18|11|2022

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# Deliverable 5.4: Recommendations for innovative fit for purpose pricing and funding models for CA-ARTI diagnostics

VALUE-Dx

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 820755. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and bioMérieux SA, Janssen Pharmaceutica NV, Accelerate Diagnostics S.L., Abbott, Bio-Rad Laboratories, BD Switzerland Sàrl, and The Wellcome Trust Limited.



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## Abbreviations

| | |
|---|---|
| AMR | Antimicrobial resistance |
| BIZNES | Warsaw University of Technology Business School |
| CA-ARTI | Community-acquired acute respiratory tract infection |
| CE | Conformité Européenne |
| CED | Coverage with Evidence Development |
| CEPS | Comité Economique des Produits de Santé (Health Products Pricing Committee), France |
| CRP | C-reactive protein |
| DRG | Diagnosis-Related Groups |
| Dx | Diagnostic(s) |
| EAP | Expert Advisory Panel |
| EHIF | Eesti Haigekassa (Estonian Health Insurance Fund) |
| EU | European Union |
| EUnetHTA | European Network for Health Technology Assessment |
| GBP | Great Britain Pound |
| GDP | Gross domestic product |
| GÖG | Gesundheit Österreich GmbH (Austrian National Public Health Institute) |
| GP | General Practitioner |
| H2020 | Horizon 2020 |
| HAS | Haute Autorité de Santé |
| HIQA | Health Information and Quality Authority |
| HTA | Health Technology Assessment(s) |
| IMI | Innovative Medicines Initiative |
| IVD | In Vitro Diagnostics |
| JAMRAI | Joint Action on Antimicrobial Resistance and Healthcare-Associated Infection |
| JPA | Joint Procurement Agreement |
| LRTI | Lower respiratory tract infections |
| MD | Medical device(s) |
| MEAT | Most Economically Advantageous Tender |
| NHS | National Health Service |
| NICE | National Institute for Health and Clinical Excellence |
| NPV | Negative Predictive Value |
| ÖGK | Österreichische Gesundheitskasse (Austrian Social Health Insurance Fund) |
| OHE | Office of Health Economics |
| PCR | Polymerase chain reaction |
| POCT | Point-of-care (diagnostic) test(s) |
| PPP | Purchasing power parities |
| PPV | Positive Predictive Value |
| PPRI MD | Pharmaceutical Pricing and Reimbursement Information Sub-group on Medical Devices |

| | |
|---|---|
| PPRI | Pharmaceutical Pricing and Reimbursement Information (network of competent authorities responsible for pricing and reimbursement of medicines) |
| QALYs | Quality-Adjusted Life-Years |
| R | Recommendation(s) |
| R&D | Research and Development |
| REA | Relative Effectiveness Assessment |
| RTI | Respiratory tract infections |
| RWD | Real-World Data |
| RWE | Real-World Evidence |
| SHI | Social Health Insurance |
| STRAMA | Swedish strategic programme against antibiotic resistance |
| TEV | Transferable Exclusivity Vouchers |
| TLV | Tandvårds- och läkemedelsförmånsverket (Dental and Pharmaceutical Benefits Agency), Sweden |
| URTI | Upper respiratory tract infections |
| US | United States |
| USD | United States Dollar |
| VODI | Value of Diagnostic Information |
| WHO | World Health Organization |
| WP | Work Package |

## List of country abbreviations

| | |
|---|---|
| AT | Austria |
| BE | Belgium |
| CH | Switzerland |
| DE | Germany |
| EE | Estonia |
| FR | France |
| HU | Hungary |
| NL | Netherlands |
| NO | Norway |
| PL | Poland |
| SE | Sweden |
| UK | United Kingdom |

# Executive summary

Antimicrobial resistance (**AMR**) is a global public health threat which is the cause of numerous deaths and medical complications. One major driver for AMR is the inappropriate use of antibiotics, such as **in** the treatment of **community-acquired acute respiratory tract infections (CA-ARTI)**.

Several measures, including AMR stewardship programs and incentives for research of novel antibiotics, have been discussed and implemented to address AMR. One important tool to tackle AMR is diagnostic testing, e.g., rapid **point-of-care tests (POCT)** applied in primary health care, such as in the practices of general practitioners, to identify if the infection is caused by a virus or a bacteria, and consequently to determine whether or not prescribing of an antibiotic is justified and needed.

The European VALUE-Dx project under the "Innovative Medicines Initiative" (IMI) framework, aims to foster the use of diagnostic tests to improve the quality of antibiotic prescribing. Its Work Package 5 (**Economic Value, Policies and Innovative Funding Models**) is aimed to **demonstrate the value of diagnostic tests** which support doctors in their prescribing decisions related to antibiotics.

Previous research and practice have identified a potential to encourage uptake of CA-ARTI POCT (point-of-care tests in community-acquired acute respiratory tract infections) and suggested possible barriers related to existing pricing and funding policies applied for these diagnostics (e.g., high prices of POCT compared to antibiotics). However, little evidence was available as to which policies in the so-called **peri-launch phase** (i.e., between the CE mark certification and placing the diagnostic on the market) have been implemented for POCT in European countries, and what their possible implications might be.

In the VALUE-Dx project, the authors shed light into this under-researched area and explore how peri-launch policies can contribute to appropriate use of CA-ARTI POCT with a view to optimising antibiotic prescribing and thus reducing AMR. **This document presents recommendations for policy action related to HTA, pricing and procurement, and funding, to facilitate the outpatient use of CA-ARTI POCT.**

The development of the recommendations was based on previous work, including a literature search and a mapping exercise of existing HTA, pricing and reimbursement policies applied for medical devices in general and for diagnostic tests in the outpatient sector in 17 European countries (cross-country comparative findings are presented in a separate VALUE-Dx technical report and a scientific article). In addition, expert interviews were conducted to identify factors with facilitating or hindering impact with regard to the uptake of diagnostics. The barriers and facilitators were analysed in the context of the health system and country setting and formed the basis for the development of fit for purpose policy recommendations with the potential to improve CA-ARTI POCT uptake. In addition to the involvement of experts from national public authorities when collecting the evidence base for the development of the recommendations, a broad review process was carried out to consider the perspectives of relevant stakeholders (e.g., policy-makers, which are the target group of the recommendations, or CA-ARTI POCT suppliers), including their assessment of feasibility of the measures. The review process included expert meetings to present and discuss the recommendations.

A total of fifteen recommendations targeted at policy-makers are proposed; ten of them have been clustered in the policy areas of HTA, pricing and procurement, and funding. Five additional recommendations refer to overarching aspects that are conducive to the successful implementation of peri-launch policies.

In the following, the peri-launch policies are briefly described separated by area addressed:

**Health Technology Assessment (HTA)**

- HTA helps to **strengthen the quality of** the **decisions** that public authorities take on the price of a health technology (e.g., a CA-ARTI POCT), and/or on their inclusion into reimbursement, as HTA supports decision-making through the generation and appraisal of evidence. However, in Europe, HTA is **rarely used** as an integral part of pricing and funding decisions on CA-ARTI POCT. This may partially be attributable to a missing pricing and funding policy framework for these diagnostics, since prices of CA-ARTI POCT are not regulated by the authorities (but freely set by the suppliers), and these POCT are not reimbursed on a product basis. Thus, as also interviews suggested, public authorities may not see a need for a systematic use of HTA in decision-making. In addition, some methodological limitations exist, as a rapid Relative Effectiveness Assessment (REA) limited to a few core domains may not fully **capture the specific character of CA-ARTI POCT** (e.g., in their inter-play with antibiotic prescribing).
- Two of the three recommendations proposed in the area of HTA focus on **methodological standards**: when HTA is conducted, it should be based **on existing methodological tools** (e.g., standards developed in EUnetHTA), thus benefiting from **previous work, harmonisation and cross-country collaboration**. Further developments may be necessary to operationalise the HTA methodology to consider appropriately the specificities of CA-ARTI POCT, such as their possible **societal value in tackling AMR**. In addition to methodological advances, one recommendation reminds policy-makers to work towards the **systematic use of HTA**, including regular re-assessments, in particular when new relevant evidence is available and decisions are made on the public funding of CA-ARTI POCT, and their price.

**Funding: reimbursement and remuneration**

- In several European countries CA-ARTI POCT are not included in a positive list which would ensure their reimbursement, but **health professionals** are **remunerated for their application**. In European countries the decision base for tariffs to remunerate GPs for the application of CA-ARTI it is not always clear. It is neither comprehensible nor transparent whether and how these tariffs are adjusted over the years. This may be due to a lack of data on benefits and costs of the POCT. Moreover, a **calculation of the tariff** that is only based on the price of the CA-ARTI POCT and does not consider further cost components related to the use of the test in a doctor's practice could be a possible barrier.
- Two of the four recommendations on funding relate to the possible changes in the design of the remuneration for outpatient doctors. One proposes a **more evidence-based design of the tariffs**, which, however, would also consider further cost components for the service of the CA-ARTI POCT beyond the price. Another recommendation invites policy-makers to explore whether or not it would be possible to **link remuneration of the doctors for antibiotic prescribing to a previous application of the POCT** in line with defined treatment guidelines. Should doctors prescribe an antibiotic without using the diagnostic recommended by the guidelines, they would not be remunerated for prescribing the antibiotic. Doctors might find this measure rather harsh, thus it would need to be well-communicated to them. However, this policy measure may not be feasible in some health care settings as it requires linking funding mechanisms for medicines (i.e., antibiotics) and devices (the tests conducted as a prerequisite). **Conditional funding** is also foreseen in a recommendation that suggests possible use of managed-entry agreements (in the form of Coverage with Evidence Development, CED) which would link (full) funding for suppliers

to data generation. One recommendation encourages policy-makers in countries with no device-specific reimbursement to explore a change in the funding system and introduce product-specific reimbursement for CA-ARTI POCT.

**Pricing and procurement**

- Suppliers of CA-ARTI POCT can freely set the price (so-called "free pricing"). There is **no price regulation for CA-ARTI POCT** apart from indirect price control by public authorities, when they act as purchasers in public procurement processes. There might be **potential to optimise procurement processes**.
- In response to concerns about prices of CA-ARTI POCT which tend to be higher compared to antibiotics, policy-makers are recommended to explore the **introduction of price regulation** for CA-ARTI POCT, at least for those POCT that are funded by public payers (e.g., in connection with product-specific reimbursement). This would allow the setting of prices at affordable levels, and, if linked with public funding, ensure predictability in sales for suppliers. Predictability to suppliers is also offered through **novel, subscription-based procurement models**, which would de-link prices from rewards for suppliers: a defined volume at a fixed price would be agreed between procurers and suppliers. Lastly, **public procurement** of CA-ARTI POCT could be **optimised by** applying more **strategic approaches**. This would include further award criteria in addition to price, multiple winners awarding contracts, pooling of expertise and volumes of procurers at national or cross-national levels and including conditionalities (e.g., regarding security of supply) into contracts.

**Overarching recommendations**

The proposed policy measures relating to HTA, funding, and pricing and procurement are accompanied by five **overarching recommendations of supportive action** relevant for most policy recommendations. They stress the importance of **communication and stakeholder involvement**, **collaborative approaches** (also across countries), and **monitoring and evaluation** as essential components of policy implementation. Furthermore, it is made clear that **policy action is inter-linked**. To achieve the intended policy objective (i.e., uptake of CA-ARTI POCT to improve quality of antibiotic prescribing), **a range of measures are needed** (from the peri-launch phase, as well as the pre-launch and post-launch phases, which were not scope of this assignment). The recommended policy measures should ideally be implemented in alignment and combination with other measures. Finally, the authors acknowledge that the feasibility of the implementation of policy measures is context-specific and varies across countries and settings.

# List of recommendations

| Policy area | RECOMMENDATIONS | |
|---|---|---|
| | In brief | Wording as proposed |
| Health technology assessment (HTA) | **R1: Enhance the harmonisation of HTA methodology for CA-ARTI POCT based on established guidance** | It is recommended to work on a harmonisation of standards for conducting HTA for POCT, including clear reporting criteria for outcomes related to effectiveness, accuracy, and other domains relevant for CA-ARTI POCT. Actions should be based on established guidance, e.g., from EUnetHTA, and aligned with needs of HTA bodies and health policy-makers. An important accompanying action is the communication of the standards, including data needs for conducting the HTA (e.g., through early scientific advice). |
| | **R2: Consider appropriately the value of POCT as tool to combat AMR** | In the further development of the HTA methodology, it is recommended to consider the contribution that CA-ARTI POCT can make as a tool to improve quality of antibiotic prescribing (personalised medicine). Methodology may be advanced to also reflect the societal value of these diagnostics in addressing AMR. |
| | **R3: Systemic use of HTA, including regular re-assessments** | It is recommended to systematically base pricing and funding decisions on HTA and conduct regular re-assessments (updated HTA) when relevant new data are available. |
| Funding | **R4: Align doctors' remuneration for use of CA-ARTI POCT to consider relevant costs** | It is recommended to explore applying a more comprehensive tariff approach for doctors which considers remuneration of further cost components that, in addition to the price of a CA-ARTI POCT, incur for their use in an outpatient physician practice. |
| | **R5: Consider linking doctors' remuneration for antibiotic prescribing to use of CA-ARTI POCT** | It is recommended to explore an adjustment of the tariff scheme for outpatient doctors, by linking their remuneration for the antibiotic prescription to preceding use of a CA-ARTI POCT in defined cases according to guidelines. |
| | **R6: Managed entry agreements with continuous data generation** | It is recommended to explore use of managed entry agreements (MEAs) with to link funding of the CA-ARTI POCT to continuous data generation (e.g., Coverage with Evidence Development, CED) under well-defined conditions. |
| | **R7: Product-specific reimbursement** | It is recommended to consider the implementation of product-specific reimbursement for CA-ARTI POCT as an incentive for their uptake. For this policy option, an appropriate policy framework needs to be in place, which includes transparent and clear reimbursement criteria and decision processes regarding the inclusion into reimbursement, and re-assessments. |

| Policy area | RECOMMENDATIONS | |
|---|---|---|
| | In brief | Wording as proposed |
| Pricing and procurement | **R8: Price regulation to achieve affordable prices** | It is recommended to explore introduction of price regulation, to make CA-ARTI POCT more affordable and competitive. |
| | **R9: Subscription-based procurement models ("Netflix" models)** | It is recommended to explore innovative procurement policies, including subscription-based procurement models, with defined volumes that are independent from per unit prices. |
| | **R10: Strategic procurement** | It is recommended to adopt a strategic approach to procurement which aligns preparation, launch of calls, assessment, and award of bids to defined objectives. Moving towards more strategic procurement includes to explore increased use of additional award criteria beyond the price, pooled procurement, market research, tenders awarded to multiple bidders and strategies to mitigate possible shortages. |
| Overarching | **R11: Holistic approach to implement a toolbox of measures** | It is recommended to adopt a holistic approach to pricing and funding policies for CA-ARTI POCT. In addition to the proposed measures in the peri-launch phase, there is a need for policy actions, including accompanying measures, along the whole value chain. |
| | **R12: Communication and stakeholder involvement** | It is recommended to accompany the recommended measures with appropriate communication activities at relevant stakeholders, including the public, and to involve stakeholders, where appropriate, to ensure acceptance and support of the measures as far as possible. |
| | **R13: Cross-country collaboration** | While funding, pricing and procurement are national competences of EU Member States, it is recommended to explore collaborative approaches across countries in terms of methodology development, sharing of data and exchange of policy experience. |
| | **R14: Monitoring and evaluation** | Policy-makers are urged to ensure that implemented policy options are assessed, based on well-defined indicators and regular data collection, as to whether or not they were successful in achieving intended policy objectives. If this is not the case, policy-makers are encouraged to adapt the policies appropriately. |
| | **R15: Country-specific context** | When implementing the policy recommendations for the peri-launch phase to improve the uptake of CA-ARTI POCT, it is advised to consider the country's context and to design the measures accordingly. |

AMR: Antimicrobial resistance; CA-ARTI: community-acquired respiratory tract infections, POC: point-of care, POCT: Point-of-care test(s), R: Recommendations

Further explanations of the recommendations including the rationale and implementation considerations are integrated in the descriptions of each policy measure in the main text of this document.

