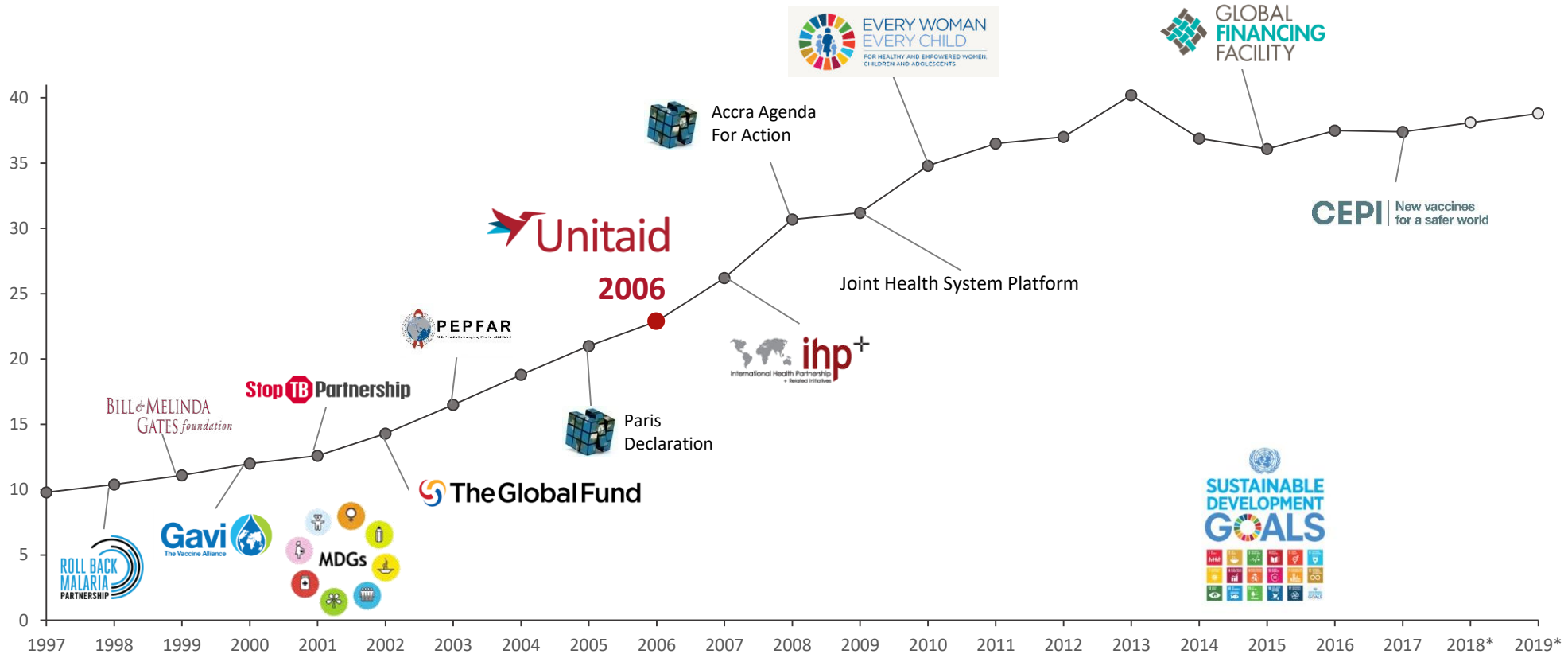
Incentivising investments in R&D for LMICs

