Approches diagnostiques innovantes et accès au marché

Innovating Diagnostic Approaches and Market Acess

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Open Innovation & Partnerships Dpt

PIONEERING DIAGNOSTICS

When we think about product access to the market, we focus on these 2 steps…

Diagnostic Evidence Continuum

Analytical Validity → **Clinical Validity**

Does the test accurately measure what it claims to measure?

- Precision, reproducibility, replicability
- Accuracy
- Analytical sensitivity, specificity

Does the test accurately identify or predict a clinical status?

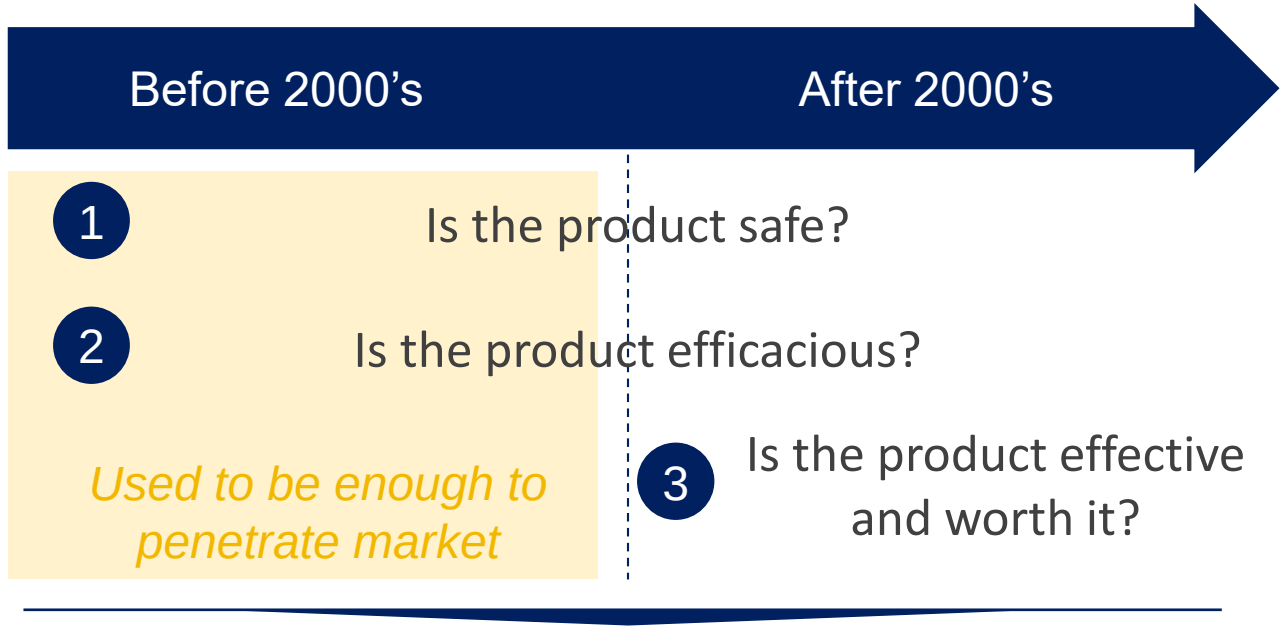
- Clinical sensitivity, specificity
- Negative predictive value (NPV), positive predictive value (PPV)

Required for Regulatory Approval

Source: Health Advances for bioMérieux

… But safety, efficacy, clinical value are no longer enough to ensure market penetration of innovative products

Key questions to be answered to penetrate market

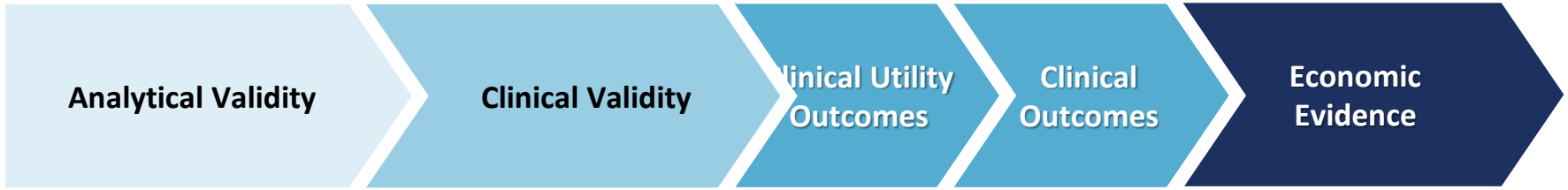


Market access is then all about **demonstrating** and **communicating** product **medical and economic value** to the **health system**

Source: Health Advances for bioMérieux

As a result, much more evidence is needed for market adoption compared to regulatory approval

Diagnostic Evidence Continuum



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Does the test alter patient management and improve outcomes?