# Acknowledgements

We gratefully acknowledge the valuable input of the experts from Austria, Estonia, France, Poland, and Sweden, who participated in the interviews and validated the authors' analysis of barriers and facilitators derived from the interviews:

- Austria: Lamiss MEJDOUBI, from *Österreichische Gesundheitskasse* (Austrian Social Health Insurance Fund / ÖGK)
- Estonia: Tanel KAJU from *Eesti Haigekassa* (Estonian Health Insurance Fund / EHIF)
- France: Jocelyn DUHAMEL from *Comité Economique des Produits de Santé* (Health Products Pricing Committee / CEPS); Cédric CARBONNEIL and Valérie PARIS from *Haute Autorité de santé* (French National Authority for Health / HAS)
- Poland: Marcin CZECH from *Warsaw University of Technology Business School* (BIZNES), previously Ministry of Health
- Sweden: Ina SCHÄFFNER from *Tandvårds- och läkemedelsförmånsverket* (Dental and Pharmaceutical Benefits Agency / TLV)

Sincere thanks go also to the members of the Task 5 working group of the VALUE-Dx project, the VALUE-Dx Expert Advisory Panel (EAP), and the members of the subgroup on medical devices of the Pharmaceutical Pricing and Reimbursement Information (PPRI) network, for their comments on a previous version of this report.

# 1. Introduction

## 1.1. Background: Antimicrobial resistance from antibiotic use in CA-ARTI

Antimicrobial resistance (AMR) refers to the ability of microorganisms to persist or grow in the presence of medicines (antimicrobial, such as antibiotics) designed to inhibit or kill them [1].

AMR is a major public health problem in Europe and globally and has been responsible for numerous deaths (estimates of 700,000 annual deaths [2]) and medical complications that cause pain and require follow-up treatments [3-5]. Furthermore, the economic impact of AMR on health care systems is substantial [6-8]. The Irish Health Information and Quality Authority (HIQA) quantified the financial burden resulting from AMR as similar to the cost of treating cancers and rheumatoid arthritis [9].

As AMR is largely caused by the use of antibiotics and transmission of (multi-) resistant pathogens between humans, animals, and the environment [10], misuse and indiscriminate use of antibiotics are major drivers for emergence and spread of AMR [11]. Antibiotics are often prescribed in cases when the disease is caused by a viral, not bacterial infection [12, 13].

For diseases related to CA-ARTI (see Box 1) large-scale inappropriate use has been documented despite high confidence of physicians in the decisions about antibiotic prescribing [14, 15]. As these infections have been identified as a critical area, CA-ARTI were selected for the VALUE-Dx project, to which the present report contributes.

**Community-acquired acute respiratory tract infections (CA-ARTI) include:**
Lower respiratory tract infections (LRTI):
- Typical infections: bronchitis and pneumonia

Upper respiratory tract infections (URTI):
- Typical infections: tonsillitis, pharyngitis, laryngitis, sinusitis, otitis media, certain influenza types, and the common cold
- Typical symptoms: cough, sore throat, runny nose, nasal congestion, headache, low-grade fever, facial pressure, and sneezing.

Influenza:
- Can affect LRTI and URTI
- Typical symptoms: fever, runny nose, sore throat, muscle pain, headache, coughing, and fatigue

*Box 1: Overview of community-acquired acute respiratory tract infections*

## 1.2. Addressing AMR through diagnostics: the VALUE-Dx project

Various approaches have been implemented or are under consideration to tackle AMR. Among others, in several countries AMR stewardship programs were implemented in health care facilities and at national levels, to promote appropriate prescribing and use of antimicrobials through evidence-based interventions [16].

An important instrument to support appropriate prescribing is diagnostics, in particular rapid point-of-care tests (POCT) [17]. They have proven to be suitable to improve the quality of antibiotic prescribing and reduce the overuse of antibiotics [18-21].

Given their role as a supporting tool for improved antibiotic prescribing, CA-ARTI POCT can be considered as "**companion diagnostics**". European legislation [22] defines a companion diagnostic as a device that is essential for the safe and effective use of a corresponding medicine, to identify patients, before or during treatment, who are most likely to benefit from the corresponding medicine or likely to be at increased risk of serious adverse reactions as a result of treatment with the medicine. Use of companion diagnostics is particularly known from precision medicine, e.g., in oncology but meanwhile the concept has also been used for infectious diseases [23].

CA-ARTI POCT, which can be designed as blood-based tests or smear-based Polymerase chain reaction (PCR) tests, have been developed and have been made available on the European markets for years. But the frequency of CA-ARTI POCT application prior to antibiotic prescription to treat CA-ARTI **differs** considerably **among European countries**, as do the antibiotic prescribing rates [15]. As POCT may enhance the quality of antibiotic prescribing decisions, there is potential to increase their uptake.

This was the rationale for VALUE-Dx, an Innovative Medicines Initiative (**IMI**) **project**, which aims to build the medical and economic case for rapid diagnostic tests as a public good in the fight against AMR. The project is focused on the outpatient sector (community care), which is defined as the first point of contact with health services. VALUE-Dx aims to demonstrate the value of CA-ARTI POCT with a view to contribute to their improved uptake.

## 1.3. VALUE-Dx analysis of peri-launch policies for CA-ARTI POCT

This report, which presents recommendations for policies, falls under the **Task 5.5** (Work Package 5 related to "**Economic Value, Policies and Innovative Funding Models**") of the VALUE-Dx project. Building on previous work done in Task 5.5A, it presents the findings of Task 5.5B.

As shown in Figure 1, Task 5.5 of the VALUE-Dx project comprises:

- Task 5.5A to survey HTA, pricing and reimbursement policies that are applied for diagnostic tests for respiratory tract infections (RTI) and CA-ARTI in the outpatient sector in European countries, and
- Task 5.5B to identify facilitators and barriers in HTA, funding and pricing policies and, based on these learnings, to develop policy recommendations.

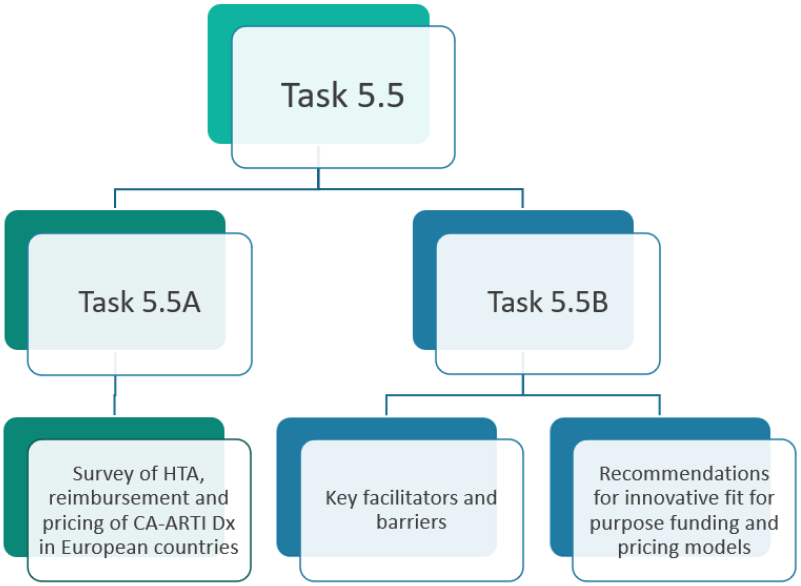
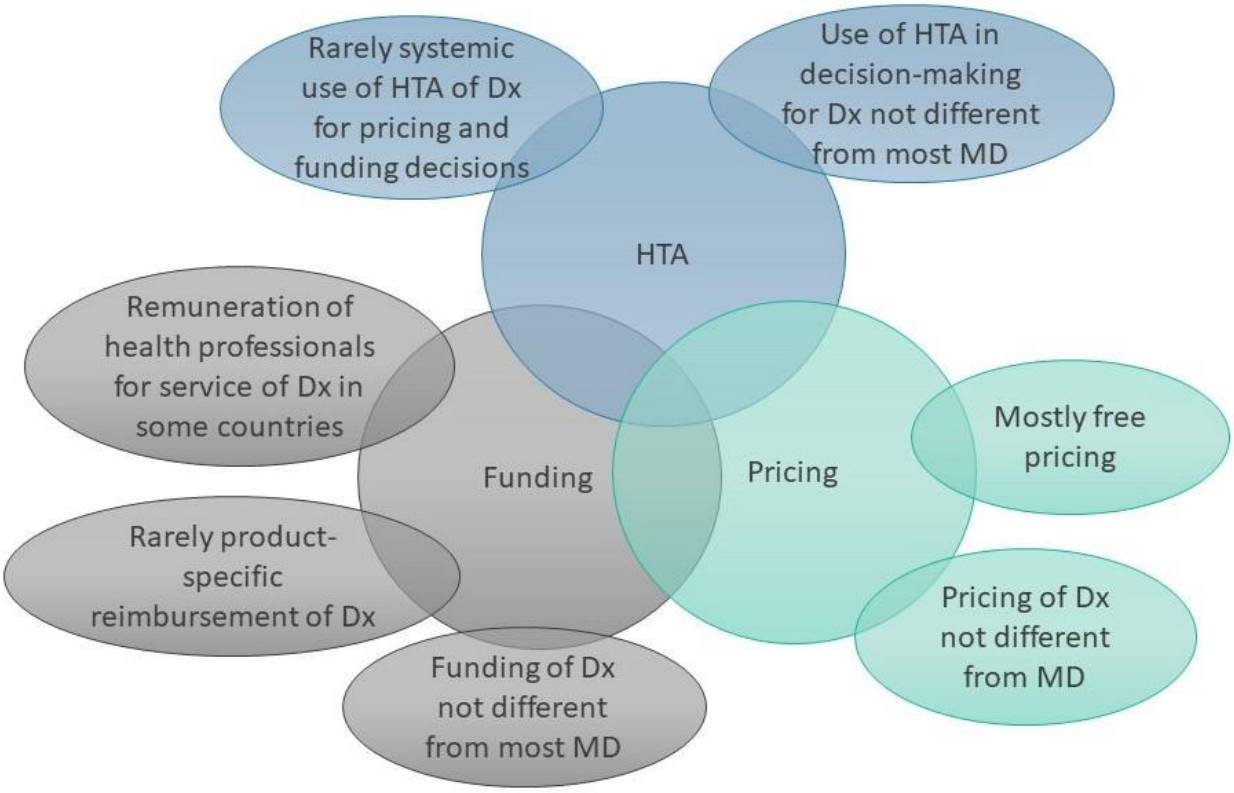



*Figure 1: Components of VALUE-Dx Task 5.5*

### 1.3.1. Findings of the European survey of peri-launch policies

The study conducted for Task 5.5A addressed policies in the so-called **peri-launch phase.** This phase starts after the certification of diagnostics (resulting in having a CE mark in Europe), and comprises a health technology assessment (HTA), pricing, funding, and procurement of the POCT (see also chapter 2.1).

The findings of Task 5.5A, which have been published as a technical report [24] and as a scientific paper [25], provided a **mapping of HTA, reimbursement and pricing of rapid diagnostic tests for RTI and CA-ARTI** based on a literature search and a survey in 17 European countries. As an additional research question, the study investigated as to whether the analysed peri-launch policies for rapid diagnostic tests differed from those applied for medical devices (MD) in general.




Dx: diagnostics (here: related to rapid diagnostic tests for RTI or CA-ARTI), HTA: health technology assessment, MD: medical devices

*Figure 2: Summary of findings from the survey and literature review in Task 5.5A*

**Key outcomes of the European survey conducted in Task 5.5A** (relating to the year 2020) were as follows (for a visualisation see Figure 2):

- **Health Technology Assessment (HTA),** which is a tool to generate and appraise evidence to support pricing and funding decisions, is systematically conducted as part of the decision-making process for selected MD and methods in a few European countries (e.g., France, Germany, Hungary, and the UK), but **not for rapid diagnostic tests for RTI and CA-ARTI.** Thus, CA-ARTI POCT are made available on the market without a prior HTA.
- Regarding **pricing**, European countries do **not impose any price regulation** for rapid diagnostic tests for RTI and CA-ARTI; this means that **the supplier can set the price** at the own discretion (so-called "free pricing"). Overall, there is limited price regulation for MD; some countries (e.g., France, Greece, Hungary, and Spain) regulate the prices of MD that have been included in the reimbursement list (i.e., are publicly co-funded). In settings with free pricing, **indirect price control** may apply **via public procurement** (e.g., Austria, Germany, Italy, and UK).
- Seven countries (Austria, Cyprus, Estonia, Finland, France, Romania, and Slovakia) reported to **reimburse** POCT for RTI or CA-ARTI **on a product-specific basis**, while a few further MD may be reimbursed. In addition, in some countries **health professionals were remunerated for the service** of conducting a diagnostic test [24, 25].

Overall, the findings offered a descriptive policy mapping, but they were not intended to be analytical in terms of possible impacts. This confirmed a **need for expert interviews** as the **basis for the recommendations** in this document (cf. also chapter 2.2).

## 1.4. Objective and outline of this report

The aim of Task 5.5B was to develop **recommendations for fit for purpose policies in funding and pricing** to improve the uptake of CA-ARTI POCT in the outpatient sector. This report presents such funding and pricing policy recommendations, which are supplemented by some further recommendations on HTA and overarching considerations. The analysis of potential barriers and facilitators, which informed the development of recommendations, is summarized in the Appendix.

# 2. Methods

The recommendations are **based on evidence from Task 5.5A and the first part of Task 5.5B** (identification of barriers and facilitators related to HTA, pricing and funding that impact the uptake of CA-ARTI POCT) of the VALUE-Dx project.

Task 5.5A provided a comparative description of HTA, reimbursement (funding) and pricing policies applied for diagnostic tests for RTI and CA-ARTI in European countries: it was mostly based on a survey with competent authorities, supplemented by a literature review. The findings were published in a technical report [24]. Task 5.5A was designed as a **qualitative cross-country system and policy analysis**.

