Diagnostics in current AMR Priority Agendas

Till T. Bachmann
University of Edinburgh

Novel Diagnostics for Infectious Diseases workshop
25 – 26 March 2024
Royal Society, London

The **Interest** in AMR Diagnostics is Huge

ECCMID 2023
ECCMID 2024

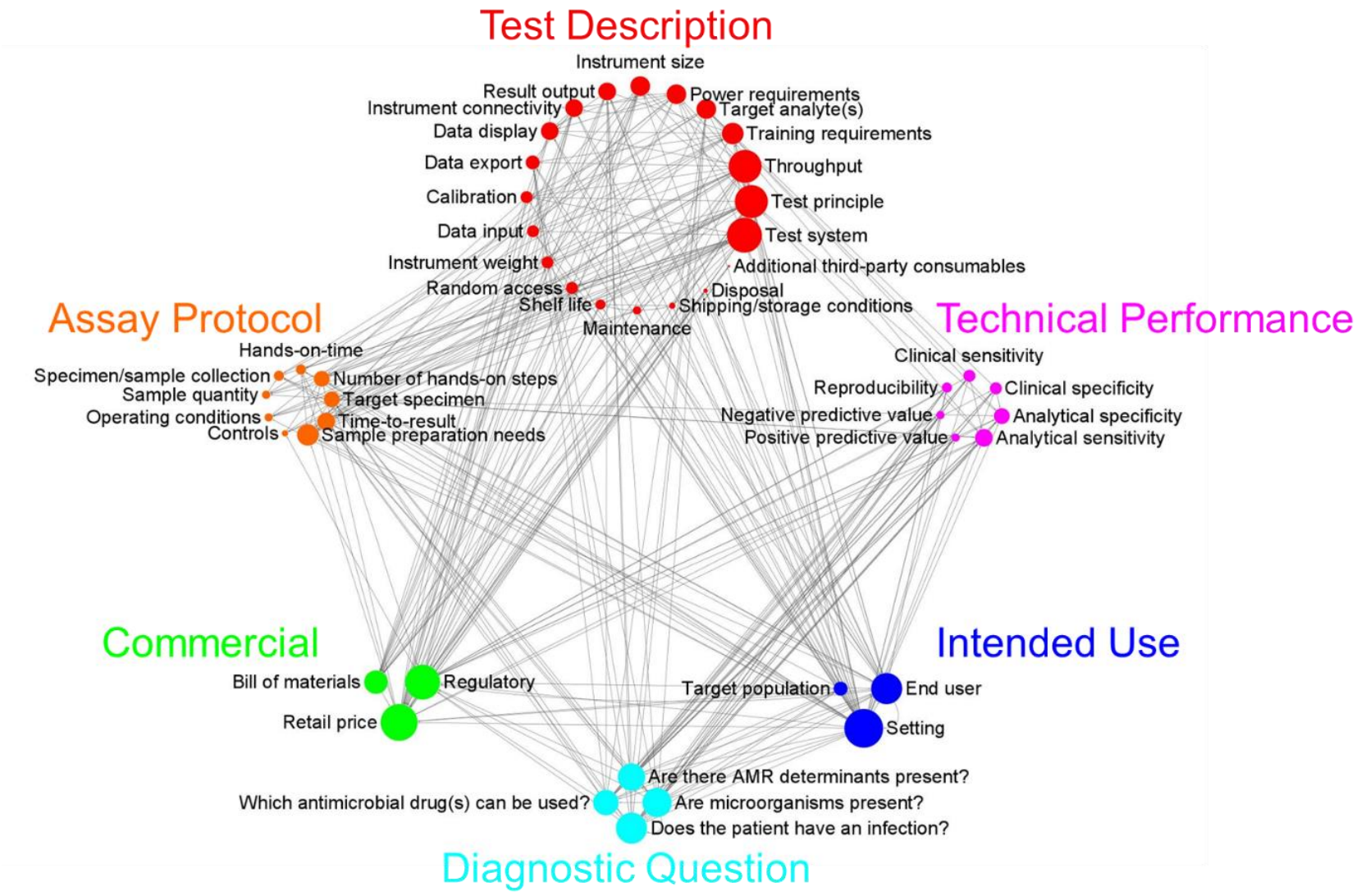
"We need high quality, strong data to tackle AMR and it all starts with diagnostics"