- Physician decision-making impact analysis
- Clinical outcomes through observational or prospective randomized controlled trials

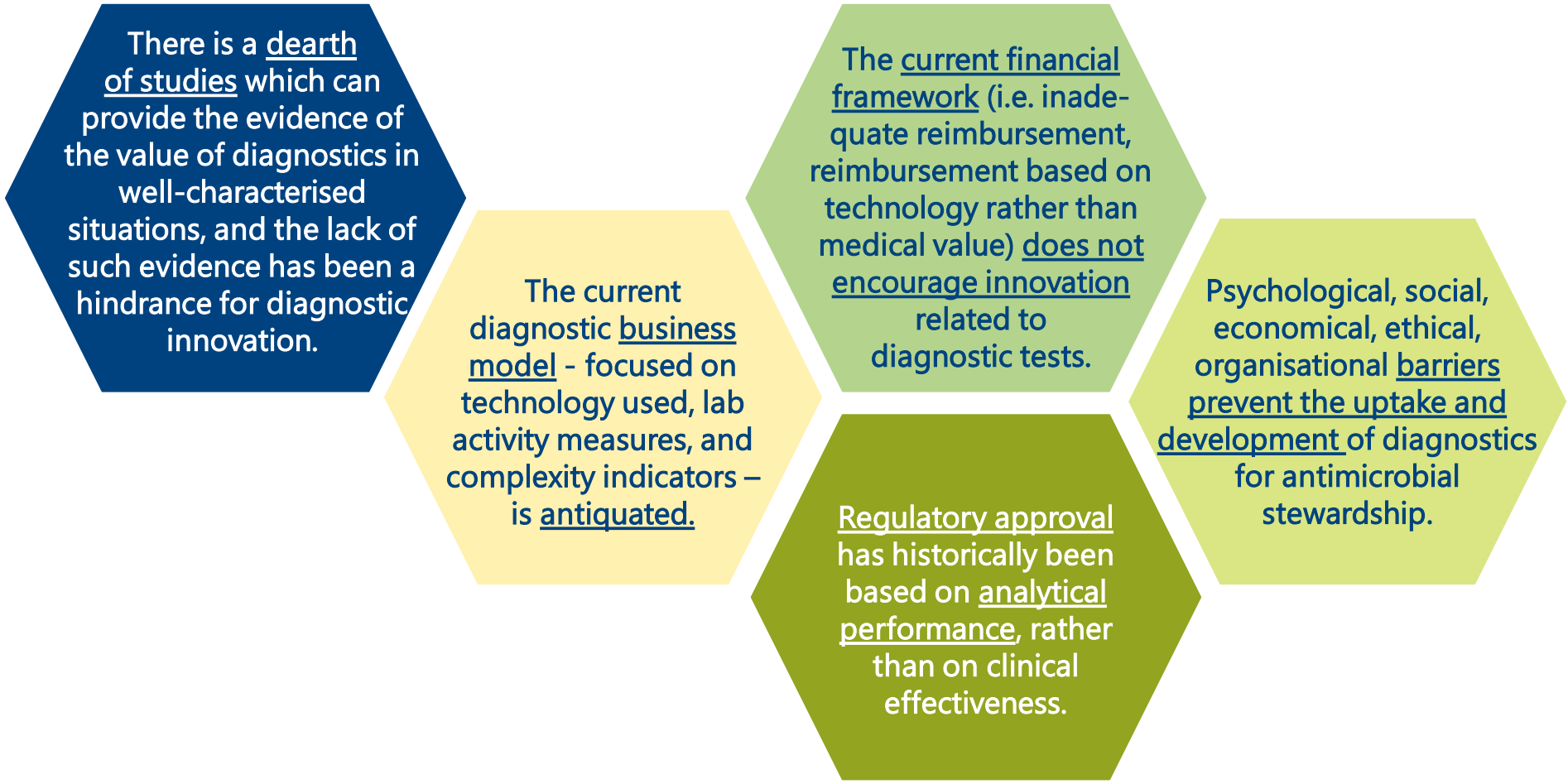
Does the test provide acceptable value or save money?