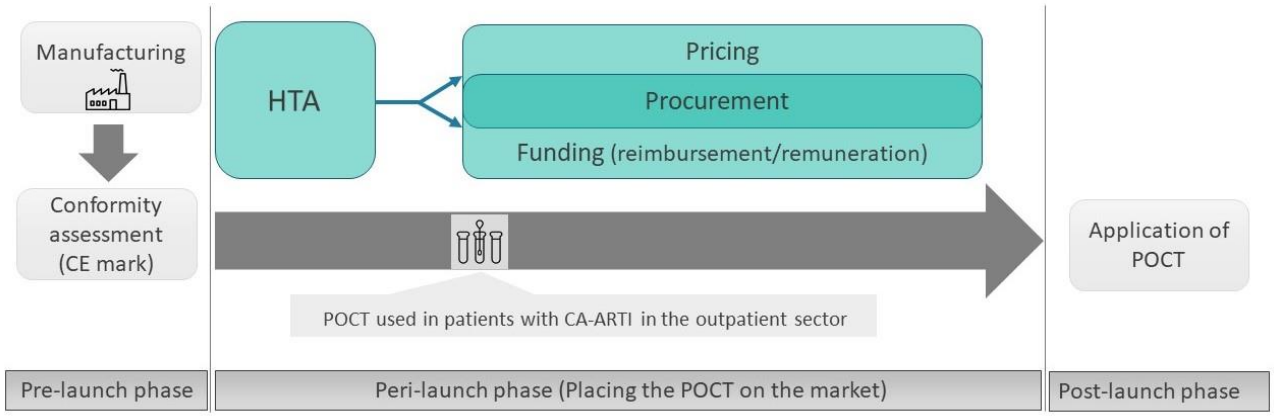
While the cross-country analysis conducted in Task 5.5A was comprehensive (i.e., comprising also smaller markets and countries less in the focus of research and policy attention) and showed the **status of implementation** of policy options specific for CA-ARTI POCT, there was a lack of granularity. As a targeted literature review on **possible barriers and facilitators did not identify sufficient information** on the selected policies (as most findings related to the AMR stewardship programs), it was decided to follow a country case study approach in Task 5.5B. The methodological choices for Task 5.5B are described below.

## 2.1. Scope and conceptional framework

The policy recommendations were developed for the specific context and scope of this VALUE-Dx task and refer to:

- The peri-launch phase (as described below);
- Infectious diseases of the respiratory tract, the diagnosis with most antibiotic applications and most likely biggest potential for avoiding inappropriate use;
- The outpatient sector (community care, primary care);
- CA-ARTI POCT (rapid tests), not those carried out in laboratories;
- CA-ARTI POCT applied during the patient visit in the general practitioner (GP) practice (other application of POCT, e.g., by other health professionals, such in community pharmacy, or by patients, were not within the scope of the project);
- POCT to identify whether or not the CA-ARTI is caused by viruses or bacteria.

The **peri-launch phase** [26] is situated between granting of the CE mark (in Europe) and placing of the device (such as the diagnostic) on the market. This is visualised in Figure 3 and was developed based on an internationally accepted framework of the value chain for medicines [27]. **Peri-launch instruments and measures include HTA (value assessment) as a supporting tool** to help determine the value of a POCT or other health technologies, and pricing, procurement, and reimbursement policies.




CE: Conformité Européenne, CA-ARTI: Community acquired acute respiratory tract infection, HTA: Health Technology Assessment, POCT: Point-of-care (diagnostic) test(s)

*Figure 3: Relevant phases along the POCT value chain*

For medicines, peri-launch policies have been studied extensively, while **for medical devices, including diagnostic tests, evidence is limited**. Thus, development of the conceptional framework for peri-launch policy action is built on learnings from the concepts applied for medicines. Literature on pharmaceutical policies [28-35] has pointed to the **inter-linkage between pricing and funding**, and, as a result, **some policies with pricing as well as funding components could be assigned to both the policy areas** of pricing and funding. Furthermore, there are different approaches as to whether to interpret procurement as a separate policy area or subsume it under pricing (or sometimes under reimbursement).

Guided by the findings of the European survey of national peri-launch policies for CA-ARTI POCT [24], the authors decided to assign the policy recommendations to the three policy areas of:

- HTA / value assessment
- Funding (reimbursement and remuneration)
- Pricing and procurement

The **term "funding"** was chosen as an umbrella notion to comprise reimbursement of the diagnostic and remuneration of the health professional for the service (for further details see Figure 7 and explanatory text in chapter 3.2). **Procurement is mentioned explicitly** because of its **importance for CA-ARTI POCT.**

For tackling AMR, policy action is being extensively discussed, however, usually more related to antibiotics, in the pre-launch and post-launch phases. The first phase includes, for instance, recommendations for financial incentives to developers for novel antibiotics, such as specific global funds and – currently under evaluation in the European Union – Transferable Exclusivity Vouchers (TEVs), whereas the latter include communication and capacity-building activities targeted at health professionals and the public, and prescribing guidelines. The development of recommendations for the pre- and post-launch phases, for which several policy proposals have already been developed, is not the scope of this assignment.

## 2.2. Country case studies

The rationale for the **country case study approach** was to **understand in detail the specificities of the policy environment** in terms of HTA, funding (reimbursement and remuneration), pricing / procurement, and **implications of** the (design of) **policies in place** in a few selected countries. This was done through interviews with country experts (in a focus group or through an interview with individual experts).

Country selection aimed to ensure a balanced mix of:

- Countries of different income,
- Countries of different size,
- Countries in different geographic areas in Europe, and
- Countries of different health systems (tax-funded or social health insurance-contribution funded).

**Austria (AT), Estonia (EE), France (FR), Poland (PL), and Sweden (SE)** were selected as case study countries. Table 1 gives an overview of included countries and the affiliation of the interview experts.

*Table 1: Characteristics of experts and countries*

| Country | Characteristics of health system * | Institution | Type of interview |
|---|---|---|---|
| **Austria** | Decentralized, contribution-based social health insurance; GDP per capita: 53,267.9 USD PPP (2021) | Österreichische Gesundheitskasse (Austrian Social Health Insurance / ÖGK) | Written questionnaire with follow-up calls for clarification |
| **Estonia** | Centralized, tax-funded Beveridge system; GDP per capita: 27,280.7 USD PPP (2021) | Eesti Haigekassa (Estonian Health Insurance Fund / EHIF) | Expert interview |
| **France** | Centralized, tax-funded Beveridge system with a national health insurance; GDP per capita: 43,518.5 USD PPP (2021) | Comité Economique des Produits de Santé (Health Products Pricing Committee / CEPS), Haute Autorité de santé (French National Authority for Health / HAS) | Focus group interview (3 experts) |
| **Poland** | Centralized, social health insurance; GDP per capita: 17,840.9 USD PPP (2021) | Warsaw University of Technology Business School (BIZNES), previously Ministry of Health | Expert interview |
| **Sweden** | Decentralized, tax-funded Beveridge system; GDP per capita: 60,239.0 USD PPP (2021) | Tandvårds- och läkemedelsförmånsverket (Dental and Pharmaceutical Benefits Agency / TLV) | Expert interview |

*Gross domestic product (GDP) for the year 2021 refers to data from the World Bank national accounts data in purchasing power parities (PPP) in current international USD) [36].

Experts for the interviews were approached through the sub-group on medical devices of the **Pharmaceutical Pricing and Reimbursement Information (PPRI) network** [37]. PPRI is a network of

competent authorities responsible for pharmaceutical pricing and reimbursement from 50, mainly European, countries, and international institutions such as the European Commission, the Organisation for Economic Co-operation and Development (OECD), and the World Health Organization (WHO), with the PPRI Secretariat affiliated to the authors' institution Gesundheit Österreich GmbH (GÖG). PPRI was established in 2005, and in 2018 the PPRI Secretariat established a subgroup on medical devices (PPRI MD) at the request of its members [38].

## 2.3. Expert interviews

Between November 2021 and May 2022, the authors conducted one **focus group interview** with three representatives from France and **expert interviews** with representatives of the respective public authorities of Estonia, Poland, and Sweden. Austria was represented by the Austrian Social Insurance, whose representative decided to reply in writing, but the expert was available for clarification queries.

Preparation of the interviews included searching the literature, including grey literature and screening websites and documents to understand the peri-launch policy environment for diagnostic tests and for medical devices in general. **Publications on relevant barriers and facilitators** for AMR POCT uptake, **best practice examples and national initiatives** identified were **also used as the knowledge base** to develop the recommendations. Documents (e.g., HTA reports, publication on programs to reduce AMR) were examined in a text analysis to identify possible barriers and facilitators.

The interviews were conducted by two researchers. Informed consent was obtained in written form before the interviews. One researcher facilitated the interview and a second researcher took manual notes (no recording). A summary of the notes, including a preliminary analysis of key features of the country policy framework for CA-ARTI POCT (displayed in a graph in the minutes), barriers and facilitators, as well as lessons learned and recommendations proposed during the interview, were shared with the interviewees for confirmation. This validation process usually also comprised the clarification of a few open questions.

## 2.4. Recommendation development

Based on the learnings from the case study countries and on literature related to some further countries, a compilation of barriers and facilitators was established. The summary is available in the Appendix (Table 2: Barriers for the uptake of CA-ARTI POCT in the outpatient sector and Table 3: Facilitators for the uptake of CA-ARTI POCT in the outpatient sector).

It should be noted that the scope of this Task 5.5B is to develop recommendations related to policies in the peri-launch phase (value assessment, pricing / procurement, reimbursement, and further funding policies). **Other areas of possible facilitators and barriers** to the uptake of CA-ARTI POCT are addressed in **other parts of the VALUE-Dx project** (Task 5.7) and previous or ongoing projects, such as the **EU Joint Actions on AMR**.

Based on the information generated as described (see Figure 4), a set of draft policy recommendations was developed, guided by the principles of enhanced cooperation [39] in the following areas, as defined in the description of actions in the VALUE-Dx project:

- Collaborative approaches between regulators, HTA bodies, pricing authorities, and payers;
- Addressing the fragmentation within countries and a lack of coordination of the activities regarding HTA, pricing and procurement, funding decisions;
- Strengthening the collaboration between EU member states by fully respecting the subsidiarity principle.


*Figure 4: Process for the development of policy recommendations*

Since the country context, such as organisation of the health system (e.g., contracted or employed doctors), largely determines the feasibility and usefulness of the policy measures in different setting, the authors do not recommend any "most important" measures that should be implemented everywhere. On the same note, another guiding principle was to refrain from ranking proposed measures, for the same reason that feasibility of the policies depends on the context, and this varies across countries.

## 2.5. Review

To **ensure relevance, feasibility, and operational practicability** of policy recommendations, **experts from different countries and backgrounds** were invited to participate in **review** processes from September till November 2022. To reach a broad audience from different countries and institutions, the draft recommendations were sent via email to various stakeholders. Furthermore, three expert review meetings were held in which the authors presented the recommendations and invited the experts to share their perspectives.

The following experts were given an opportunity to review and comment on the recommendations:

- The interviewed experts,
- Experts from the subgroup on medical devices from the Pharmaceutical Pricing and Reimbursement network (PPRI MD),

- The Expert Advisory Panel (EAP) of the VALUE-Dx project, which provided input and was invited to participate in the discussion,
- Members of the VALUE-Dx consortium, including the WP 5 working group.

For all core areas (HTA, funding, pricing, and procurement), experts from authorities, industry, and academia provided comments.

The authors took the **feedback** on board and **integrated it into the recommendations** as far as possible and where appropriate. For a few points that could not be easily addressed or where there were questions of understanding, the reviewers and authors exchanged views verbally and found a solution that was acceptable and supported by both sides.

Most comments can be clustered in three major groups:

- Several reviewers were concerned about **unintended consequences** of the proposed measures, in particular potential overuse of the CA-ARTI POCT. As a result, the authors **carefully considered the impact of their proposed policy options** and added and stressed prerequisites and other relevant criteria in the implementation considerations.
- Some recommendations presented in the **draft version** were **not sufficiently clear** to reviewers and caused misunderstanding. In response, the authors **worked on improving clarity**.
- Regarding some of the novel policy options proposed (e.g., innovative procurement arrangements such as the “Netflix” model and performance-based managed-entry agreements), reviewers had **mixed perception on the feasibility** of the measure (often with regard to the country that they were affiliated to).

As part of the efforts to improve clarity, the revision also comprised editorial changes, in the course of which some separate recommendations were combined. As a result, the overall number of recommendations decreased.

## 2.6. Limitations

The development of the recommendations has a few limitations. It must be remembered that the process for the recommendation development, as shown in Figure 4, included the generation of evidence by conducting expert interviews.

First, the **scope and terminology are not entirely consistent** in the mapping report produced in Task 5.5A [24] and in this report. In the **previous report** in Task 5.5a the term "reimbursement" was used as a synonym for funding. In the course of the project, the terminology has evolved to be more specific about what is meant.

Secondly, in the interviews it was confirmed that the **country context plays a crucial role** in determining which policies would be feasible and appropriate for implementation. Thus, some of the proposed measures cannot, or can hardly, be implemented in some of the countries, or their implementation would not be meaningful. For example, financial incentive schemes, such as bonuses for the use of POCT prior to antibiotic prescribing, would have a very different impact in a health system where GPs can charge for services rendered compared to a system with fixed salaries for employed GPs.

A third limitation was the **lack of evidence**, in terms of literature, as well as the difficulty to find experts for the interviews. The latter was partially linked to **limited time availability of the experts**, and also that the **technical experts** approached who work in **public authorities** did not always feel confident about talking about peri-launch activities for POCT, especially in the context of AMR, since **AMR was rather perceived as a topic for health care practitioners**. Still, it was important for ue to address representatives of public authorities for learning about barriers and facilitators, as the recommendations are targeted at policy-makers. Perspectives of health care practitioners have been considered in other tasks of the VALUE-Dx project (in particular Task 5.7).

The **scope of this research** in the VALUE-Dx project was **GP practices**. However, in several countries, **further health professionals**, including community pharmacists, **could also offer CA-ARTI POCT** and thus contribute to improved uptake. There is room for further research and policy development.

Despite these limitations, the authors trust that developed recommendations offer guidance to national policy-makers to address AMR through improved use of diagnostics.

# 3. Recommendations

Based on the methodological approaches described above, policy recommendations were developed, taking into account the country-specific differences in the health systems where CA-ARTI POCT are used. For instance, in some countries, CA-ARTI POCT are applied in GP practices, which are, in principle, private but in a contractual relationship with one or more social health insurance funds. Before use, the CA-ARTI POCT are bought by the doctors or patients. Other countries have primary health care centres, where employed doctors, who receive a fixed salary, use the CA-ARTI POCT, which are purchased by the local, regional, or national administrations.

When developing the recommendations, the authors aimed to consider the different settings and to ensure feasibility and applicability as far as possible. However, the differences across countries and health systems posed a challenge. In addition, the individual policies on HTA, pricing and procurement, and funding, and overarching topics (such as awareness of AMR in the population, existence of an institution that could implement measures to prevent AMR or launch campaigns to improve health literacy in the field) are inter-linked. The different remuneration systems also importantly influence if and to which extent financial incentives targeted at doctors would have an effect on the uptake of CA-ARTI POCT. In countries with fixed salaries for GPs (e.g., UK), financial incentives may be far less justifiable to public payers than in a system like Sweden, where an infrastructure is in place to provide feedback to doctors if their antibiotic prescribing behaviour is comparable to peers.

In the following subsections, 15 recommendations are presented, one by one. They are grouped into four areas:

- HTA / value assessment (3 recommendations),
- Funding (4 recommendations),
- Pricing and procurement (3 recommendations) and
- Overarching topics (5 recommendations).

Recommendations related to overarching topics were included to highlight the **necessity of policy action along the life-cycle and of accompanying measures** that are important to support successful implementation. For each of the recommendations the rationale and implementation considerations are described. Figure 5 provides an overview of the recommendations. As the assignment of Task 5.5B in the Value-Dx project was to develop recommendations for innovative policy recommendations on funding, pricing, and procurement, these policy options are highlighted in Figure 5 by being placed in the centre.