Katerina Galluzzo
28th of May 2019



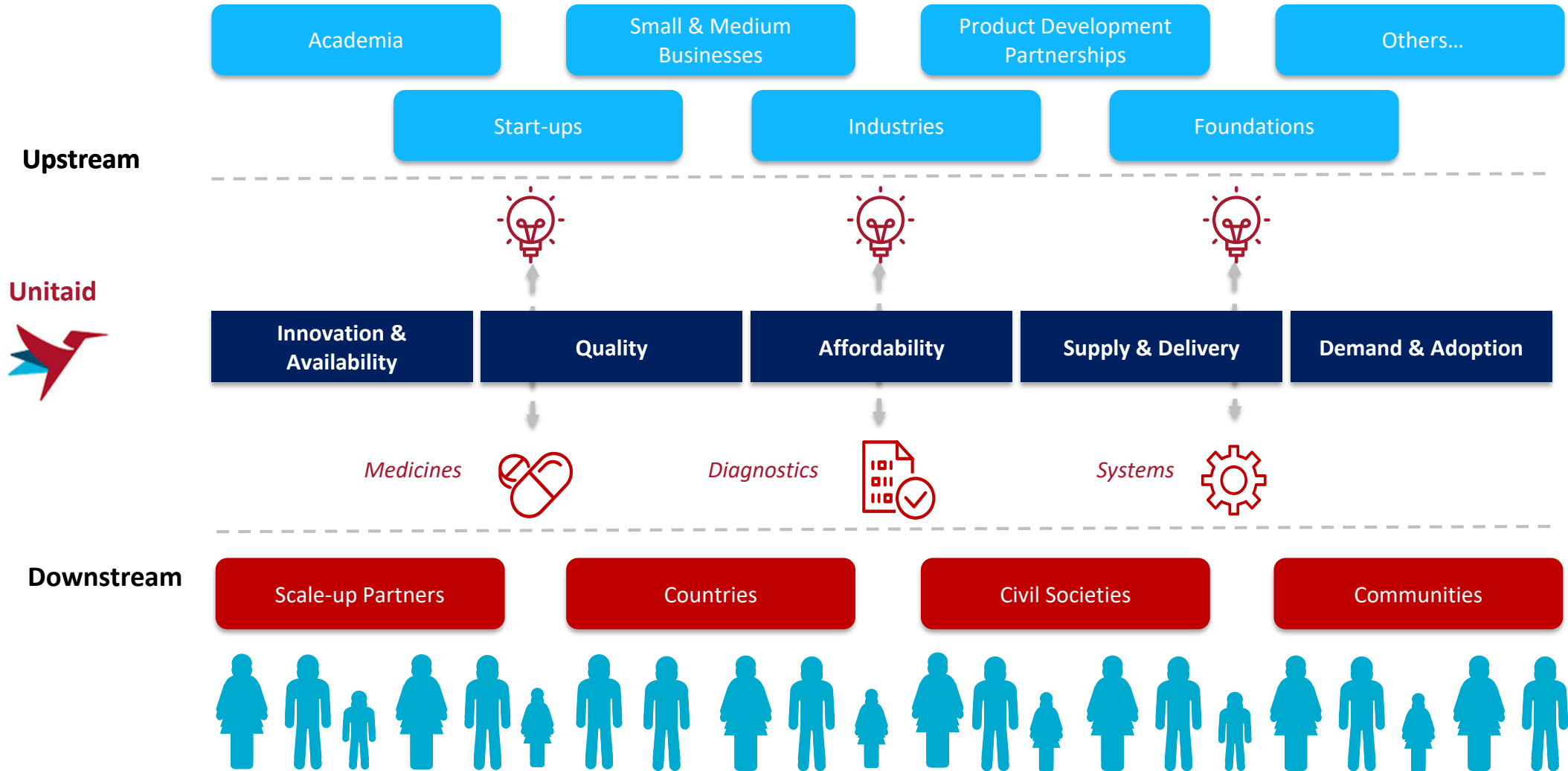
Growth in development assistance

Development assistance for health (\$B)