Diagnostics Pipeline Corner

ECCMID 2024 >>> Diagnostic Pipeline Corner 27/04/2024 12:15 -13:15

Target Product Profiles for AMR Diagnostics

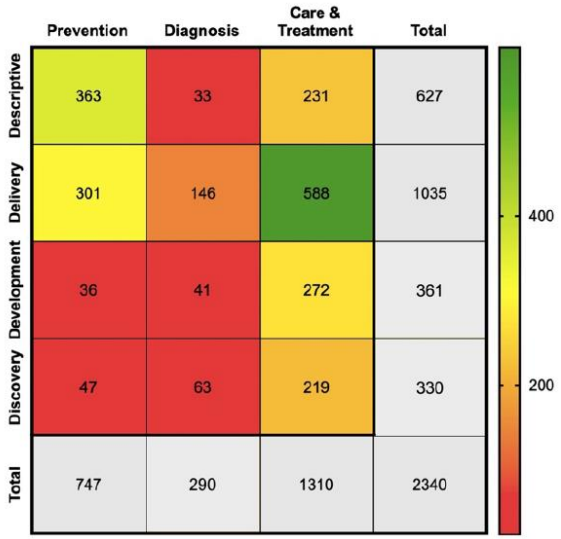
Mind the Interdependencies

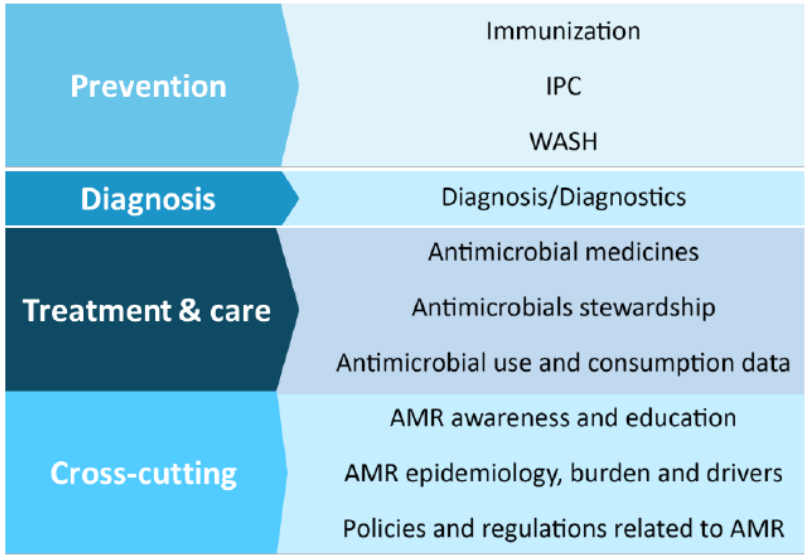


Bachmann TT, Mitsakakis K, Hays JP, van Belkum A, Russom A, Luedke G, Simonsen GS, Abel G, Peter H, Goossens H, Moran-Gilad J, Vila J, Becker K, Moons P, Sampath R, Peeling R, Luz S, van Staa T, Di Gregori V, Expert Guidance on Target Product Profile Development for AMR Diagnostic Tests, BMJ Glob Health. 2023 Dec 18;8(12):e012319. doi: 10.1136/bmjgh-2023-012319

WHO global research agenda for **AMR in human health**

- **Identify and prioritize research topics** to inform health policies and evidence-base interventions in the human health sector
- **Catalyse investment** and scientific interest among scientific community and funders
- Scoping Review → Review and consolidation → Prioritization





World Health Organization

Hamers RL, Dobreva Z, Cassini A, Tamara A, Lazarus G, Asadinia KS, Burzo S, Olaru ID, Dona D, Emdin F, Van Weezenbeek K, Bertagnolio S. Global knowledge gaps on antimicrobial resistance in the human health sector: A scoping review. Int J Infect Dis. 2023 Sep;134:142-149
Hamers RL, Cassini A, Asadinia KS, Bertagnolio S. Developing a priority global research agenda for antimicrobial resistance in the human health sector: protocol for a scoping review. BMJ Open. 2022 Jun 2;12(6):e060553.