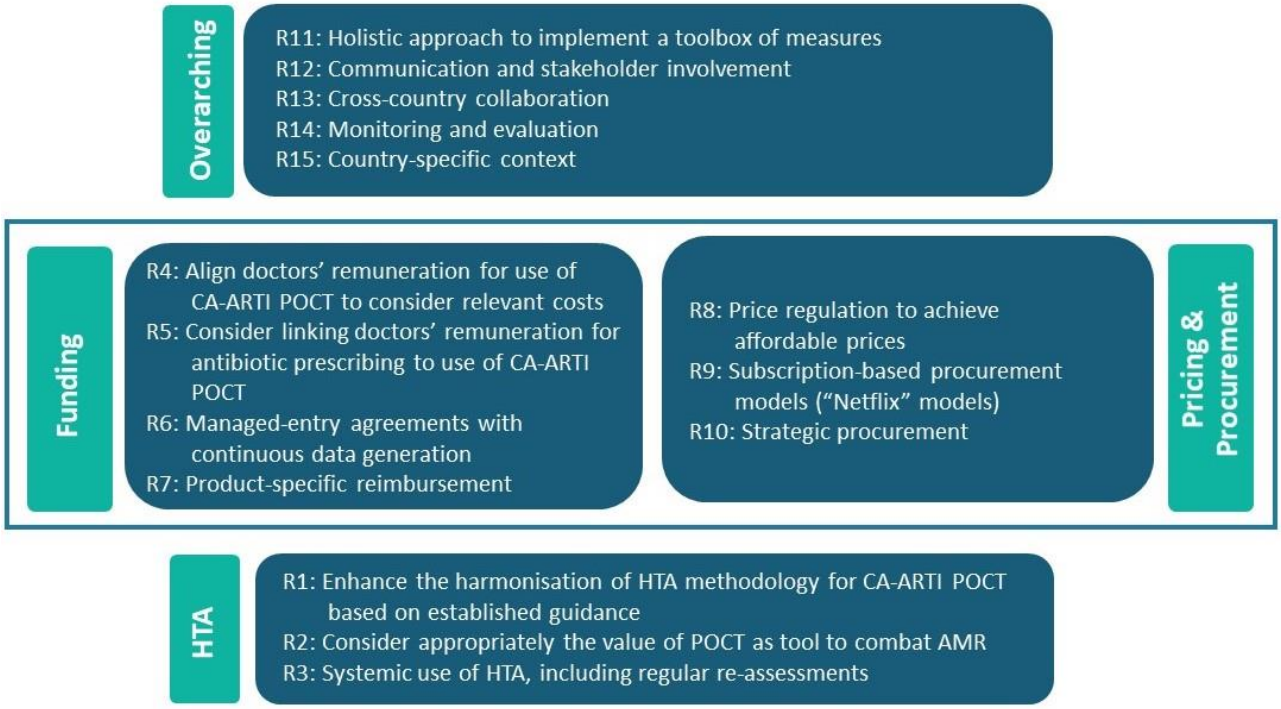



*Figure 5: Recommendations for policies in the peri-launch phase to enhance uptake of CA-ARTI POCT*

The 15 recommendations should not be seen separately: policies in the peri-launch phase are **linked** to each other and each policy recommendation is related to other measures. The strong influence of the country context as to which policies are reasonable and feasible makes a ranking or a selection of some top measures for all of Europe inappropriate. When selecting and designing policies, the setting of the country in which the policy is aimed to be implemented should be taken into account as determinant for achieving the goals, such as savings through collaboration or security of supply through more strategic approaches.

## 3.1. Health Technology Assessment (HTA) / Value assessment

Health technology assessment (HTA) is a tool to determine the value of a diagnostic or any other health technology to support regulatory and policy decisions. It offers systematic and transparent collation and appraisal of evidence. Over the years, definitions of HTA have evolved, with varied versions of the definition being used in different organizational contexts. In 2020, a new definition of HTA, as agreed upon by the international HTA community, was announced (see Box 2).

**What is Health Technology Assessment?**

"HTA is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system.

Note 1: A health technology is an intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organize healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, program, or system.

Note 2: The process is formal, systematic, and transparent, and uses state-of-the-art methods to consider the best available evidence.

Note 3: The dimensions of value for a health technology may be assessed by examining the intended and unintended consequences of using a health technology compared to existing alternatives. These dimensions often include clinical effectiveness, safety, costs and economic implications, ethical, social, cultural and legal issues, organizational and environmental aspects, as well as wider implications for the patient, relatives, caregivers, and the population. The overall value may vary depending on the perspective taken, the stakeholders involved, and the decision context.

Note 4: HTA can be applied at different points in the lifecycle of a health technology, that is, pre-market, during market approval, post-market, through to the disinvestment of a health technology."

*Source: O'Rourke et al. 2020 [40]*

*Box 2: Updated definition of Health Technology Assessment*

Findings in Task 5.5A highlighted the following features with regard to HTA for CA-ARTI POCT: There is large variation in the institutional setting of HTA across and even within European countries. The uptake of an assessment performed by the HTA body and its consideration for further funding and pricing / procurement varies across the countries, overall. HTA for CA-ARTI POCT, if conducted, are rarely factored in funding and pricing / procurement decisions [24].

In addition, literature [41] and experts in the interviews pointed to challenges and limitations related to assessments for diagnostics, including CA-ARTI POCT. Based on these learnings, three recommendations with regard to HTA are proposed, with the first two being strongly inter-connected.

### 3.1.1. Enhance the harmonisation of HTA methodology for CA-ARTI POCT based on established guidance (R1)

*Recommendation 1*

It is recommended to work on a harmonisation of standards for conducting HTA for POCT, including clear reporting criteria for outcomes related to effectiveness, accuracy, and other domains relevant for CA-ARTI POCT. Actions should be based on established guidance, e.g., from EUnetHTA, and aligned with needs of HTA bodies and health policy-makers. An important accompanying action is the communication of the standards, including data needs for conducting the HTA (e.g., through early scientific advice).

*Rationale*

Despite major progress in the development of HTA methods, primarily driven and further developed by the members and working groups of the European Network for Health Technology Assessment (EUnetHTA), there are **methodological challenges related to HTA for POCT**. While this recommendation may be less important for other settings where guidance is available, the relevance of methodological challenges related to CA-ARTI POCT was mentioned as a barrier to the uptake of CA-ARTI POCTs by the experts from France, Poland, and Sweden.

Interviewed experts from France and Poland noted that, independent of a potential lack of evidence to be used in HTA, **usually** there is **no comprehensive HTA conducted for diagnostics**. In Sweden it depends on the regions whether or not HTA is conducted and a health technology may be evaluated in parallel by several regions. Experts stated **methodological difficulties in assessing the value of POCT** and the **lack of uniform regulation on HTA methodology** for In Vitro Diagnostics (IVD) / POCT between HTA authorities within a country or between countries (Sweden, France), especially regarding the **operationalisation of the patient benefit**, which is often unclear for POCT.

There is **no consensus among HTA authorities**, **what outcome data is considered acceptable** by decision-making organisations to show the value of a POCT. Relevant outcomes would need to be agreed with the decision-makers and the operationalization would have to be aligned between HTA authorities to enable collaboration, but, e.g., in Sweden the requirements even differ between HTA bodies and regions.

In other countries, e.g., France, **knowledge on HTA skills** and the **interpretation of evidence** to describe the value of POCT is missing. For example, it is unclear if accuracy data alone, which might be potentially linked to decision-analytic models on long-term outcomes, is sufficient for the value assessment, or if there is a need for direct data on the impact of the test on outcomes of interest (e.g., morbidity, antibiotic use etc.). There would be a **need for capacity-building to create new resources in HTA compilation** according to the **information needs of decision-makers**.

In general, there is a **lack of clarity as to which data and evidence are to be considered in the assessment** and limited common understanding and agreement of an appropriate methodology, for example, regarding the impact of using a test (compared to current care) on long term outcomes, not solely immediate impact / performance of the test. This could be due to a situation that HTA is not commonly used for non-high-risk medical devices such as CA-ARTI POCT. This has major

implications since HTA outcomes are used downstream for funding, pricing, and procurement decisions.

A commonly accepted HTA methodology for CA-ARTI POCT is essential if HTA for these devices is established. There needs to be clear and transparent **information on what is expected** from the HTA by policy-makers and which evidence on the studied CA-ARTI POCT is required (e.g., from regulatory bodies or diagnostic developers or suppliers). Moreover, it is to be ensured that new evidence can be generated, e.g., based on real-world data (RWD).

According to the definition of HTA, the multi-disciplinary process and the comprehensive scope of potentially relevant dimensions that constitute the value of a health technology highlight how broad the value of a health technology can be defined. The **different dimensions** are often inter-linked. A potential for describing the value of AMR POCT more comprehensively in HTA reports is to extend the scope to the "intended and unintended consequences of using a health technology compared to existing alternatives", which is also part of the HTA definition [40]. Applying a CA-ARTI POCT in primary care may also have a societal value (see also Recommendation 2 in chapter 3.1.2).

Clear and harmonized standards (e.g., on which dimensions to assess) and reporting criteria would also facilitate **cross-country** writing or re-use of **HTA**. Within Europe, collaboration in guideline development for HTA and for conducting joint assessments, called rapid **Relative Effectiveness Assessments (REA)**, has been developed during three Joint Action programs in the European Network for Health Technology Assessment (**EUnetHTA**) [42], which has been funded by the European Commission.

If an HTA is conducted for CA-ARTI POCT, the **evaluation of clinical effectiveness and safety** would benefit if it is conducted **as joint European REA** according to EUnetHTA standards [43] as described in Box 3, as this saves resources, strengthens the HTA production and avoids redundancies.

The **EUnetHTA HTA Core Model®** [43] application for rapid **Relative Effectiveness Assessment (REA)** [44] with additional elements from the **HTA Core Model® Application for Diagnostic Technologies Version 3.0** [45] has successfully made the proof of concept of the methodological framework of the compilation of an HTA report on AMR-related POCT [46].

Although POCT are not high-risk diagnostics, it has proven useful to incorporate diagnostic-specific elements from the HTA Core Model® Application for Diagnostic Technologies Version 3.0.

REA include the domains, which are to be adapted to diagnostics:

- Description and technical characteristics of technology
- Health problem and current use of the technology
- Clinical Effectiveness
- Safety
- A checklist for potential ethical, organisational, patient and social, and legal aspects.

*Box 3: Guidance from the EUnetHTA HTA Core Model® to assess diagnostics*

*Implementation considerations*

**Existing up-to-date guidance on HTA methodology**, e.g., as published by EUnetHTA [42, 43] or which is used by a comparable HTA report [46], is recommended to be used when planning HTA on POCT, within a country or across countries to foster methodology developments. There could be a

need for **capacity-building on EUnetHTA standards** in HTA agencies. While evidence from randomised controlled trials (RCT) is state of the art for the assessment of clinical effectiveness in HTA (also in the EUnetHTA Core Model [43]), a trade-off between study costs and value of information needs to be managed. Standardised collected **real-world evidence** (RWE) from surveillance systems or medical records or evidence generated in managed entry agreements (see Recommendation 6) could be an option to address the challenge of lack of evidence to assess health technologies, including POCT. Thus, given limited evidence (e.g., RCT), RWD could be considered as the best available evidence and used in HTA. **Standardised data collection on key parameters** would also enable the use of evidence generated in HTA for pricing and procurement.

**Supportive factors** on the way to developing and implementing standardised and harmonised HTA methodology, which is mainly provided by EUnetHTA in Europe, is the active involvement of national HTA bodies in joint assessments and their consideration of use the EUnetHTA guidance, e.g., the EUnetHTA HTA Core Model® [43], as well as aligning national standards to the European and international ones. Despite common standards in Europe, **available resources for conducting HTA** might differ significantly between countries. When developing a commonly applied HTA methodology, challenges of **countries with lower capacity** in HTA need to be addressed, for example, by focusing on a limited set of standards and reporting criteria, which can be fulfilled more easily.

In areas with potential for differences between HTA bodies a **common understanding** is essential for collaboration. Such areas are, inter alia, the selection of the diagnostic-specific domains to be assessed, or the operationalisation of the primary and secondary outcomes, e.g., whether or not the outcomes would focus on effectiveness and accuracy of the CA-ARTI POCT or if a broader approach such as assessing the impact of the application of POCT on the course of the disease is chosen.

Possible **challenges** that may emerge in the development of an HTA methodology for CA-ARTI POCT include (non-exhaustive list):

- Limited or no evidence is available on the assessed domains,
- The comparators (different health technologies/POCT) in the studies differ,
- The quality of evidence is low with a high risk of bias,
- Outcomes used for the assessment of clinical effectiveness are operationalized differently,
- Patient groups or documentation of study parameters,
- Different threshold values for a positive or negative test result (further explained below),
- Differences in framework factors such as staff training,
- No accessibility to data (language, rights, data protection, technical or financial reasons).

Regarding the **operationalization of the outcomes** used to assess POCT, **accuracy,** i.e., the correctness of the test result, which is measured by sensitivity and specificity of a test**,** and **consistency of the test results** in different populations are essential and common practice to evaluate the clinical utility and validity of a diagnostic tests [47]. Even if misclassification due to false test results is a problem in diagnostic testing, there is no gold standard POCT indicating the true antibiotic susceptibility, but there are measures to describe test performance. The degree of acceptable false negative and false positive results is defined according to the positive predictive value (PPV) and the negative predicted value (NPV) **of a POCT.** In the context of POCT for CA-ARTI

patients, the most commonly used test performance indicator is the NPV, which is the proportion of false negative test results in all patients with negative test results [47].

In developing methodological standards for conducting HTA for CA-ARTI POCT, information needs of HTA bodies and health policy-makers across Europe could be surveyed with a view to adapt guidance and communicate needs for evidence generation and operationalization of a relevant benefit to stakeholders including the selection of the study population, outcomes relevant for health policy decision making, and which comparators shall be included in the assessment. **Early communication and interaction between stakeholders** can improve availability of relevant evidence used for a value assessment and ensure that the right questions are asked in HTA but also in trials, which form the evidence base for HTA. In this context, stakeholders are diagnostic developers, academics, regulators, HTA agencies, health system clinicians, patients, and payers.

A **best practice example** for a **joint REA** in line with EUnetHTA standards was the one conducted **for CA-ARTI POCT** by the Irish HTA body HIQA [46] and collaboration partners in 2019, as described in Box 4. Guidance from EUnetHTA has been adapted to IVD. The Main Association of Austrian Social Security Institutions, a collaboration partner in the production of the HTA, published a short German version of that HTA report [48], which also included country-specific assessments and considerations. This is an efficient approach to fulfil national requirements and benefit from the comprehensive assessment. The implementation of the new **EU Regulation on Health Technology Assessment** (EU) 2021/2282 from 2022-2025 may also offer the opportunity to promote joint HTA on medical devices.

**HTA for AMR POCT as Joint Rapid Relative Effectiveness Assessment (REA)**

**Scope of the HTA**: C-reactive protein-POC tests in primary care to support decision making in CA-ARTI

**Methodological guideline**: EUnetHTA Core Model® [43-45] and other guidance documents published by EUnetHTA on HTA for IVD

**Leading authority for REA**: HIQA; partners from other countries collaborated

**Assessed domains were:**

- The description of the technology assessed
- The problem treated by the POCT
- Clinical effectiveness and safety
- Diagnostic test accuracy
- Analytical performance of the POCT
- Safety
- Ethical, organizational, patient and social aspects, and legal aspects (if applicable)
- Economic aspects and financing

With moderate evidence, the results of the HTA indicate that the use of CRP-POCT leads to a statistically significant reduction in the number of antibiotic prescriptions to CA-ARTI patients in primary care (at the initial consultation). The analytical performance of the CRP-POCT evaluated is broadly comparable to testing from the laboratory. However, adequate training is required to avoid operator's errors. Enhanced skills to apply POCT seem to have an impact on the accuracy and, therefore, on the impact of the diagnostic on antibiotic prescriptions.