- Cost-effectiveness analysis
- Budget impact modeling and analyses

Required for Regulatory Approval | **Required for Market Adoption**

Source: Health Advances for bioMérieux

Challenges of diagnostics



VALUE-Dx :

Pioneering Public-Private Partnerships to quantify the value Diagnostic

(and combat Anti-Microbial Resistance by optimising antibiotic use)

The VALUE-Dx Consortium

Vision & purpose of VALUE-Dx project

The **vision** is to transform clinical practice, improve patient outcomes, and combat AMR, through the widespread use of clinical and cost-effective innovative diagnostics strategies to achieve more personalised, evidence-based antibiotic prescription and use in community care settings.

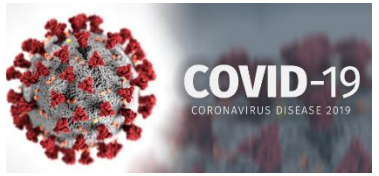
The **purpose** is to facilitate and accelerate the rigorous assessment and implementation of (new) diagnostic technologies into healthcare settings, by establishing the infrastructure, methods, processes and approaches needed to understand, evaluate, assess, and demonstrate the multi-faceted value of diagnostics and overcome the associated barriers to their widespread adoption and use.

The **focus** is on realising its vision and purpose on community-acquired acute respiratory tract infections (CA-ARTI).

Therefore, VALUE-Dx will focus on diagnostic strategies relevant to reducing AMR in CA-ARTI in community care settings, referred to as “CA-ARTI-Dx”

Case Study : Community-Acquired Acute Respiratory Tract Infections (CA-ARTI)

- CA-ARTI has an important incidence / public health impact
- Overprescribing of antibiotics is mostly flagrant (~ 50% inappropriate / unecessary)
- Various parameters can be measured to demonstrate impact of IVD
  - ❑ Dose, # days of antibiotic prescribed to patient
  - ❑ Proportion of patients NOT receiving antibiotics
  - ❑ Development of antibiotic resistant colonization
  - ❑ Pathogen mutation
  - ❑ Patient outcome
  - ❑ Health care-associated costs.
  - ❑ …



Objectives of VALUE-Dx

Helping to build the economic case for rapid diagnostics as a public good in the fight against AMR