WHO global research agenda for AMR in human health - **Diagnostics**

Prevention

1. Investigate the impact and contribution of community WASH and waste management interventions on the burden and drivers of antimicrobial resistance
2. Investigate implementation strategies and the impact of WASH-related interventions in health-care settings on the burden of health care–associated infections and antimicrobial medicine prescribing
3. Identify (cost-) effective, acceptable and feasible multimodal infection prevention and control strategies and the relative effect of their components on reducing health care–associated infections
4. Assess the impact of vaccines on colonization and infection by resistant pathogens, and on reducing the use of antimicrobial medicines, health-care encounters and health system costs

Diagnosis

5. Investigate and evaluate rapid point-of-care tests to discriminate bacterial versus non-bacterial infections
6. Investigate and evaluate rapid antimicrobial susceptibility testing methods from blood cultures
7. Investigate and evaluate diagnostic tests for detecting pathogens and antimicrobial susceptibility testing
8. Investigate and evaluate diagnostic tests for detecting fungal pathogens
9. Investigate the clinical and diagnostic value of phenotypic antifungal susceptibility testing
10. Investigate, assess and evaluate the implementation of novel rapid point-of-care assays and optimal testing approaches for (resistant) *Neisseria gonorrhoeae*

Treatment and Care

11. Investigate antimicrobial stewardship interventions that are context specific, feasible, sustainable, effective and cost-effective in outpatient and inpatient settings
16. Investigate approaches to effectively use antimicrobial consumption and antimicrobial resistance surveillance data to inform stewardship and guidelines

Drug-resistant TB

35. Investigate how the diagnostic performance of molecular assays can be improved to detect drug resistance among people with extrapulmonary and pulmonary TB
36. Determine optimal diagnostic and treatment delivery models to improve the access, effectiveness, cost–effectiveness, feasibility and acceptability of drug-resistant TB treatment

Cross-cutting

24. Investigate factors driving colonization and infection by resistant WHO bacterial priority and fungal pathogens
25. Identify optimal surveillance methods to generate accurate and reliable data on the epidemiology and burden of antimicrobial resistance
28. Determine the most (cost-) effective behavioural change interventions to mitigate antimicrobial resistance emergence and spread
29. Evaluate the implementation of antimicrobial resistance–related policies and regulations and their effectiveness in mitigating antimicrobial resistance and improving health outcomes
30. Investigate implementation strategies for national policies, legislation and regulation to improve infection prevention, patient care and the use of antimicrobial medicines
31. Identify the most (cost-) effective interventions and an investment case to mitigate antimicrobial resistance globally and across countries
32. Investigate strategies to integrate antimicrobial resistance interventions into broader health, health financing, development and welfare structures and evaluate their impact
33. Investigate how regulatory frameworks, marketing incentives and financing models affect the sustainable development, availability, equitable access and use of new antimicrobial medicines

Antimicrobial-resistant bacterial and fungal infections

World Health Organization

Launch of 'Global research agenda for antimicrobial resistance in human health' **22 June 2023**, https://www.who.int/publications/m/item/global-research-agenda-for-antimicrobial-resistance-in-human-health

Diagnosis of **Bacterial Infections**

1. Investigate and evaluate
   - **rapid point-of-care diagnostic tests** (including biomarker-based tests) and diagnostic algorithms to
   - discriminate between **bacterial**, **fungal** and **viral** infections and **non-infectious syndromes**,
   - which are **feasible for use in limited-resource settings** and
   - among different sub-populations (including children and neonates), and
   - to monitor **treatment response***

*Priority for in low-resource settings.