*Source: HIQA (2019) [46]*

*Box 4: Best practice example conducting an HTA as joint assessment based on EUnetHTA guidance*

### 3.1.2. Consider appropriately the value of POCT as tool to combat AMR (R2)

*Recommendation 2*

In the further development of the HTA methodology, it is recommended to consider the contribution that CA-ARTI POCT can make as a tool to improve quality of antibiotic prescribing (personalised medicine). Methodology may be advanced to also reflect the societal value of these diagnostics in addressing AMR.

*Rationale*

CA-ARTI POCT contribute to **improved antibiotic prescribing**, especially if the test result is available sufficiently timely to support and confirm the therapeutic decision. Compared to tests that are sent to laboratories, receiving the test result within a few minutes, i.e., during the patient's visit in the doctor's practice, largely determines the value of the POCT applied in the outpatient (community) sector. The decision for further treatment (i.e., if an antibiotic is needed) can be made promptly, and there might be reduced need for a follow-up conversation via phone or a second visit.

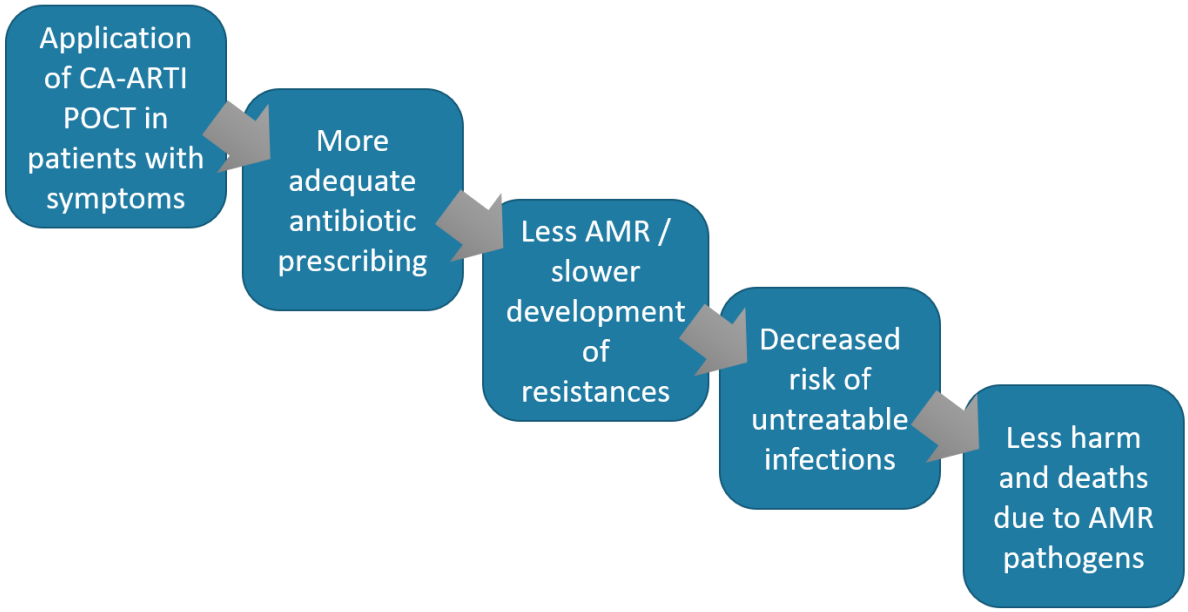
In terms of tackling AMR, the contribution of POCT to impact the further treatment process, which may include refraining from prescribing an antibiotic when not beneficial, is an important aspect of CA-ARTI POCT. As these POCT help optimise treatment for the patient, they serve as kind of

**companion diagnostic** (see also chapter 2.1). Such an approach to targeted "personalised medicine" has been promoted in the EU (cf. Box 5).

> *"A medical model using characterization of individuals' phenotypes and genotypes (e.g., molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.*
> *Personalised Medicine should be seen as an evolution of medicine, rather than a revolution, and many challenges remain before its successful application across healthcare systems."*
> *Source: EU Health Ministers in their Council conclusions on personalised medicine [49]*

*Box 5: Definition of personalised medicine*

The value of POCT to reduce antibiotic misuse goes far beyond the aspect of clinical effectiveness, safety, accuracy and easy applicability of the IVD in daily practice and avoiding side effects of antibiotics. They also offer a **societal value** in terms of avoiding and/or reducing AMR for society in the future. Figure 6 summarises different benefits of POCT which results in societal value.




Source: authors based on Neri et al. 2019 and Wurcel et al. 2019 [50, 51]

*Figure 6: The societal value of CA-ARTI POCT use*

*Implementation considerations*

When developing an HTA methodology for CA-ARTI POCT which considers several dimensions including societal value, HTA bodies can **draw from existing similar work** in this area. Experts of the Office of Health Economics (OHE) have worked on **models to consider the societal value of novel antibiotics** in HTA [50, 52, 53]. Furthermore, there are proposals from the AB-DRIVE project [54].

Taking into account the societal value of diagnostics, the **value of diagnostic information (VODI) framework** might offer some guidance. The VODI framework was developed with the aim to have a tool to recognize the intrinsic value of diagnostics to treatment decisions and to improve informed decision-making in healthcare [51].

The VODI framework is rather broad and considers as societal benefits whether individuals can return to work earlier or if there are savings for welfare programs. However, there is frequently no evidence available for these outcomes. But if the VODI is considered adequately in HTA and a need for high-quality data is recognised, this may create an incentive to generate evidence. The risk of false-positive and false-negative results always exists, but the proportions of false results can be influenced by setting the threshold value [47]. The consequences of having a false result need to be considered in the VODI framework to improve understanding [51].

### 3.1.3. Systemic use of HTA, including regular re-assessments (R3)

*Recommendation 3*

It is recommended to systematically base pricing and funding decisions on HTA and conduct regular re-assessments (updated HTA) when relevant new data are available.

*Rationale*

As stated earlier, the European mapping found that HTA is not (systematically) used for policy decisions on CA-ARTI POCT. This may be due partially to the limited implementation of pricing policies (free pricing for CA-ARTI POCT) and funding policies (product-specific reimbursement for CA-ARTI POCT only in some countries).

As HTA contributes to **improved policy decisions**, authorities should base pricing and funding processes, whether in place now or introduced in future, on HTA. Better informed and more evidence-based decisions are also important in terms of **accountability** of public authorities.

In addition, regular re-assessments of available evidence as part of the HTA process at pre-defined frequencies are proposed because **developments in health technologies**, CA-ARTI POCT in this case, can make a difference for the determination of value and eventually for the uptake in practice.

The nature of these **changes may differ**, but their relevance can only be appropriately considered in pricing, procurement, and funding decisions if these contributions are measured and described **transparently**. If new evidence relevant for the assessment of clinical effectiveness and safety is collected regularly through a **systematic review** as a standard of policy implementation action, pricing, procurement, and funding decisions can indeed be based on the best available evidence.

A re-evaluation of appropriateness of use and dispensing ensures the link from clinical practice to HTA and reimbursement decisions.

*Implementation considerations*

Policy-makers could do a mapping exercise as to which pricing and funding policies are in place in their country, and how they could integrate HTA in the processes. **Clarity on the type of the HTA** (mini-HTA or full HTA) needs to be reached; for CA-ARTI POCT no full HTA may be needed.

Whenever policy-makers **introduce new pricing and funding policies**, considerations should be made to take the opportunity and link them to a systematic use of HTA.

With regard to the **timing of the re-assessment**, it is beneficial to plan from the beginning to conduct regular assessments at **fixed intervals** (e.g., every three to five years) or based on **defined events** that trigger a re-assessment.

However, the **trade-off between re-assessment and** optimal use of **resources** is to be considered. This could be addressed by a more regular comparative re-assessment of the clinical effectiveness of all CA-ARTI POCT, whereas ethical, legal, social and patient aspects might not need to be re-assessed that frequently.

Re-assessment of POCT is more beneficial if **evidence** is **continuously produced**, which could be a result of managed entry agreements (see Recommendation 6).

## 3.2. Funding: reimbursement and remuneration

Leverage for the use of devices is public funding (i.e., coverage of all or parts of the costs by a public payer such as a social health insurance fund). In the context of CA-ARTI POCT, the term "funding" comprises two components: "reimbursement" and "remuneration" (see Figure 7 and Box 6).

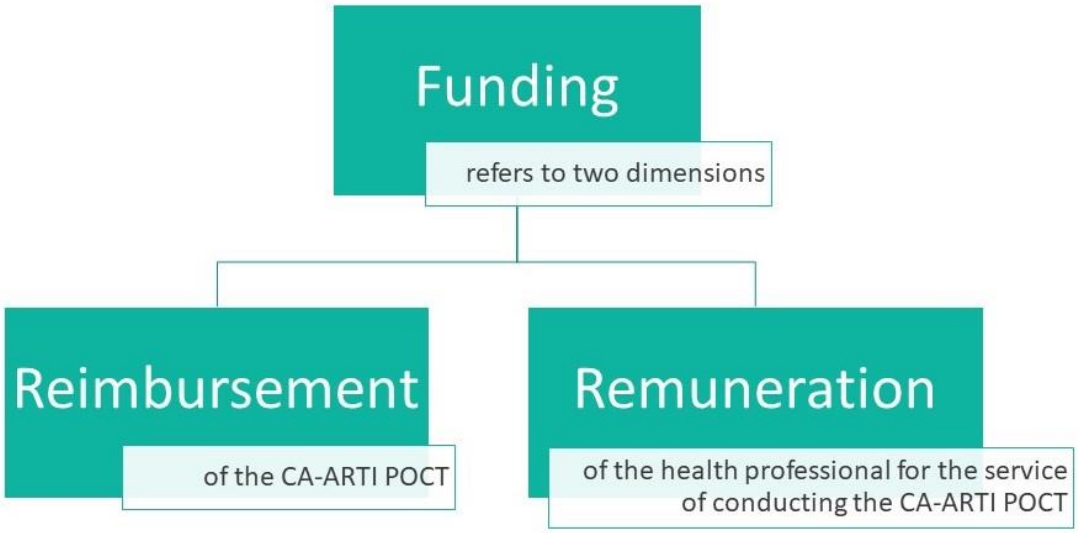



*Figure 7: Funding dimensions*

**Reimbursement** is the **payment for a product:**

- to the supplier, which can be the manufacturer or supplier,
- for the provision of the health technology (e.g., a CA-ARTI POCT).

**Remuneration** is the **payment for the use** of a device:

- to a health care professional, e.g., a general practitioner
- for the application of POCT including administrative tasks, conducting a test, logistics, maintenance of the equipment.

*Source: Vogler and Windisch 2022 [25]*

*Box 6: The difference between reimbursement and remuneration*

The findings on funding for CA-ARTI POCT in the European survey [24, 25] conducted in the VALUE-Dx Task 5.5A, confirmed by the country case studies, showed the following policy situation with regard to funding for CA-ARTI POCT in the outpatient sector (community setting):

- **Product-specific reimbursement** of diagnostic tests for CA-ARTI is applied in few European countries.
- **Remuneration of the health professional for the service of conducting a diagnostic test** is a funding mechanism for CA-ARTI POCT in the community in some countries.

The policy recommendations developed for the area of funding consider these two components of reimbursement and remuneration.

### 3.2.1. Align doctors' remuneration for use of CA-ARTI POCT to consider relevant costs (R4)

*Recommendation 4*

It is recommended to explore applying a more comprehensive tariff approach for doctors which considers remuneration of further cost components that, in addition to the price of a CA-ARTI POCT, incur for their use in an outpatient physician practice.

*Rationale*

Expert interviews suggested that it may not be sufficient to consider solely the price of a POCT for the calculation of the tariff for remunerating health care professionals for their use of CA-ARTI POCT. There are **further cost components** as well as primarily **infrastructure and staff cost** (see Box 7).

**The following cost components may be relevant in GP practices:**

- IT equipment
- Staff (time for applying the CA-ARTI POCT, investment in training)
- Logistics (e.g., transportation, distribution via wholesalers, storage, in GP practice)
- Technical equipment in GP practices for delivering CA-ARTI POCT (e.g., machines to analyse test results plus consumables to run the tests, test kits)
- Time incurred for monitoring and documentation of test results and antibiotic prescribing

*Source: Data collection through expert interviews in the case studies*

*Box 7: Components of infrastructure relevant for CA-ARTI POC testing in outpatient practices*

The **perception of doctors that additional costs would not be sufficiently remunerated** was identified as a potential **barrier** for the uptake of CA-ARTI POCT. This was, for instance, reported from Poland, where further infrastructure costs could hinder doctors to procure and use CA-ARTI POCT. In other case study countries, with high uptake (e.g., Sweden, Estonia), GPs were remunerated for the use of CA-ARTI POCT, including coverage of additional costs, e.g., storage costs or staff time. In Estonia, the remuneration tariffs were adjusted on an annual basis, with the involvement of stakeholders. While experts were careful to stress in the interviews that

remuneration was not sole factor impacting use, it can still constitute an important facilitator or barrier.

*Implementation considerations*

Payers and policy-makers involved in funding decisions need to **understand which cost factors** are **relevant for prescribers**, as basis for designing the tariff scheme to remunerate them. Based on this information, policy-makers can then opt for the most appropriate form of ensuring remuneration for prescribers (e.g., which components of the infrastructure to be funded).

The **cost factors** can be **country- and context-specific** and may differ, e.g., depending on the size of the practice (small or large) or its geographic location (urban or rural area). Overall, this measure is only applicable in countries where doctors are remunerated on a fee-for-service basis for applying the POCT.

**Regular re-evaluations** of the reimbursement tariffs, given possible changes of underlying cost factors, can be beneficial. Defined intervals are helpful from a practical perspective, e.g., it is done annually in Estonia. Furthermore, policy-makers would benefit from a **pro-active approach** to evaluate cost components than rather respond to requests of physicians.

The latter implies establishing a **reporting and surveying system to collect information on a regular basis**. The implementation of a **feedback system** for an exchange between physicians and public authorities on an annual basis, as established in Estonia, can be considered as a good practice example in this respect to defining reasonable tariffs. Communication between physicians reporting actual costs including prices of POCT and costs for application and policy-makers responsible for adjusting the tariffs can be a win-win situation for both parties.

As a word of caution, **any decision about remuneration should be underpinned by careful data and research**. Unintended consequences should be **avoided**, which may, for instance, incentivize **overuse**. In this context, thoughts should also be given to **what equipment is required** to perform CA-ARTI POCT adequately and appropriately. There is no need to equip GP practices (or community pharmacies) with laboratory infrastructure that far exceeds what is necessary for responsible prescribing.

A **variant** of the proposed policy measure (i.e., to adapt the tariff scheme for doctors in a system, in which they are remunerated for this service) would be the **introduction of a separate tariff** for the use of the CA-ARTI POCT in a setting where this had not been in place before. This would be a context in which doctors are solely paid on a capitation basis and/or in which for CA-ARTI POCT no separate tariff has been defined in the remuneration scheme. While feasibility of this measure in such settings is yet to be explored, it may offer **unintended incentives**. One reviewer suggested that, if such a model were introduced, it should be introduced on a pilot basis for a limited period of time, with voluntary participation for physicians and accompanied by an evaluation.

### 3.2.2. Consider linking doctors' remuneration for antibiotic prescribing to use of CA-ARTI POCT (R5)

*Recommendation 5*

It is recommended to explore an adjustment of the tariff scheme for outpatient doctors, by linking their remuneration for the antibiotic prescription to preceding use of a CA-ARTI POCT in defined cases according to guidelines.