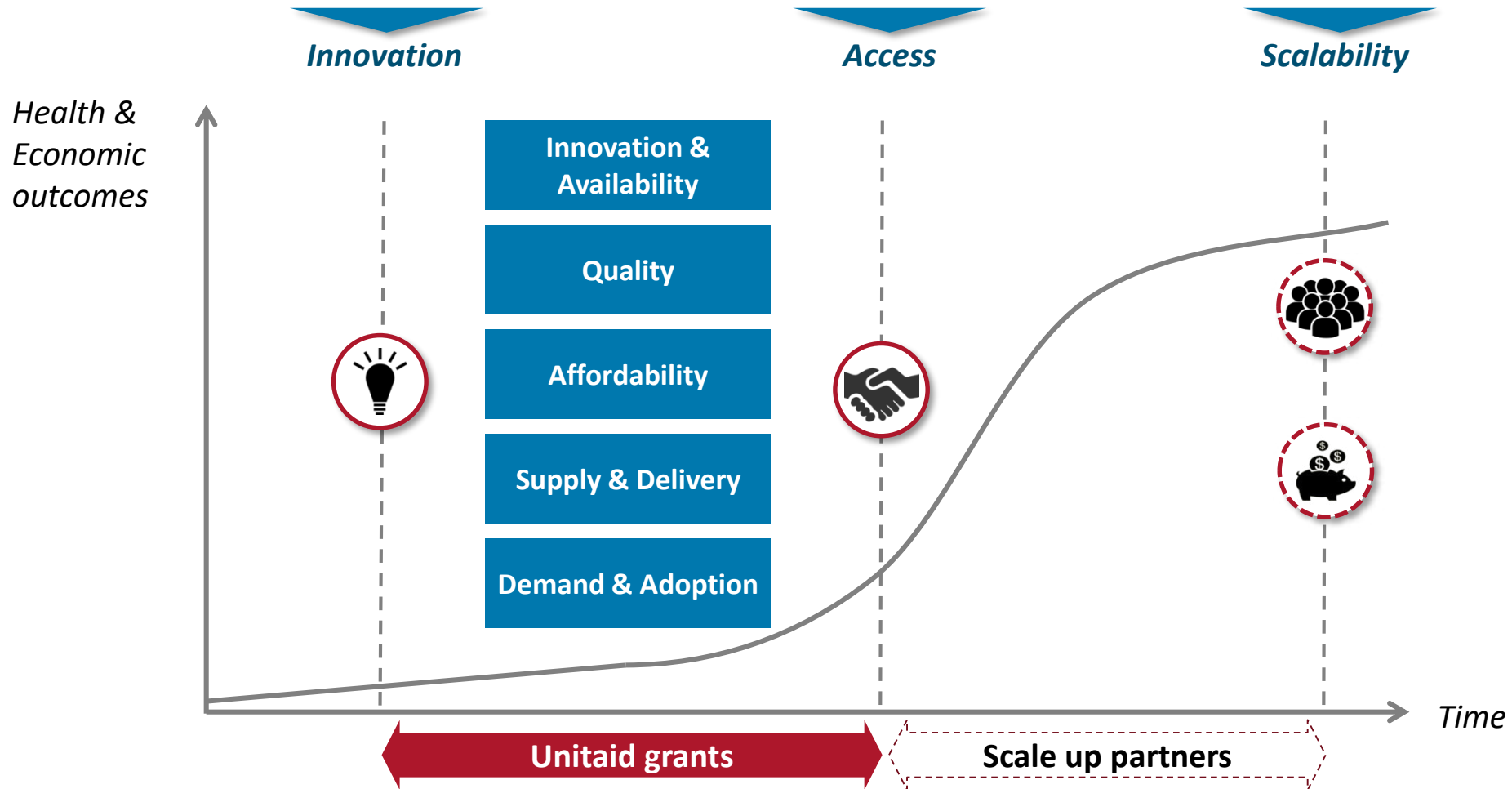
Source: IHME (Institute for Health Metrics and Evaluation), *projections

Unitaid's role in global health



Unitaid's strategy and positioning

Unitaid's mission: maximize the effectiveness of the global health response by catalyzing equitable access to better health products