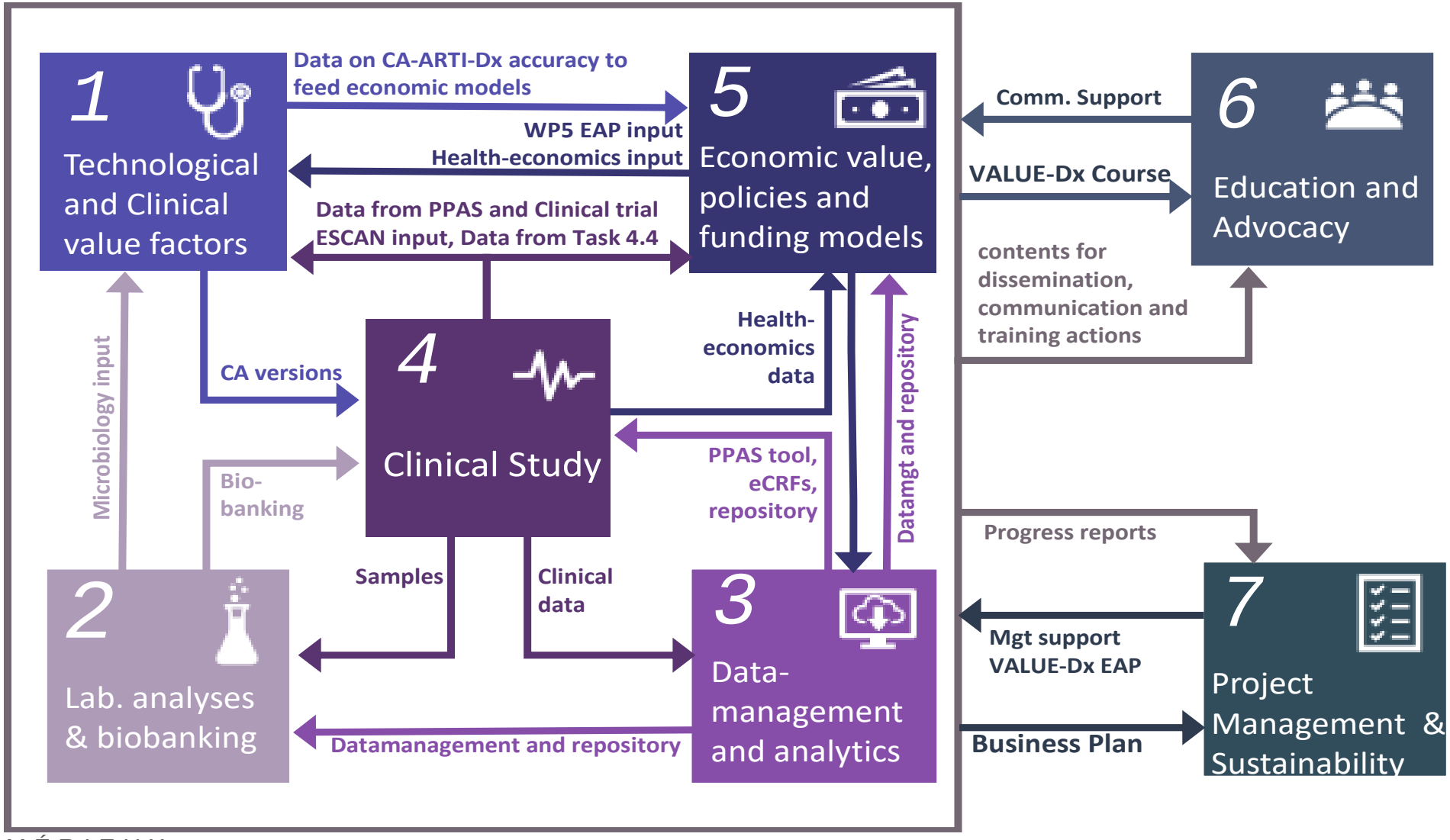
1. To **design a health-economic framework (HEF)** to assess and demonstrate the value of diagnostics both for individual patients and for public health impact by reducing antibiotic use and subsequent antibiotic resistance among patients.

2. To **establish a sustainable European Standardised Care Network** adequately trained and resourced to conduct clinical trials evaluating the value of diagnostics.

3. To **design and implement clinical studies to demonstrate the value of diagnostics** in the optimal management of Community-Acquired Acute Respiratory Tract Infections (CA-ARTIs)

4. To **explore, define and attempt to resolve the psychological, ethical and social barriers** which prevent the more widespread adoption of diagnostics delivering healthcare to the population.

Project structure and interactions

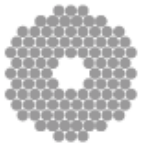


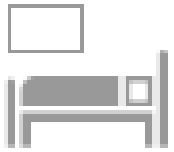
Community care settings

- Defined as the first point of contact with health services.
- This includes both in and out of office hours care.
- **Settings**: general practice, urgent care centres, accident and emergency rooms and other acute services in hospitals, paediatric care centres, and rehabilitation and long-term care facilities.