*Rationale*

This recommendation is built on the idea to **link remuneration of doctors**, particularly for their antibiotic prescribing, **to the proof of precedent use of the CA-ARTI POCT** where relevant and stipulated in the treatment and prescribing guidelines: Only doctors that first use, when necessary, a CA-ARTI POCT, will be remunerated for prescribing of an antibiotic.

This policy recommendation is guided by positive **experience of financial incentives**, as, for instance, reported from Sweden (however, implemented in a different way, see below). Financial incentives are a signal of public payers in their strategy to address AMR. But it goes beyond as it is intended to sanction doctors financially if they do not comply with treatment and prescribing guidelines.

*Implementation considerations*

The proposed measure is novel and may require major changes in the legislation with regard to medicines and diagnostics.

The feasibility of this measure **depends on the country-specific** organisational and funding **setting of the health care system**, as it addresses the services of the prescription of an antibiotic and use of a companion diagnostic. For example, this measure is not possible in settings where doctors are not remunerated for the service of issuing a prescription, e.g., where employed physicians work in NHS primary health centres.

To ensure successful implementation, **clear and transparent rules and procedures** are necessary, also with a view to prevent potential overuse of POCT. **Treatment guidelines on antibiotic prescribing** need to be accompanied by **exemption criteria** that define the situations in which doctors are permitted to refrain from conducting the POCT. These rules can be laid down in legislation or other regulatory frameworks.

The **documentation system for doctors** to report and justify use, or non-use, of the CA-ARTI POCT, needs to be implemented in a way that it does not lead to additional **administrative burden**.

Furthermore, it needs to be accompanied by **capacity-building and communication** measures.

In countries, where this measure cannot be not implemented given the existing policy framework, **other financial incentives** may be an option. In Sweden, for instance, a premium is paid to doctors for achieving quality indicators such as low antibiotic prescription rates based on POCT in patients presenting with CA-ARTI.

### 3.2.3. Managed-entry agreements with continuous data generation (R6)

*Recommendation 6*

It is recommended to explore use of managed entry agreements (MEAs) to link funding of the CA-ARTI POCT to continuous data generation (e.g., Coverage with Evidence Development, CED) under well-defined conditions.

*Rationale*

There is a need for further research on the use of CA-ARTI POCT, including their (clinical) benefits which may vary across different health care settings, as this allows learnings for further development. However, it is usually difficult to collect data from the primary care sector.

One innovative model could be to develop a funding model that draws from the principles of managed-entry agreements (MEAs), in particular those that link funding to progress, or collection data (performance-based MEAs). MEAs are known from the pharmaceutical sector, where they are used to manage the market entry of medicines with high price tags (to contribute to affordability) and/or to **manage uncertainty** (Box 8).

A managed-entry agreement (MEA) is defined as "an arrangement between a manufacturer and payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions"[55].

These arrangements can use a variety of mechanisms and are usually classified into financial-based and performance-based MEA. Flat discounts, capping and price–volume agreements are examples of the first, whereas the latter include arrangements such as coverage with evidence development, risk-sharing and pay-for-performance schemes). The idea of performance-based MEA is that the health outcomes after some time of treatment affect the funded price (discount) and whether the health technology remains in public funding.

*Sources: Klemp 2011 [55], WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies [56]*

*Box 8: Definition of managed-entry agreements (MEA)*

Since performance-based MEAs can contribute to **generate evidence**, this policy could be transferred to CA-ARTI POCT, with the focus on data generation. In the expert interview, France reported to consider agreeing on **Coverage with Evidence Development** (CED), a performance-based type of an MEA, for medical devices (however, not for diagnostics).

*Implementation considerations*

The idea of MEA is to link funding to conditionalities. In the context of POCT, it may be organised to link either product-specific reimbursement (see also R7) or remuneration for health professionals, such as to doctors, to the collection of needed data in primary care in utilisation of the CA-ARTI POCT, after they have been made available.

While MEAs would be novel for CA-ARTI POCT, MEAs have been applied for medicines in several countries for years. Thus, there are important **learnings** from this field [57-62] that policy-makers can take on board when concluding and using MEAs.

A major limitation of, particularly performance-based, MEAs is their administrative burden. Thus, it is to be ensured that the **administrative burden** related to documentation is not too large for purchasers and health professionals. A trade-off between data collection and resources has to be made.

MEAs are strongly criticized for their **limited transparency**, mainly of the discounted prices agreed, and also of further details of the contracts as well as the generated data. Policy-makers and payers are encouraged not to agree into confidential deals as they have been concluding for medicines (where there is also an interest of manufacturers to price discriminate across countries given the wide-spread use of the external price referencing policy [63], which is rarely applied for diagnostics [24]). Thus, it is important to provide for **transparent processes and outcomes** and to contractually define the **availability of generated data**, i.e., at the time of concluding the MEA contract.

Transparency also implies that **data generated are publicly made available**.

Upon implementation of a performance-based MEA, policy-makers and payers need to closely monitor that **data are actually generated**. Experience from the field of medicines showed that this was not always the case [64, 65].

If data do not meet defined objectives, policy-makers are responsible for stopping funding of the health technology.

Given the novelty of this policy for CA-ARTI POCT, in the starting phase MEAs should be concluded on a **pilot** basis and adopted with first lessons learned.

### 3.2.4. Product-specific reimbursement (R7)

*Recommendation 7*

It is recommended to consider the implementation of product-specific reimbursement for CA-ARTI POCT as an incentive for their uptake. For this policy option, an appropriate policy framework needs to be in place, which includes transparent and clear reimbursement criteria and decision processes regarding the inclusion into reimbursement, and re-assessments.

*Rationale*

The survey conducted in Task 5.5A showed a **limited application of the product-specific reimbursement** for CA-ARTI POCT in the outpatient sector as in the majority of the studied European countries they were not eligible to be included in a positive list, which would provide (at least) public coverage for the included POCT [24, 25].

Reimbursement of a health technology on a product-specific basis (i.e., through inclusion into a positive list) offers an important **incentive for** its **uptake**, as the example of so-called "DRG carve-outs" shows (see Box 9). Though the example relates to mainly medicines and the hospital sector, the same incentivizing mechanism applies.

**How product-specific reimbursement can foster uptake – Example from "DRG carve-out" in French hospitals**

Hospitals are usually funded through a diagnosis-related groups (DRG) funding scheme, and this also applies for French public hospitals. DRG schemes constitute bundled funding, which means that hospitals are remunerated for defined services (procedures), regardless of how much they actually spend on the medicines and medical devices used in these services.

France applies a specific "additional" reimbursement list (so-called "liste en sus") in hospitals for defined medicines and medical devices used whose uptake is aimed to be encouraged. This national list includes medicines with high price tags (e.g., cancer medicines) and also novel antibiotics to foster their use instead of standard antibiotics. This policy, also referred to as "DRG carve-out", has incentivized the uptake of medicines and medical devices that were granted such product-specific reimbursement.

However, in France, inclusion of health technologies on this "additional list" was intended as a temporary measure. After some time, the technologies should be transferred back into the bundled funding scheme, with a view to allowing inclusion of novel products instead. However, in practice, this happens rather rarely, and medicines and medical devices continue to be reimbursed on a product-specific basis.

While it is acknowledged that this example relates to the hospital sector, there are some learnings for CA-ARTI POCT in the community: It highlights the potential of product-specific reimbursement to serve as an incentive to foster uptake, while it also indicates the risk in cases when this measure is not discontinued upon changes of conditions: It may result in increased public spending, as well as potential overuse.

*Sources: Vogler et al. 2020 [66], Vogler et al. 2021 [29]*

*Box 9: Example for product-specific reimbursement from the field of medicines (in France)*

*Implementation considerations*

For implementation of product-specific reimbursement, **well-defined conditions and transparent criteria** are necessary, also to mitigate the risk of overuse.

Systematic collection and appraisal of evidence in **HTA** supports and strengthens the decision on which diagnostics are eligible to be included in the product-specific reimbursement scheme.

Furthermore, the reimbursement list must be subject to **regular monitoring and re-assessment**, which then actually results in the delisting of a health technology for the benefit of novel diagnostics. This needs to be embedded in a **disinvestment strategy**.

The implementation of this policy depends on the health care setting. It is **easier to be introduced in countries where** for other medical devices **product-specific reimbursement is already in place**, and this policy option introduced for CA-ARTI POCT can build on existing rules and processes for other devices. Moreover, there is experience from those areas available to inform policy-makers.

Given the risk of potential overuse (and overspending), as also shown in the example in Box 9, this measure may also be considered to be combined with a mechanism to determine the price on behalf of the authorities and public payers (e.g., price regulation), see also the next chapter (3.3).

## 3.3. Pricing and procurement

Pricing relates to policy action by public authorities to set the price of a health technology (such as a CA-ARTI POCT), e.g., statutorily (e.g., based on a legislation) or through price negotiation [56]. A kind of indirect price regulation is public procurement, i.e., purchase of health technologies such as CA-ARTI POCT, by contracting authorities [56].

Given the linkage between pricing and procurement, recommendations for these two policy areas are presented in this chapter. Two of the three recommendations proposed relate to procurement, since in some countries (e.g., with primary health centres with employed doctors) procurement of the CA-ARTI POCT plays a role.

### 3.3.1. Price regulation to achieve affordable prices (R8)

*Recommendation 8*

It is recommended to explore introduction of price regulation, to make CA-ARTI POCT more affordable and competitive.

*Rationale*

Concern has been expressed in the literature that limited uptake of POCT is linked to their prices, which are high compared to the prices of antibiotics. High prices may limit uptake [35]. Vice versa, as phrased by an expert from a case study country, affordability would encourage the acceptance of health professionals to use the CA-ARTI POCT.

A key policy intervention to **ensure affordable prices** is price regulation, which can be exercised through different pricing policies. The rationale behind pricing regulation is to make prices affordable for those who pay for the health technologies – may these be public payers, health professionals and/or patients (depending on the organisation of the health system, with the possibility of (partial) public coverage for private purchasers).

The opposite of price regulation is free pricing, where the suppliers set the price of the health technology at their discretion [56]. This is the current pricing policy approach for CA-ARTI POCT, i.e., **free pricing, in combination with** indirect price control through **public procurement**. The survey, which was conducted in Task 5.5A, found that free pricing is applied for outpatient CA-ARTI POCT in the 17 studied European countries [24, 25]. In light of the concern about limited affordability of POCT as a barrier to (increasing) uptake, changes in the pricing policy framework in European countries might offer leverage for change.

To make CA-ARTI POCT more affordable and also competitive compared to antibiotics, which appear to be the first option for many prescribers, policy-makers are encouraged to reflect on whether or not price regulation for CA-ARTI POCT could be a policy option to move forward, and to decide which pricing policy would be most appropriate in the respective health care setting.

*Implementation considerations*

In principle, there is a **range of pricing policies**, and policy-makers need to **select** the most appropriate policy. In doing so, policy-makers can draw from the **learnings** in other areas (in particular medicines) in which sufficient experience and evidence on impacts is available (see, for instance, the WHO Guideline on Country Pharmaceutical Pricing Policies [35].

Every policy has benefits and limitations, and, when designing and implementing a policy, it is important to avoid, or at least **mitigate**, **unintended effects**.

In particular, policy-makers are challenged to carefully **balance the trade-off between affordability for the health system and availability**. If suppliers consider (regulated, negotiated or tendered) prices as too low, there is the risk that they perceive the market as unattractive, and decide to withdraw. In managing this trade-off, policy-makers need to consider policy options based on a combination of measures. For instance, potentially lower prices resulting from policy action would be compensated by predictability (through novel procurement models, see next chapters 3.3.2 and 3.3.3) and public funding (instead of patient out-of-pocket payments).

As implementation of price regulation tends to be met by opposition of suppliers, as known from similar situations for other technologies, policy-makers are urged to be well prepared, with an **implementation plan**, which comprises stakeholder information and dialogue at due time.

### 3.3.2. Subscription-based procurement models ("Netflix" models) (R9)

*Recommendation 9*

It is recommended to explore innovative procurement policies, including subscription-based procurement models, with defined volumes that are independent from per unit prices.

*Rationale*

There is an interest to increase uptake of POCT, and this can be supported by several measures, as also described in the other policy recommendations. However, **higher use may likely increase overall spending** for public payers (or patients), given the higher total volumes even if per unit prices might decrease due to competition.

An option to address this challenge is through subscription-based procurement models (sometimes referred to as "Netflix" model) which allow purchasing health technologies with **defined maximum volume, independent from per unit prices**. A defined lump-sum payment can reward use of potentially large volumes of a health technology while offering **predictability** of reward to suppliers and predictability of costs to the health system (public payer). This policy option could be used for low-priced products such as CA-ARTI POCT, especially if the incidence of the disease is high and uptake shall be enhanced.

Experience from practical examples is limited but there are a **few pilots** (mainly for medicines), which are presented in the box below (Box 10). Examples of subscription-based procurement models from England and Sweden relate to **antibiotics** (and were recommended by the Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI) [67, 68]), where

there is interest to keep use as low as needed but provide sufficient reward for suppliers. Other procurement models (hepatitis medicines in Australia and some US states, and AMR laboratory diagnostics in Germany [29]) have been introduced with the aim to encourage use of health technologies at affordable spending for the public payers. Given the focus on increased uptake, the latter can be considered as models to be transferred to CA-ARTI POCT.

Characteristic of subscription-based models is the de-linkage of the price from procured (and consumed) volumes. Such a model offers the benefit that the revenue for the supplier of a POCT and the budget required by the public payer are usually transparent and predictable. Below, four examples of an implementation of this procurement model are presented (three for medicines and one for diagnostics), however with different focus (to compensate industry while keeping uptake low, and other arrangements to ensure higher use at fixed overall spending).

**Hepatitis C medicines:**

**Australia** was a pioneer in developing a subscription-based procurement scheme (later internationally known under the name of "Netflix" or "All-you-can-treat" models).
Australia decided to conclude this procurement agreement to address the objective to eliminate hepatitis C by 2030. Five suppliers of hepatitis C medicines were offered a fixed revenue for treating an unlimited number of patients with hepatitis C medications within a period of five years (from March 2016 till February 2021). In return, the manufacturers were granted a fixed sum (1 billion Australian dollars) for this period of time.

In 2019, in the United States, first **Louisiana** and later **Washington** signed similar five-years contracts for hepatitis C medicines.

**Antibiotics:**

A pilot on a fixed annual subscription fee for market entry and supply of novel antibiotics in **England**, also called "commercial model" was launched in 2019. It has the following features:

- It is based on the concept that the supplier receives a fixed annual fee for granting access to an unlimited volume of antibiotics (if needed).
- The amount of the annual subscription fee was planned to be impacted by the outcomes of an HTA that would be performed by National Institute for Health and Clinical Excellence (NICE). As the standard HTA methodology does not account sufficiently for the particularities of novel antibiotics (see also chapter 3.1.2), NICE was asked to develop a new cost-effectiveness evaluation methodology specific to novel antibiotics.
- The amount paid for such a contract can be up to GBP 10 million per product and year.

After a rigorous process involving expert clinical input, the first two medicines (cefiderocol and ceftazidime with avibactam) were selected for the HTA. Based on the HTA conducted, at the beginning of 2022, the AMR Evaluation Committee made a judgement on the value of the medicines to the NHS, measured in quality-adjusted life-years (QALYs). The conclusions informed commercial negotiations between NHS England and the companies resulting in an agreement of payment levels in subscription-style contracts. The procurement contracts took effect from July 2022.

**Sweden** piloted procurement contracts with an annual revenue guarantee to suppliers of antibiotics used as reserve antibiotics.