Partner engagement is key through the entire process



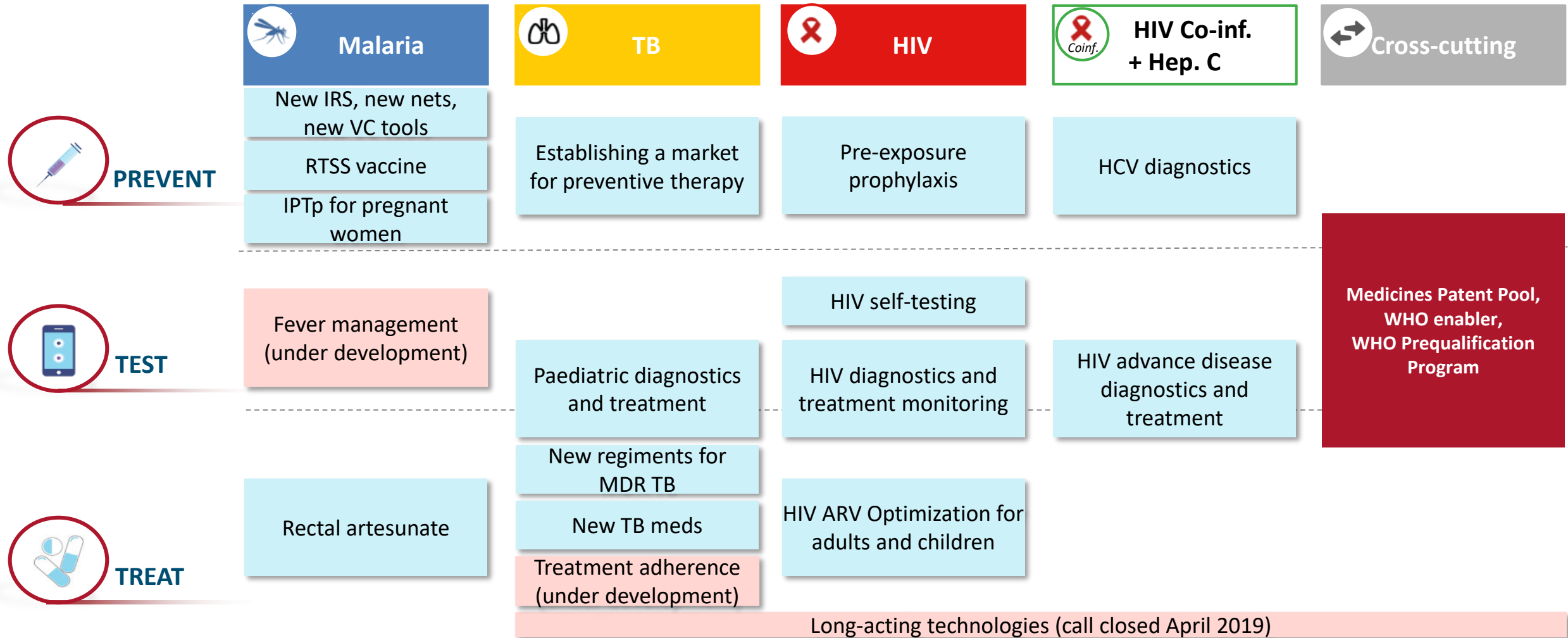
Anticipate and respond to country needs

Anticipate upstream innovation

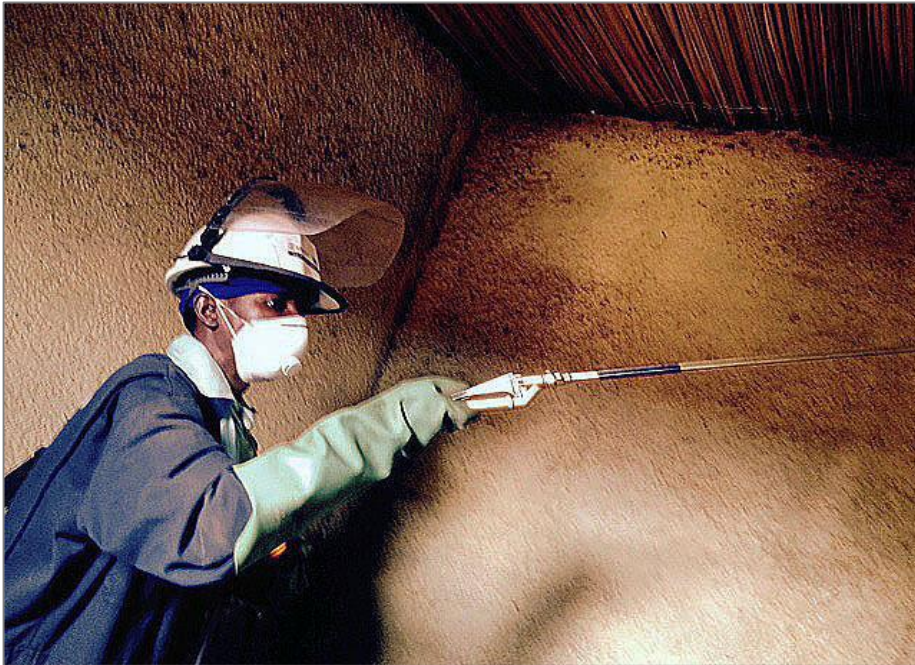
Ensure readiness to scale-up including funding





Unitaid's core investment areas and AMR (non-exhaustive)

As of 2019, ~60% (\$0.7b) of Unitaid's portfolio are related to resistance issues