*Tests to tell if **antibiotic treatment is needed** and if the **treatment works** and which can be done **anywhere***

Sample ⇨ ⇨ *Answer*

Disposable

Analytical markers
Time to result
Cost
Storage stability
Operational stability
Training
Manufacturing
Distribution
Regulatory
…

example dosa-diagnostics.org

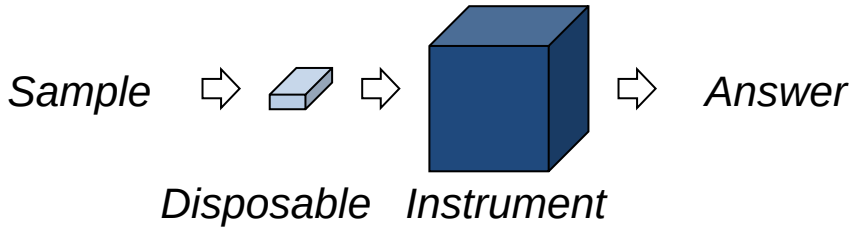
Diagnosis of **Bacterial Infections**

2. Investigate and evaluate
   - **diagnostic tests** for the
   - **isolation, identification, antimicrobial susceptibility testing and/or resistance detection** of
   - bacterial pathogens (including multiplex panel-based tests, and tests utilizing novel technologies) that are
   - **rapid**, **affordable**, **feasible** for use in **resource-limited settings** and among
   - different sub-populations, and from a
   - variety of specimen types*

*Priority for in low-resource settings.

Tests to tell if antibiotic treatment is needed and if so ***which one to use****.*

Increasing *information demand*
Increasing *complexity*
Many *analytical targets*
Evolving *analytical targets*
Increasing *resource demand*

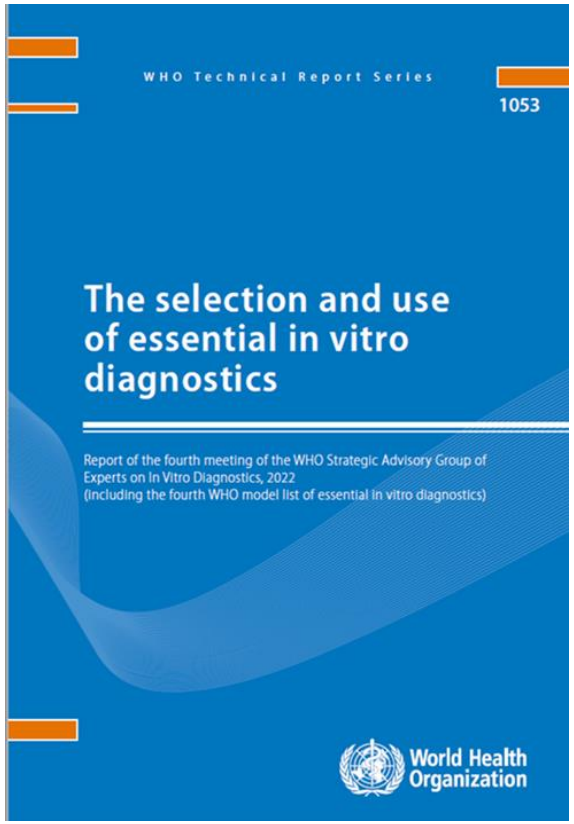


Diagnosis of **Fungal Infections**

4. Investigate and evaluate
   - **rapid, (near) point-of-care diagnostic tests** (including antigen and multiplex panel–based tests) for
   - detecting drug-resistant **WHO fungal priority pathogens** with critical importance for antimicrobial resistance (such as *Candida auris*, *Aspergillus fumigatus* and *Cryptococcus neoformans*)
   - feasible for use in **limited-resource settings** and among different subpopulations.

5. Investigate and evaluate the
   - the **clinical utility and diagnostic accuracy** of
   - **phenotypic antifungal susceptibility testing** (including determining minimal inhibitory concentration breakpoints and testing for in vitro and in vivo synergy between antifungal medicines) and
   - their **impact on clinical outcomes**.

WHO **Essential Diagnostics List** (EDL)