- The model aims to make the rather small market of rarely used novel antibiotics attractive for suppliers to ensure access for the population.
- A fixed annual sales volume was guaranteed to suppliers while "guaranteed annual sales" for the antibiotic were calculated based on the cost of a "safety stock", whose price is fixed 50% above the average European list price. Unexpectedly high sales exceeding the

guaranteed annual revenue would be rewarded by a bonus equal to 10% of the "safety stock" price.
- In July 2020, framework agreements were established with five manufacturers for a period of two years.

**Diagnostics:**
There is no example for an explicit subscription-based procurement model for diagnostics, but the regulation in Germany that laboratory diagnostics for antibiotics are exempt from "profitability control" is based on a similar understanding to allow for unlimited, publicly funded use without justification. The "profitability control" implies that prescribers must motivate and justify their prescribing behaviour; an exemption permits unlimited use of these diagnostics without justification.

*Sources: for the models on Hepatitis C medicines [29, 69-71], for antibiotics in England and Sweden [72-75], for the laboratory diagnostics [29]*

*Box 10: Examples for subscription-based procurement models*

*Implementation considerations*

Towse et al. 2017 expressed hesitancy and called for further research on the impact of the subscription-based models before they could be recommended for implementation [76]. Meanwhile, however, experience has been gained, and some **lessons** were learned. The reviewers of this report also had mixed perspectives on whether, or not, such procurement models would be able to deliver intended objectives.

Thus, it is recommended to **launch a pilot** of a subscription-based procurement model with a clear **evaluation strategy** to assess the benefits gained. Furthermore, a **market consultation** can be supportive.

When developing such a procurement model for the CA-ARTI POCT, **the specificities** of these diagnostics are to be taken into consideration.

To maximize benefits for society, **further funding and procurement components** can be included in the design of these procurement models, e.g., continuous data collection, or the procurement contracts are **accompanied by supportive policies**. Australia, for instance, combined the subscription-based procurement model for hepatitis C medicines with managed-entry agreements, and in England, HTA was integrated as a key component (Box 10).

Developing an appropriate subscription-based procurement model has to be based on **detailed estimates** of expected volume and costs. This can be a **time-consuming** exercise but it is essential to model the payments as accurately as possible [77]. Attention should be given to the potential risk that returns could be considered as too low for suppliers, and they would withdraw. At the same time, there are the concern that a de-linkage would incentivize overuse (up to the defined limit). Therefore, policy-makers must carefully design the subscription-based model to balance this **trade-off between limited incentives to suppliers and "over-incentivizing"**. A higher level of **accuracy of predictive data** can help mitigate these two risks.

An **institution** has **to be defined** to negotiate the contract with the suppliers, and it should be ensured that this institution has access to necessary information and estimations. Central

purchasing bodies may be suitable institutions for managing a subscription-based procurement contract.

### 3.3.3. Strategic procurement (R10)

*Recommendation 10*

It is recommended to adopt a strategic approach to procurement which aligns preparation, launch of calls, assessment and award of bids to defined objectives. Moving towards more strategic procurement includes to explore increased use of additional award criteria beyond the price, pooled procurement, market research, tenders awarded to multiple bidders and strategies to mitigate possible shortages.

*Rationale*

**Public procurement** (i.e., defined as all aspects surrounding the process of purchasing by a contracting authority, such as a body of public law (e.g., government, local health authority, or social health insurance institution) or an institution affiliated to the public sector (e.g., not-for-profit institution [79]) has been criticised for **driving down the prices** which risks that suppliers might consider markets as not sufficiently attractive and would withdraw or not offer their product.

While tendering is indeed a **competitive** practice, competition is not necessarily limited to price competition, but other (value and quality related) aspects can also be considered when bids are evaluated. In a more strategic procurement approach trade-offs between different objectives, such as achieving more competitive prices and ensuring long-term availability of products, could be better balanced.

Strategic procurement means that procurement policies and techniques are selected aligned to defined objectives that are aimed to be achieved. Strategic procurement is therefore **not a stand-alone policy but an approach that combines different public procurement practices and even further policies and instruments** (such as HTA, pricing and funding policies, and measures to optimise prescribing, e.g., through treatment guidelines).

One important aspect of strategic procurement concerns the **award (evaluation) criteria**. The concern of price-driven tendering decisions is addressed by the so-called **Most Economically Advantageous Tender (MEAT)** concept, which is defined in the 2014 **EU Public Procurement Directive** [78].

The MEAT criteria approach allows and even encourages **explicit consideration of several criteria (in addition to the price) when evaluating offers and awarding contracts**. While the price is still an important award criterion, it is not the sole decision-impacting factor. Applying the MEAT criteria implies to also **consider further aspects**, such as security of supply, environmental criteria, evidence on relevant aspects from HTA **and** to **weight them appropriately**, aligned to overall (public health) objectives. EU public procurement legislation requires that all criteria and their weighting are defined and published by the procuring institution (see Box 11).

**Background information on MEAT:**
Application of MEAT criteria in public procurement is laid down in the Directive 2014/24/EU of the European Parliament and of the Council of 26 February 2014 on public procurement and repealing (Directive 2004/18/EC) [80]:

*"Contracts should be awarded on the basis of objective criteria that ensure compliance with the principles of transparency, non-discrimination and equal treatment, relative value of the tenders in order to determine, in conditions of effective competition, which tender is the most economically advantageous tender."*

**Possible components of MEAT award criteria:**

- Effectiveness of CA-ARTI POCT
- Security of supply
- Costs or cost-effectiveness, also measurable via a life-cycle costing, which includes all costs over the life cycle of works, supplies or services
- Environmental criteria, e.g., packaging (size and materials used), recyclability, CO2 footprint of production and transport
- Social criteria, e.g., support of a national supplier, providing of employment

*Box 11: Most Economically Advantageous Tender (MEAT) criteria*

Another frequently mentioned element of strategic procurement is **pooled (or joint) procurement**. It creates **larger markets** through economies of scale and increases the **purchasing power** of the procurers while suppliers may benefit from larger volumes which improves **predictability** of orders and facilitates planning capacities.

Pooled procurement across countries is included as one of the procurement techniques in the European Parliament *Directive 2014/24/EU on public procurement and repealing* [78]. It can be implemented by two or more countries on a bilateral basis (for medicines, successful cross-country joint procurements have been achieved by the Baltic countries and some of the Nordic countries, see Box 12). For procurement of medical countermeasures against serious cross-border health threats, countries can conduct pooled procurement through the Joint Procurement Agreement (JPA) of the European Commission.

Pooled procurement usually refers to collaboration **across countries**, but it may also be centralisation in procurement **intra-country**. The recommendation to consider pooled procurement is particularly relevant for **small markets** which may not be considered attractive for suppliers on their own. Small markets exist in countries with lower numbers of inhabitants and in fragmented health systems, e.g., Sweden and Austria, where health care provision is largely the mandate of the regions.

Beyond pooling volumes, joint procurement allows **pooling of capacity and expertise** of participating procurers and can be accompanied by authorities' collaboration in other areas (e.g., joint HTA production, see also the overarching Recommendation 13 in chapter 3.4.3).

**Pooled procurement** refers to the formal arrangement where financial and non-financial resources are combined across various purchasing authorities to create a single entity for purchasing health products (e.g., medicines) on behalf of individual purchasing authorities [35].

**Reasons for and benefits of pooled procurement** [81-83]:

- Small markets that seem to be unattractive to suppliers may be supplied
- Reductions in unit purchase prices and public spending
- Reduction of operating costs and administrative burden (e.g., delegation to central purchasing body), if done wisely (in the beginning there may be increased costs)
- Improved governance in procurement
- Equity considerations (all countries / procurers are treated equally, whereas normally large markets in high-income countries tend to have a better status)
- Rationalized choice through better-informed selection and standardization
- Improved quality assurance
- Eventually improved access to health technologies

**Example for voluntary joint procurement initiatives in Europe are the following:**

- The **Baltic Procurement Initiative** (involving Estonia, Latvia, and Lithuania) conducted several cross-country procurements for vaccines that are in the immunization schedule of at least two of the countries.
- Countries of **Nordic Pharmaceutical Forum** (Denmark, Iceland, Norway) concluded joint Nordic tenders, mainly on "old" hospital medicines. In these tenders, they also piloted new approaches, such as consideration of environmental award criteria.

*Box 12: Pooled procurement – definition, benefits and examples*

*Implementation considerations*

Performing procurement, policy-makers and procurement agencies are advised to offer **incentives for suppliers so that these are interested to bid** in order to avoid a situation of having no or a limited number of bids. Thus, a strategic procurement approach applies a **long-term view** about how to manage the market for the POCT through tenders and further procurement practices.

Strategic procurement has **several components** and when implementing a strategic procurement approach, the full range of procurement tools and practices should be considered. MEAT and pooled procurement form important elements of strategic procurement but there are several others approaches and tools (see Box 13).

**Characteristics of strategic procurement**

- Application of the **Most Economically Advantageous Tender (MEAT) criteria**, i.e., further award criteria in addition to the price
- **Pooled procurement**, i.e., collaboration of public procurers at intra-country or cross-country levels
- **Multiple winner awards,** i.e., division of the market among different suppliers by granting the contract to several bidders (e.g., through defined quota, different conditions) to avoid monopolies and incentivize suppliers to submit bids and serve the market
- Strategically chosen **duration** of the contracts (to manage the trade-off between competition, achieved by contracts of shorter duration, and security of supply, supported by longer-term contracts)
- Transparent and clear **procedures** and rules (contract management)
- Strategic choice of the **procurement practices and tools** (e.g., open tender procedures versus framework agreements), aligned to policy objectives intended to be achieved.
- Linkage to **clinical treatment guidelines**, e.g., as conducted in Denmark and Norway where guidelines published by specialist societies define the prerequisites for the prescription of a medicine or application of a POCT (recommendation based on the most economically advantageous tendered product)
- A well-organised **needs assessment**, based on a realistic assessment on volumes
- Information technology is supportive, and **e-procurement** is a prerequisite for good procurement practice
- Collaboration and **sharing of experiences** of other procurers (e.g., on piloting novel procurement practices and techniques)
- Data collection and analysis of **key performance indicators**
- **Market consultation**, **dialogue** with suppliers

*Sources: WHO Europe (2016), Vogler et al. (2022a), Vogler et al. (2022b), [84-86], expert interviews*

*Box 13: Strategic procurement – examples of key elements*

Strategic procurement is not straight-forward and requires skills and resources. For instance, use of the MEAT award criteria is **challenging and time-consuming**, both **for procurers as well as for bidders**. For procurers, it requires efforts to define the additional award criteria, and their relative importance (weighting). Procurers who aim to value information by applying MEAT may be confronted with the **limited availability of information** on HTA domains and further sources on the value of POCT to substantiate the award criteria.

While use of the MEAT criteria contributes to other policy objectives than affordability (price) of health technologies (e.g., potential societal value of CA-ARTI POCT), policy-makers and procurers need to be aware of a potential **trade-off between the price and further objectives** (i.e., higher prices to be paid in return for operationalization of "value").

Calls which indicate further award criteria (e.g. environmental award criteria) may be challenging for suppliers since they need to supply additional data. **Market consultations** with suppliers before the launch of a MEAT criteria-based call may be helpful for both parties. From the medicines area, there is the good-practice example of the Danish procurement agency, Amgros, which held for six weeks hearings with suppliers before the launch of a complex call for a cross-country tender. In

particular for joint or innovative procurement, it is beneficial to **consult early with suppliers to ensure their participation in tenders**.

For conducting more strategic procurement, policy-makers need to ensure that involved public procurers **build capacity**. Important elements of capacity-building can be **sharing of experience** among procurers and **learnings** from other purchasers, e.g. on pilots.

Policy-makers should acknowledge and be prepared that pooled procurement is challenging to implement, in particular for cross-country procurements where **different legislations** apply. For pooled procurement, it is crucial to decide in the planning phase on a **lead procurer** that is granted the appropriate mandate.

Key learnings from pooled procurement initiatives suggested to **plan much more time** for preparing a joint tender than for normal procurements, e.g., recommended by the central procurement body Amgros for the inpatient sector. Also, **sufficient staff resources** need to be planned.

## 3.4. Overarching recommendations

While this policy document offers recommendations on innovative fit for purpose pricing and funding models for CA-ARTI POCT, the analysis has highlighted the inter-linkage of some of the areas. Thus, overarching action which goes beyond addressing a specific peri-launch policy, and accompanying measures are needed. To account for a broader perspective, five overarching recommendations are proposed.

### 3.4.1. Holistic approach to implement a toolbox of measures (R11)

*Recommendation 11*

It is recommended to adopt a holistic approach to pricing and funding policies for CA-ARTI POCT. In addition to the proposed measures in the peri-launch phase, there is a need for policy actions, including accompanying measures, along the whole value chain.

*Rationale*

The umbrella term “holistic approach” relates to **coordinated action** to ensure that **an intervention in one area is supported by further measures in other areas**, e.g.:

- Inclusion of evidence from HTA into clinical practice guidelines
- Feedback loops for information on security of supply from users, e.g., physicians and wholesalers, to procurers
- Implementation of public awareness programs on AMR and antibiotic stewardship programs in addition of the implementation of CA-ARTI POCT in guideline recommendations
- Annual adjustment of funding to current prices

- Use of evidence from HTA for reimbursement decisions or tenders based on MEAT award criteria
- Early scientific dialogue of payers, HTA bodies and regulators with suppliers and developers to ensure that the right questions are being asked in the trials and any further early interaction between diagnostic developers, academics, regulators, HTA agencies, health system clinicians and payers
- Use of horizon scanning to inform payers and procurers on what is in the pipeline

The holistic approach implies an understanding the **different steps and policies along the value chain from an integrative perspective**, in which one policy follows smoothly onto the previous one or works as kind of gatekeeping, e.g., outcomes of an HTA can impact funding decisions (see the "Nye Metoder" approach in Norway (Box 14) as an example for the implementation of policies that are well aligned in a holistic approach.

**Nye Metoder for the managed introduction of new health technologies in Norway**
The "Nye Metoder" [New Methods] system in Norway ensures a smooth managed introduction of health technologies, including medicines and medical devices, into the health system.
Important tools are the horizon scanning (i.e., systematic identification of health technologies in the pipeline), whose outcomes then determine the type of HTA (mini-HTA, single technology assessment or full HTA) to be conducted. The outcomes of the HTA are important for funding decisions.
*Sources: Documents on "Nye metoder" [87, 88]*

*Box 14: Holistic policy approach along the value chain in the Nye Metoder system in Norway*

The **specificities of CA-ARTI POCT**, with their potential to contribute to more appropriate prescribing, strongly suggest a holistic view on the "pair" of antibiotic and diagnostic ("personalised medicine", see also Recommendation 2 chapter 3.1.2).

*Implementation considerations*

A **clear understanding** needs to be established and promoted that the recommended measures can enhance their impact if applied in a well-designed policy package.

In addition, from a practical point of view, understanding needs to be developed on **how actions can impact other areas**. For example, if evidence from HTA is implemented in clinical treatment guidelines, it should be clear who has the responsibility to implement so. If policy-makers delegate this task to the healthcare professional society, there needs to be clear communication to the society and also sufficient resources need to be provided to fulfil this task.

Among the instruments that are available in the peri-launch phase, there should be a clear understanding that **HTA is a tool**, not a policy to support more evidence-based decision-making in funding and pricing / procurement. Thus, HTA should not be an academic exercise, but inform decisions.