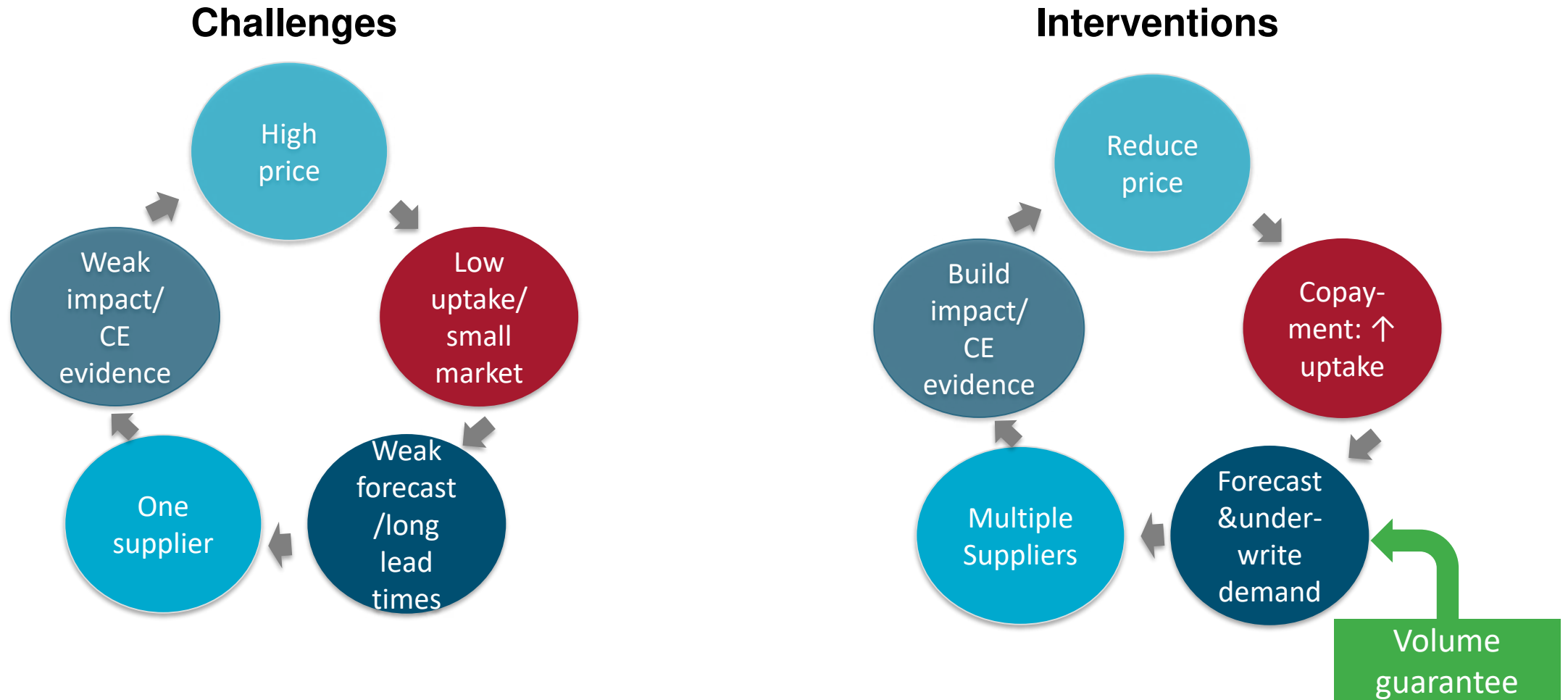


Example: NgenIRS - improving affordability of new insecticides for resistance management



 Lead grantee	IVCC
 Grant period	2016 – 2020
 Grant value	US\$ 65.1M
 Target coverage	50m people, 16 African countries

Incentivising investment through an innovative and complementary mix of strategies



Thank you
galluzzok@unitaid.who.int



Powered by **CARB-X**

PRESENTATION MADE AT GLOBAL AMR R&D HUB MEETING

GENEVA – MAY 28TH 2019



FLOW OF PRESENTATION

- The AMR landscape in India
- India's role in supporting a vibrant AMR ecosystem
- What sort of models are possible in a LMIC like India?
 - 1.35Billion people, 5th largest GDP in the world, ~20% people below poverty
 - Spends just 1.2% of GDP on Health
 - Biggest study in contrast!

AMR IS A GLOBAL CHALLENGE

NEWS 'Nightmare bacteria' are trying to spread in the U.S., CDC says

'Nightmare bacteria' are trying to spread in the U.S., CDC says

Aggressive testing at hospitals and clinics can stop superbugs



CNN Health • Food • Fitness • Wellness • Parenting • Live Longer

Superbugs kill 33,000 in Europe every year

By Lianne Kollirin, CNN
Updated 8:25 AM ET, Tue November 6, 2018



More from CNN

- Argentina's missing submarine found a year after it vanished...
- NFL Players Who Just Need a Change of Scenery

THIS IS NOT A BED

Superbugs kill more in India than globally, mortality rate is 13%

Durgesh Nandan Jha | TNN | Updated: Nov 18, 2018, 09:08 IST

✉ 🖨️ A- A+

Ad

State Farm ® Here to help life go right. ®

STATE FARM INSURANCE



HIGHLIGHTS

- The overall mortality rate due to drug resistant bacteria in India was 13% in 2015.
- Most of the patients who died were either old or admitted to ICUs when they were diagnosed with the infection. The corresponding figure in advance nations ranged between 2% and 7%.