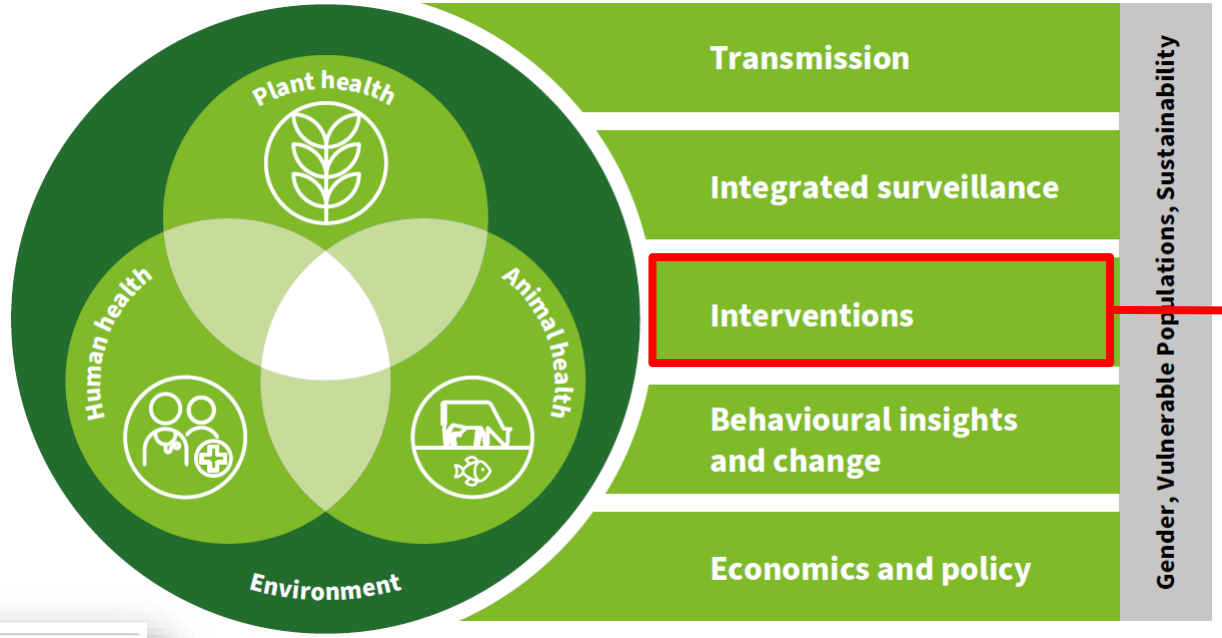
- List of categories of IVD tests
- Recommendations on assay format, test purpose, specimen type and health-care setting
- EDL version 4 - October 2023

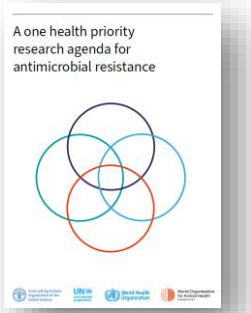
- Bacteriological/mycological tests in settings without laboratories
  - Urinalysis test strips
  - *Vibrio cholerae* antigen (RDT)
  - Cryptococcal antigen (RDT)
  - Group A *Streptococcus* antigen (RDT)
  - Antibodies to *Treponema pallidum* (RDT)

- Bacteriological/mycological test in settings with laboratories
  - Staining/microscopy
  - Urine body fluid microscopy
  - Culture, blood culture
  - Antimicrobial susceptibility testing
  - CT/NT NAT
  - *T. pallidum*
  - *Pneumocystis pneumonia* NAT

https://www.who.int/news/item/19-10-2023-who-releases-new-list-of-essential-diagnostics--new-recommendations-for-hepatitis-e-virus-tests--personal-use-glucose-meters
https://www.who.int/news-room/articles-detail/survey-bacteriology-and-mycology-tests