Syndromic Testing

Syndromic testing is a symptom-driven broad grouping of probable pathogens into one, rapid test that **maximizes the chance of getting the right answer in a clinically relevant timeframe**

One sample  > One comprehensive test  > 1 h for results  > Multiple results in one report 

Better patient management 

Provide more timely and effective treatment
Limit the use of unnecessary antibiotics
Prevent secondary spread of infection
Reduce costs of unnecessary tests
Shorten hospital stays

Diagnostic Intervention in Emergency Department

1. **BioFire FilmArray Pneumonia Panel plus** (PP): Sputum (and/or ETA or BAL sample)

2. **BioFire FilmArray Respiratory Panel 2.1. plus** (RP2.1 plus): Nasopharyngeal swab

BIOFIRE®
FILMARRAY® Torch

Respiratory Panel 2.1*plus* (RP2.1*plus*)

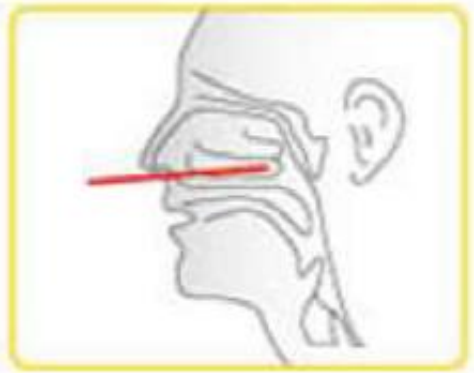
Viruses

- Adenovirus
- Coronavirus 229E
- Coronavirus HKU1
- Coronavirus OC43
- Coronavirus NL63
- **Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)**
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Human Metapneumovirus
- Human Rhinovirus/ Enterovirus
- Influenza A
- Influenza A/H1
- Influenza A/H1-2009
- Influenza A/H3
- Influenza B
- Parainfluenza 1
- Parainfluenza 2
- Parainfluenza 3
- Parainfluenza 4
- RSV

Bacteria

- *Bordetella parapertussis* (IS*1001*)
- *Bordetella pertussis (ptxP)*
- *Chlamydia pneumoniae*
- *Mycoplasma pneumoniae*

23 targets
~45 min



Nasopharyngeal swab

Overall: 97.1% Sensitivity | 99.3% Specificity[a]
SARS-CoV-2: 98.4% PPA | 98.9% NPA[b]

CE mark (IVDD)
July 2020

FDA De Novo granted

Pneumonia panel *plus* - 34 targets

In One Hour

Bacteria

15 Common Bacteria with "binned" results

Semi - Quantitative

- *Acinetobacter calcoaceticus-baumannii* complex
- *Serratia marcescens*
- *Proteus* spp.
- *Klebsiella pneumoniae* group
- *Enterobacter aerogenes*
- *Enterobacter cloacae*
- *Escherichia coli*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Klebsiella oxytoca*
- *Streptococcus pyogenes*
- *Streptococcus agalactiae*

Atypical Bacteria

Qualitative

- *Legionella pneumophila*
- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*

3 Qualitative Bacteria that cause Atypical Pneumonia

Viruses

Qualitative

- Influenza A
- Influenza B
- Adenovirus
- Coronavirus
- Parainfluenza virus
- Respiratory Syncytial virus
- Human Rhinovirus/Enterovirus
- Human Metapneumovirus
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