CIDRAP Center for Infectious Disease Research and Policy

News & Perspective Infectious Disease Topics Antimicrobial Stewardship Ongoing Programs

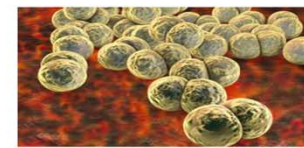
FEATURED NEWS TOPICS Zika Yellow Fever MERS-CoV

In world first, UK reports high-level gonorrhea resistance

Filed Under: Gonorrhea, Antimicrobial Stewardship
Lisa Schriming | News Editor | CIDRAP News | Mar 29, 2018

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Health officials in the United Kingdom announced today that they are investigating a gonorrhea infection contracted abroad that marks the first global detection of high-level resistance to recommended dual-antibiotic treatment as well as to other commonly used drugs.



Dr. Microbe / iStock

Gwenda Hughes, PhD, consultant scientist at Public Health England (PHE) and head of its sexually transmitted infection section said in a statement that the patient's *Neisseria gonorrhoeae* infection is very resistant to first-line treatment, a combination of two antibiotics—azithromycin and ceftriaxone.

"We are following up this case to ensure that the infection was effectively treated with other options and the risk of any onward transmission is minimised," she said, adding that the PHE actively monitors the spread of antibiotic resistance in gonorrhea and potential treatment failures.



17-18 FOOD AND DRUGS > GLOBAL SUPERBUGS

BABIES HIT THE HARDEST BY INDIA'S ANTIBIOTIC RESISTANCE CRISIS

Science

Drug resistance in sick babies - an increasing cause of worry for India

Maitri Porecha | New Delhi | Updated on January 26, 2019 | Published on January 24, 2019



The babies acquire these infections from mothers who have been subjected to unhygienic practices in the labour rooms and neonatal intensive units in hospitals - iStockphoto

'Drug-resistant bugs make treatment hard'

More babies are struck with neonatal sepsis, a series of blood stream infections, within the first month of birth in India than anywhere else in the world. Several of them die

Updated November 14 2018
Ilen Davies



The study found that the burden of respiratory illnesses is highest in areas of low socio-demographic status. Photo: Priyanka Parashar/Mint

India saw most deaths due to respiratory illnesses in children under 5 in 2015: study

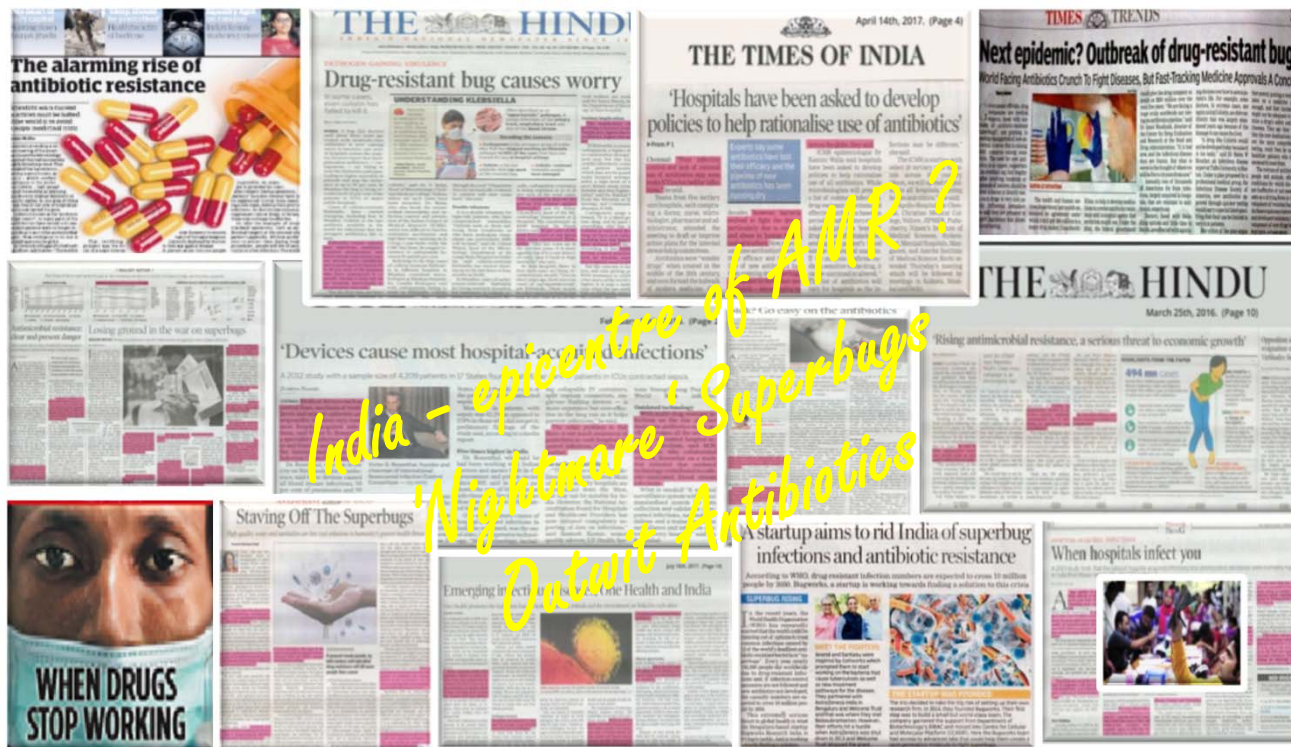
2 min read . Updated: 28 Aug 2017, 12:09 AM IST