One Health Priority Research Agenda for Antimicrobial Resistance





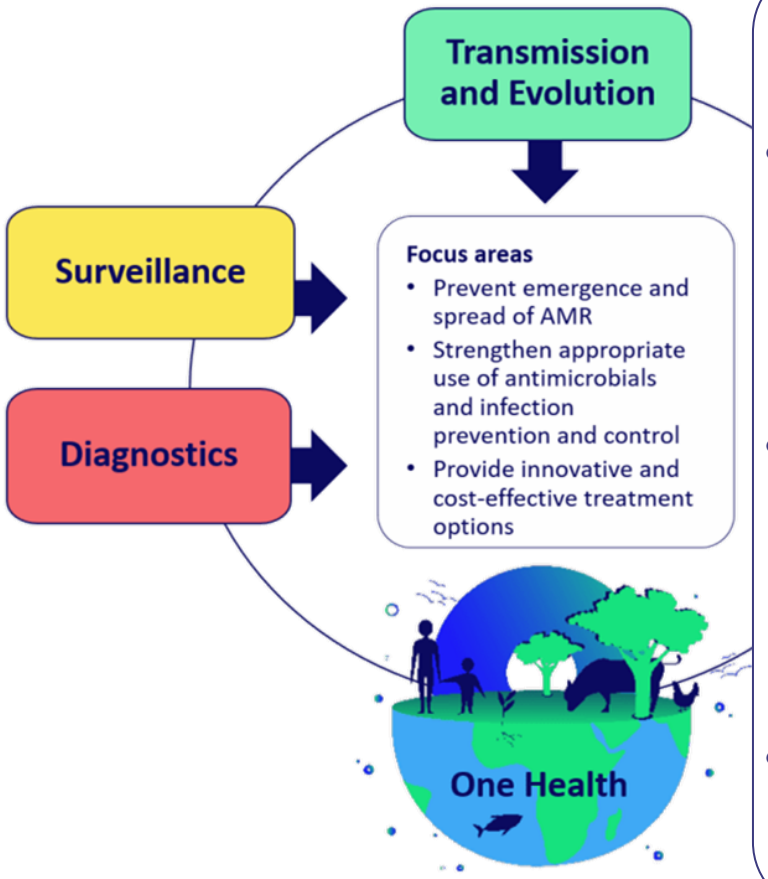
Launched 28 June 2023
https://www.who.int/publications/i/item/9789240075924

Methodology development	How can **research capacity** in LMICs be strengthened to catalyse locally tailored collaboration and cooperation between One Health-related sectors?
	What criteria should be used to **assess interventions** that aim to prevent and control AMR at the One Health interface?
	What **mix of evidence** and evaluation is needed to understand how to implement One Health AMR solutions most effectively in LMICs?
Operational research	How can One Health interventions that have proven impactful for AMR control and mitigation most effectively be **translated and scaled up in different contexts** or differently resourced settings?
	What are the minimal resource interventions required for supporting national integrated, multisectoral One Health AMR/AMU **surveillance** systems?
Evaluation	What challenges exist to the **systematic collection** and analysis of data for risk assessment and intervention impact assessment (epidemiological, economic, social, including equity) in LMICs?
	What have been the **most impactful interventions** to prevent, control and mitigate AMR at the One Health interface?
Framework conditions	How can we **improve early adaptation and innovation** for the prevention, control and mitigation of AMR across human health, animal health, plant health and the environment in LMICs?

The Horizon Europe Candidate Partnership: **One Health AMR**

Strategic Research and Innovation Agenda & Draft Roadmap of Actions

- Discover, design, and evaluate **new diagnostics** and improve the uptake and effectiveness of existing ones
- **Evaluate field performance**, feasibility, and impact of diagnostics
- Identify and overcome **barriers to implementation**, acceptance, uptake, and use of diagnostics



Objectives

- 1. To improve understanding of the mechanisms and drivers responsible for the emergence and spread of AMR
  2. To design or identify cost-effective social and **technical interventions** aiming to prevent the emergence and spread of AMR

- 1. To understand the behavioural and social/societal factors driving overuse and misuse of antimicrobials in humans, animals, and plants
  2. To develop or identify cost-effective technical innovations, including **diagnostics**, and social/ societal innovations aiming to a more prudent use of antimicrobials in humans, animals, and plants
  3. To develop or identify **cost-effective technical tools** or social/societal interventions aiming to improved prevention of the infectious diseases in humans, animals, and plants

- 1. To improve the current treatment strategies (increased efficiency, decreased risk to develop secondary resistance) and understand the barriers to access to therapeutic solutions
  2. To develop new antimicrobials, novel treatment protocols or alternative treatment therapies along with their respective **diagnostics**