9 Viruses
- **Same as in RP2*plus***
- **No Sub-typing**

Antibiotic Resistance Genes

7 antimicrobial resistance markers

Methicilin Resistance

- *mecA*/*mecC* and MREJ

ESBL

- CTX-M

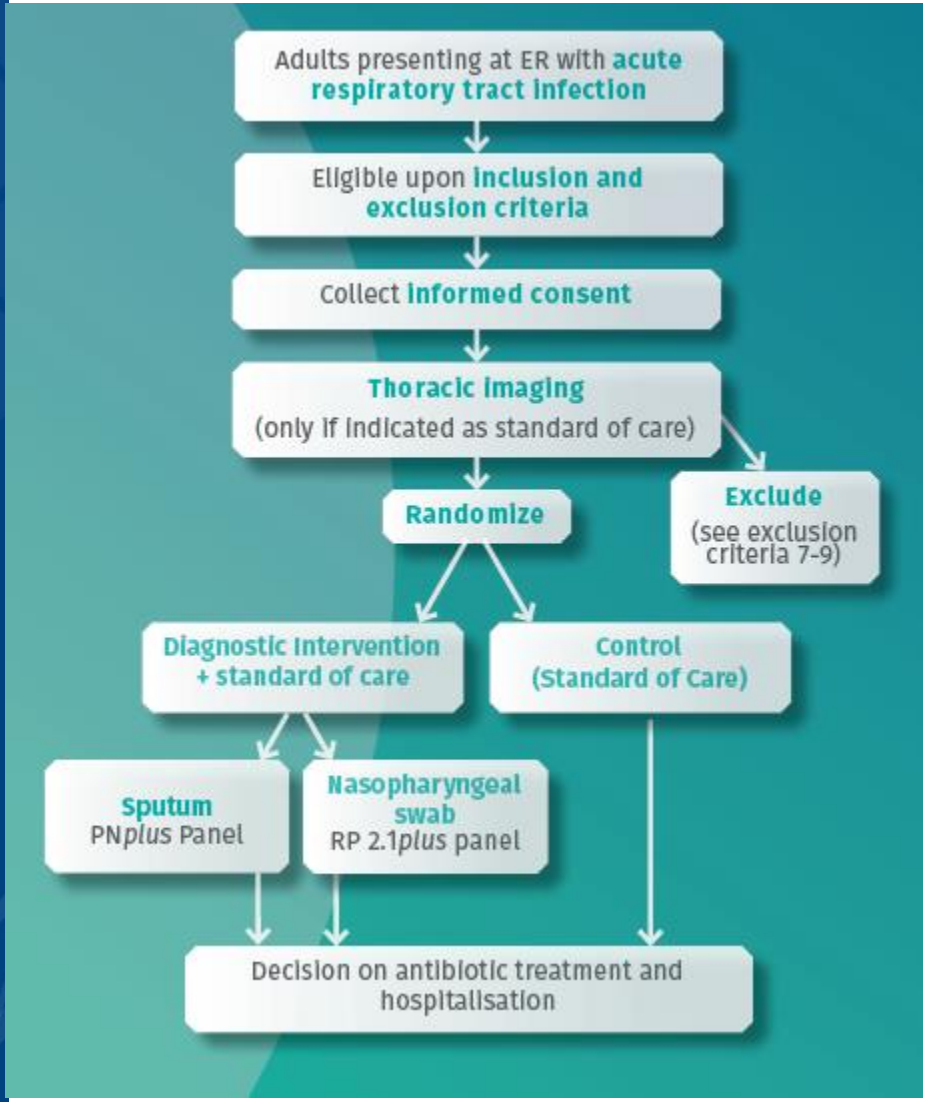
Carbapenemases

- KPC
- NDM
- Oxa48-like
- VIM
- IMP

SAMPLE TYPE

- **Sputum-like**
- **BAL-like**

ADEQUATE – Advanced Diagnostics for Enhanced QUality of Antibiotic prescription in respiratory Tract infections in Emergency rooms



Objective: assess the impact of rapid syndromic testing in patients presenting with CA-ARTI in the ER on:

1. days in hospital within 14 days after study enrolment
2. days with antibiotic therapy within 14 days after study enrolment
3. occurrence of adverse outcome within 30 days after study enrolment

Co-primary endpoints:

1. Days alive out of hospital (superiority endpoint), within 14 days
2. Days on Therapy with antibiotics (superiority endpoint), within 14 days
3. Adverse outcome (non-inferiority safety endpoint)

- For initially non-admitted patients: any admission or death within 30 days

- For initially hospitalized patients:

  - i) any readmission
  - ii) ICU admission >= 24 hours after hospitalization, or
  - iii) death, all within 30 days

VALUE-Dx

https://value-dx.eu/

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www.imi.europa.eu

www.value-dx.eu

A few take-home messages…

- Analytical performance is non longer enough for product commercialization
- Registration of (innovative) products requires extensive studies to demonstrate its medical value
- Market adoption also relies on economical value assessment in a wide frame that takes into acount extensive parameters including Quality of Life
- Pan-European / across-countries approaches are key to accelerate product adoption (and public health impact especially for communicable diseases)
- Clinical networks / cross-sectorial collaboration are key to demonstrate the important value of diagnostics (information) in the continuum of healthcare.
- Patient-centric initiatives with PROMs and PREMs are essential
- Health Economic and Outcome Research is a growing disciplin of utmost importance

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