Neetu Chandra Sharma

In India, about 82,448 children died of Pneumococcal pneumonia in 2015, shows study published in Lancet



* India loses too many people to superbugs



- Density of population
- Hand hygiene
- Easy availability – human and animal health
- Complex interplay of Access, Excess, lack of regulation, socio-economic behaviors

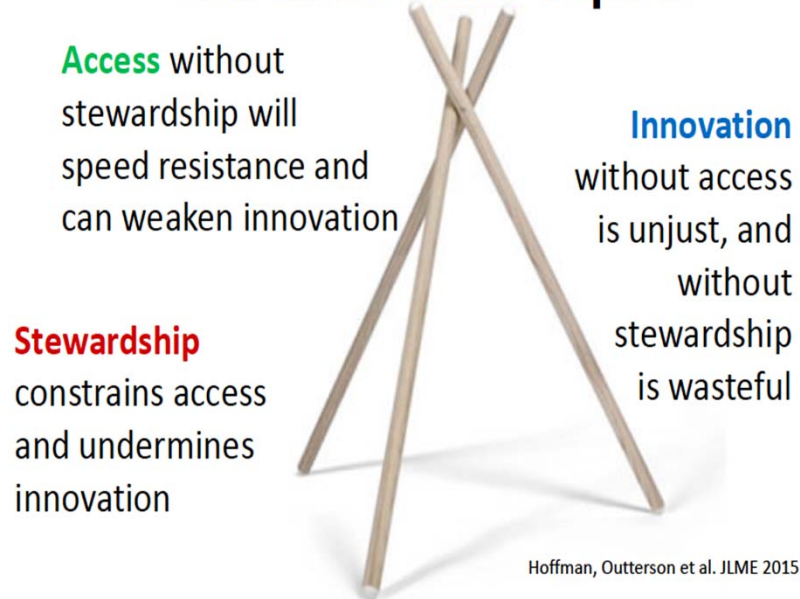
OUR EXPERIENCE WORKING WITH CLINICAL ISOLATES – SCARY!

- Ciprofloxacin
 - >90% E.coli, >70% K. pneumoniae, ~30% P. aeruginosa,
 - >80% **A. baumannii**, ~30% E. cloacae, & ~50% S. marcescens
- Levofloxacin
 - 90% E.coli, >70% K. pneumoniae, ~30-70% P. aeruginosa,
 - ~50-90% **A. baumannii**, ~30% E. cloacae, & ~50% S. marcescens
- Meropenem
 - ~15-25% E.coli, ~30-70% K. pneumoniae, ~50% P. aeruginosa
 - ~50-90% **A. baumannii**, ~30% E. cloacae, & ~60% S. marcescens
- Ceftazidime
 - ~90-100% of all species resistant to Ceftazidime
- *Increasing resistance to Colistin - at about 15%*
- *Urgent measures required on all fronts – Prevention, Access, Stewardship and Innovation of new therapies*

* ~1000 isolates per drug, from across 2 large tertiary hospitals in Bangalore

A PICTURE HELPS TO REMIND US WHY WE ARE HERE!

The antibiotic tripod



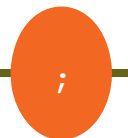
- 10 years, \$500M, < 5% success rate
- Regulatory challenges galore
- Need to make it accessible/affordable
- Use as 'last resort drugs'
- No volume but HUGE value
- Big pharma have left
- Most SME's barely alive
- But Value created by new antibiotic
 - Difference between Life & Death
 - Very edifice to modern medicine

* With permission from CARB-X

* Market Entry Rewards desperately needed



BUGWORKS TEAM!



FIRST NOVEL CLASS OF BROAD-SPECTRUM ANTIBIOTICS IN DECADES....