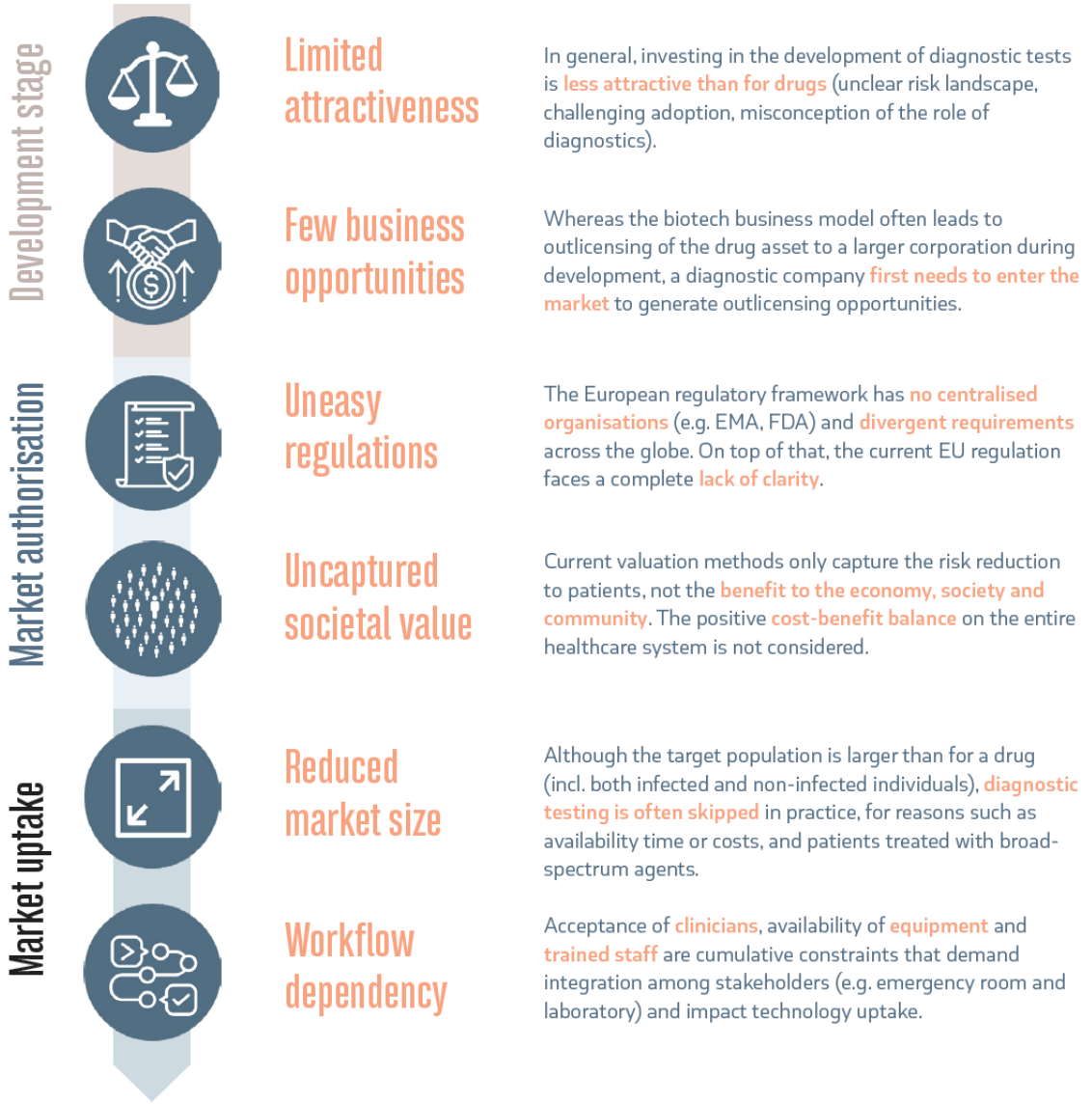
jpiamr DESIGN OH AMR

https://www.jpiamr.eu/activities/one-health-amr/design-oh-amr/
https://www.jpiamr.eu/activities/one-health-amr/

BEAM Alliance Task Force Diagnostics

Three main goals:

1. To **list the gaps** and needs in developing and marketing AMR-focused diagnostic solutions
2. To define a **common narrative** to be used in awareness raising campaigns.
3. To present and discuss implementable **solutions** with policy makers.



https://beam-alliance.eu/beam-alliance-is-launching-a-new-task-force-to-address-issues-from-the-amr-diagnostics-segment/

Many **Thanks** & **Take Home** for the London Declaration

Diagnostics for infectious diseases and AMR

- save lives
- save money
- save future drugs