Critically and Seriously Unmet Medical Need: Infections	WHO	CDC	Lead Compound
<i>Acinetobacter baumannii</i> , carbapenem-R	Critical	Serious (MDR)	Yes
<i>Pseudomonas aeruginosa</i> , carbapenem-R	Critical	Serious (MDR)	Yes
<i>Enterobacteriaceae</i> , carbapenem-R, 3 rd -gen ceph-R (ESBL+)	Critical	Urgent (carbapenem-R)	Yes
<i>Enterococcus faecium</i> , vancomycin-R	High	Serious (VRE)	Yes
<i>Staphylococcus aureus</i> , methicillin-R, vancomycin-I/R	High	Serious (MRSA)	Yes
<i>Helicobacter pylori</i> , clarithromycin-R	High	Serious	Yes
<i>Campylobacter</i> spp., fluoroquinolone-R	High	Serious (drug-R)	Yes
<i>Salmonellae</i> spp., fluoroquinolone-R	High	Serious (drug-R)	Yes
<i>Neisseria gonorrhoeae</i> , 3 rd -gen ceph-R, fluoroquinolone-R	High	Urgent (drug-R)	Yes
<i>Streptococcus pneumoniae</i> , penicillin-NS	Medium	Serious (drug-R)	Yes
<i>Haemophilus influenzae</i> , ampicillin-R	Medium	Concerning	Yes
<i>Shigella</i> spp., fluoroquinolone-R	Medium	Serious	Yes
<i>Clostridium difficile</i>		Urgent	Yes
Group A <i>Streptococcus</i>		Concerning (erythro-R)	Yes
Group B <i>Streptococcus</i>		Concerning (clinda-R)	Yes

- Completing preclinical tox and IND filing by late 2019
- Entering Phase 1 in early 2020
- TPP considerations including cUTI, HAP/VAP, IAI, Blood Stream, Melliidosis etc



DEPARTMENT OF BIOTECHNOLOGY
Ministry of Science & Technology



DBT -BIRAC Joint Call

1. New Antibiotics
2. Alternatives to Antibiotics
 - a) Therapeutic antibodies
 - b) Phage therapy
 - c) Anti-biofilms



Research and Innovation for Therapeutics

Bio -repository

Research and Innovation for Diagnosis

National Priority List for AMR Specific Pathogens

Mission AMR



NCMR, NCCS -Pune

National Centre for Microbial Resources of National Centre of Cell Sciences, Pune has been notified to function as **"Bio -repository for Resistant Microbes/ infective agents (bacteria /Fungi)"** .

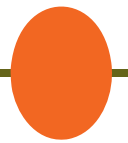


Development of Diagnostics



WHO Country office

Help Identification of priority area for future research and Innovation





INDIA'S ROLE IN SUPPORTING A VIBRANT GLOBAL AMR ECOSYSTEM

- Grants to support surveillance, devices, diagnostics and discovery – BIRAC, ICMR
- Lack of private funding for AMR; government looking at increasing funding pools
- CARB-X accelerator in Asia Pacific region - CCAMP
- Multi and Pan-drug resistance repository open to the world – NCCS Pune
- Regulatory frameworks adapting urgently to allow for faster and cheaper human trials
 - We have the highest disease burden and patients with MDR diseases – Gram Negative, MRSA, TB
 - Cost and time of trials can be a fraction of what it is in the west
 - Is it possible to complete a 'directed' Phase II, Phase III to registration in < \$100M
 - Can single development program address the requirements of different authorities – ICH route
 - Can frameworks like QIDP, LPAD be adopted locally?
 - Alternate pathways for paediatric drug approvals – crisis like situation with Sepsis!
- Enforce strict regulation on hand-hygiene, access and stewardship



Models to make new antibiotics a sustainable business proposition

- Top selling IV broad spectrum : Global sales ~2B, India \$200M
- A novel antibiotic could replace X% of that market (DR patients)
- Innovator has to think like a bio-pharma and take product to market (Manufacturing/Distribution to happen *with local large players*)
- *Multi-tiered pricing* models required
 - Govt and Charitable Trust at (Cost Price +X%)
 - Private hospitals – charge same pricing as currently being paid for Mero
 - Wouldn't work for big pharma, but suitable for SME
- Dovetail into the public-health insurance scheme being rolled out now
 - To insure 500 Million people over next 3 years
 - Pooled purchase plans are the only way to go – the TB model!
 - Government will assure 'stock pile' if (**cost + low-margin**) method adopted





THANK YOU FOR YOUR TIME