Applying a holistic approach to tackle AMR, any discussion on funding and pricing models would be incomplete without mentioning the **importance of antibiotic and AMR stewardship programs** (see Box 15, and their role in informing and offering capacity-building to professionals and patients (see

also the next Recommendation 12 in chapter 3.4.2 on the importance of stakeholder communication).

**AMR stewardship programs as holistic approaches** have the aim to achieve **responsible use** of antibiotics to optimise antibiotic prescriptions, with an **emphasis on societal implications** instead of focusing on the individual prescriptions [17, 89].

A systematic review by Dyar et al. suggested defining antimicrobial stewardship as:
"a strategy, a coherent set of actions which promote using antimicrobials responsibly" [89].

There are several options how AMR stewardship can be created [89], e.g.:

- By implementing patient monitoring
- By considering what is the most appropriate application form (infusions or orally)
- Taking into account the spectrum of the antibiotic
- By ensuring the diagnosis is appropriate to prescribe antibiotics.

*Box 15: Antibiotic stewardship programs*

Further reflections from a holistic perspective concern the **R&D funding proposals**, thus addressing the pre-launch phase. A novel measure would be a programme similar to the AMR Action Fund [90] that would not only target the development of new antibiotics, but would be designed to **support the joint development of the pair of an antibiotic and companion diagnostics** (e.g., POCT). Such an approach could draw from the learnings of the AMR Action Fund [90] which was developed in collaboration with the WHO, the European Investment Bank, and the Wellcome Trust to ensure a sustainable pipeline of new antibiotics to fight superbugs. The AMR Action Fund was established with the objective to overcome key technical and funding barriers of late-stage antibiotic development.

Policies proposed in this document **add to other measures suggested in other projects** (e.g., DRIVE AB [54]; Joint Action on Antimicrobial Resistance and Healthcare-Associated Infection (JAMRAI) [91], and vice-versa.

### 3.4.2. Communication and stakeholder involvement (R12)

*Recommendation 12*

It is recommended to accompany the recommended measures with appropriate communication activities at relevant stakeholders, including the public, and to involve stakeholders, where appropriate, to ensure acceptance and support of the measures as far as possible.

*Rationale*

There is a large body of evidence on policies in the health system and beyond, which were not successful due to their **non-acceptance or opposition of targeted stakeholders**. To **manage stakeholder reactions**, including potential opposition, information activities, dialogue and involvement is key. In fact, good communication and stakeholder involvement has proven to serve as a **prerequisite for successful policy implementation**.

Stakeholder involvement does not only contribute to acceptance and endorsement of policy measures but can also **improve the quality of implementation** (e.g., expert input to adapt the design of policies).

Some of the proposed policy measures are rather new in Europe or are still in a pilot phase. Given the novelty, health care professionals and further stakeholders may have misperceptions on the concepts and/or are not (sufficiently) informed about the planned implementation steps. Communication and capacity-building helps to contribute to clarity.

*Implementation considerations*

Communication relates to addressing and/or involving of different stakeholder groups as, e.g., patients, physicians, society, professional societies, industry, and public institutions. Ideally, the development of a **communication and stakeholder involvement plan** accompanies each policy planned that is aimed to be introduced and/or changed.

Communication can be considered successful if the relevant information reaches the targeted people. **Structures and processes for feedback from stakeholders** can be built into the communication channel and allow improved **interaction**.

A prerequisite to address the right stakeholders is to know who they are, and which type of input is expected from them. The communication plan benefits from being based on a **stakeholder mapping** in which the different roles and inputs of identified stakeholders have been analysed.

In the communication plan, **different types of involvement** (ranging from information to education and active participation in change processes) can be identified per relevant stakeholder group, which allows developing appropriate measures to ensure the intended type of involvement.

**Early communication and involvement** before implementation of measures is beneficial. Communication and stakeholder involvement includes but is not limited to communication activities in the peri-launch phase, e.g., referring to the early interaction mentioned in recommendation 1 (chapter 3.1.1) to improve stakeholder involvement in HTA between diagnostic developers, academics, regulators, HTA bodies, clinicians and payers. Communication on AMR and the potential of application of CA-ARTI POCT includes also **dissemination and capacity-building activities targeted at the public**, through social media campaigns, public advertising, and providing information material for improved health literacy.

### 3.4.3. Cross-country collaboration (R13)

*Recommendation 13*

While funding, pricing and procurement are national competences of EU Member States, it is recommended to explore collaborative approaches across countries in terms of methodology development, sharing of data and exchange of policy experience.

*Rationale*

In the last years, a move to enhanced collaboration across public institutions of different countries on peri-launch policies and tools (e.g., procurement, price negotiations, as well as HTA) has been observed. Examples for initiatives where countries are collaborating are listed below (Box 16).

**Examples for collaboration of European countries in areas related to peri-launch policies and beyond include:**

- EUnetHTA: methodology development [42]
- Cross-country collaborations joint procurement or joint negotiation for medicines (as described in Box 12), some of them also collaborate in other areas *[81, 82]:*
  - The Baltic Procurement Initiative (Estonia, Latvia, and Lithuania) collaborates in the case of shortages and lends medicines to the other countries free of charge
  - The Beneluxa Initiative also established, as a spin-off, the International Horizon Scanning Initiative and collaborates in the areas of horizon scanning, HTA, pricing and reimbursement (negotiations) and information sharing.
  - The Fair and Affordable Pricing (FAAP) initiative, which comprises countries in central and eastern Europe (Czechia, Hungary, Poland and Slovakia) and aims to perform joint HTA reports and price negotiations.
  - In the Valletta Declaration, ten countries in southern and eastern Europe aim to collaborate on horizon scanning, HTA and price negotiation to increase transparency of information on medicine prices.

*Box 16: Examples of cross-country collaborations on peri-launch policies*

Cross-country collaboration has **strengthened the purchasing power** of the involved countries and has contributed to **more informed decisions and capacity-building**. Furthermore, from a psychological perspective, working together has **inspired** and enhance the motivation of the members in a cross-country collaboration [82]. Despite several challenges (see also below), there have been **good practice experience** of public authorities that have collaborated.

Cross-country collaboration in the health care sector (e.g., on specific policies such as procurement) has been strongly **promoted by supranational institutions** such as the WHO [92, 93] and the European Commission [94].

*Implementation considerations*

Cross-country collaboration does not always require **new processes**; rather, collaboration can be **built on established existing structures**. Indeed, the structures and processes of a country's healthcare system need to be taken into account (Recommendation 15).

Depending on the policy and the type of collaboration (more technical or rather political), **different approaches** can be chosen. Existing **methodological guidance** is key. For example, HTA bodies that collaborate in joint assessments are well advised to follow the structures and guidance documents of EUnetHTA (as described in more detail in Recommendation 1 in chapter 3.1.1 “Enhance the harmonisation of HTA methodology for CA-ARTI POCT based on established guidance (R1)”).

**Phase 1: From need to vision: pre-establishment phase**

- Analysis of benefits and challenges of cross-country collaboration
- Decision on moving forward

**Phase 2: From vision up to launch: setting up a collaboration**

- Securing political support
- Definition of objectives and areas of work
- Establishment of the cross-country collaboration

**Phase 3: Taking action: getting started**

- Definition of the governance structure and working modalities
- Establishment of the working structure
- Involvement of the political level and further relevant institutions
- Analysis of national procedures and legal framework
- Reassessment of contributions and resources
- Strengthening internal communication
- External communication

**Phase 4: From preparation to piloting: cross-country collaborative action**

- Harmonization and overcoming legal barriers
- Performing pilots
- Evaluation of existing work and adaptations

*Source: Vogler et al. (2020) [82] (for the full checklist see pages 28-30)*

*Box 17: Phases within cross-country collaborations and aspects to consider*

In general, for cross-country collaborations different actions are necessary. A **guidance document** has been published **by WHO Europe** [82], which includes a checklist of steps to be followed for each of these phases. Box 19 provides an overview of these phases, and related action.

Cross-country collaboration can be challenging, for a couple of reasons, e.g., different languages and national legislations and procedures, additional work on top of national activities. Key prerequisites are thus secure political support of policy-makers and sufficient human resources [82].

In this respect, **experience from existing collaborations** can be very valuable, e.g., regarding the lead of the cooperation, to which degree responsibility for the impact on the own market is transferred to other partners and other characteristics.

### 3.4.4. Monitoring and evaluation (R14)

*Recommendation 14*

Policy-makers are urged to ensure that implemented policy options are assessed, based on well-defined indicators and regular data collection, as to whether or not they were successful in achieving intended policy objectives. If this is not the case, policy-makers are encouraged to adapt the policies appropriately.

*Rationale*

Depending on the design of a policy measure, the organisation of the health system and external factors from outside the health care sector, **same policies may have different impacts**. Even if a policy or a set of policies may initially be successful in achieved intended policy objectives, their **effect may fade out** after some time, and **adjustments** may become necessary. Thus, monitoring and evaluation is essential and should be followed by further measures, if needed.

*Implementation considerations*

To measure the progress of a policy, its **objectives** that are aimed to be achieved should be specified and operationalised in advance.

Thus, before the development and implementation of a policy measure, **indicators** are to be defined. There is no need to develop a large set of indicators, as there is the trade-off between evidence generation and resources but a few meaningful indicators that are feasible to be continuously collected and regularly analysed is helpful. For the purpose of the policy objectives of the VALUE-Dx project, a key indicator would be to measure antibiotic prescribing (outcome measures, ideally classified by characteristics of prescribers and patients), depending on the use of CA-ARTI POCT. Also, measurement should also consider capturing possible unintended effects, e.g., overuse of POCT in this case.

An **evaluation strategy** should be planned from the very beginning, which clearly outlines the responsibilities regarding who conducts the evaluation and when, to ensure impartial assessment. This strategy may benefit from launching a **structured process to receive feedback** from stakeholders (e.g., to discuss with prescribers their antibiotics prescribing behaviour compared to peer based on a benchmarking exercise).

**Transparent publication of the findings** of the evaluation results allows to share knowledge with a broader audience and to **use the assessment for communication purposes** in a country and across countries. Data from the evaluation can and should be used as basis for adapting policies.

### 3.4.5. Country-specific context (R15)

*Recommendation 15*

When implementing the policy recommendations for the peri-launch phase to improve the uptake of CA-ARTI POCT, it is advised to consider the country's context and to design the measures accordingly.

*Rationale*

There is **no one-size-fits-all policy**, and same policies may lead to different outcomes in different countries.

Interviewed experts emphasized the **importance of the country context** for the success of policy measures, including their acceptance by stakeholders, e.g., by GPs. For example, GPs in Poland were used to be provided with equipment and consumables free of charge by the Ministry of Health, and if additional storage is required, the GPs will be rewarded for the costs. It was reported that Polish GP likely have a similar expectation for CA-ARTI POCT.

Thus, these aspects need to be taken into account in policy implementation.

*Implementation considerations*

As shown in the mapping, funding, and pricing policies for CA-ARTI POCT vary across countries, and even if the same policy is in place, its design may differ. There are also difference in the culture of a health care system, which may result from practices that have been established over many years.

To **consider the respective country setting and relevant country specificities related to CA-ARTI POCT,** an **analysis of the national policy framework** (e.g., a SWOT analysis) and a **feasibility assessment** conducted before implementation of a new policy measures is helpful. It will inform if a new measure can build on an existing framework (as an add-on, which increases feasibility) or if it requires a long-term implementation and major legal, organisational, and funding changes to allow implementation of one measure.

A **stakeholder mapping** is a key component of a feasibility study, as there should be **clarity on the role of involved health care professionals and institutions**.

# 4. Conclusions

AMR is a global public health threat to which the international community needs to respond through a range of measures. One approach is to **encourage GPs to base their antibiotic prescribing on the outcome of diagnostic tests**, in particular rapid POCT in the community care setting, with a view to ensuring that antibiotics are only prescribed when needed. The VALUE-Dx project aims to support improved uptake of CA-ARTI POCT. In Task 5.5B of this project, recommendations for national policies in the peri-launch phase were developed to contribute to improved availability and affordability of CA-ARTI POCT.

Research conducted as basis for the development of the recommendations has identified several **barriers** that hinder appropriate use of CA-ARTI POCT in the outpatient sector, and some of these are related to the **underlying pricing and funding policy framework** in the European countries. For instance, in several countries prescribers are financially disincentivized to conduct a POCT (e.g., costs to cover the price of the diagnostic, staff costs, logistics) compared to prescribing a (low-priced) antibiotic without a test.

The study identified **seven policy options in pricing and funding** that policy-makers could explore to encourage the use of CA-ARTI POCT. Importantly, these **measures are not mutually exclusive**, and several of them could be **combined to reinforce their impact**. To compensate for possibly lower prices of POCT resulting from price regulation, suppliers could be granted reimbursement (i.e., public funding) for the POCT, potentially supplemented by an innovative procurement arrangement, which allows predictability on a fixed volume range, to name one example of a policy mix. One of the proposed innovative policy measures, whose feasibility is yet to be proven, would even target the funding environment for medicines, as it suggests to remunerate doctors for an antibiotic prescription only if its need was confirmed by a CA-ARTI POCT, a companion diagnostic, used in line with guidelines.

To stress the importance of the inter-linkage between the measures, this document additionally offers **recommendations on HTA**, which is a tool for evidence generation and appraisal to support pricing and funding decisions, and **some overarching considerations**. The latter include the reminder of the **country context** for any implementation of a policy measure. For instance, countries that grant product-specific reimbursement for other medical devices, ideally for IVD, are in a better position to extend this model to CA-ARTI POCT than countries whose funding does not include reimbursement for any medical device. Moreover, **some measures may not be appropriate in certain country contexts**. For example, financial incentives (or penalties) for prescribers are not relevant in systems where primary health care is provided through health centres with employed doctors, whereas these clauses could typically be included in a contract between the doctor and the public payer.

While in this report the reinforcing character of the recommended policies, where feasible, is emphasized, policy measures were deliberately **not ranked**, given assumed limited feasibility of some measures in certain country contexts. Due to the heterogeneity of health systems in Europe the recommended policy measures address various challenges in the peri-launch phase, which may be relevant in one country but negligible in others.

Even if the implementation of some of the recommended policy options may be difficult or even **not feasible in certain settings**, they were nonetheless tabled, with the aim to trigger the discussion and offer policy-makers a range of options to select from, or at least, to reflect on. The assignment for this deliverable was to propose innovative pricing and funding models, and the authors believe that a **future-proof set of policy recommendations** benefits from inclusion of policy options whose implementation is not routine but may require major changes in the organisation and funding of a health care system. There is no guarantee that all proposed policy measures, even if successfully implemented, would always achieve the intended objectives but there is **leverage for policy-makers to learn** (through evaluation) and **adapt policies** in case of unintended developments.

Despite their relevance, pricing and funding measures to encourage use of CA-ARTI POCT are only one component of AMR-related policies. They complement several other approaches, some of which are ongoing, such as AMR stewardship programs and incentives for research of novel antibiotics. Ultimately, it requires efforts from different policy domains to tackle AMR.

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# 6. Appendix

Table 2 and Table 3 include the barriers and facilitators for CA-ARTI POCT uptake derived from the expert interviews.

*Table 2: Barriers for the uptake of CA-ARTI POCT in the outpatient sector*

| | BARRIERS | SOURCE |
|---|---|---|
| **Key dimensions** | | |
| **HTA / Benefit assessment** | HTA for diagnostics is not uniformly regulated, usually there is no comprehensive HTA for diagnostics | Expert interview PL |
| | No or scarce evidence base for describing the necessity and benefit of POCT | Expert interview PL |
| | Limited clinical data, no tradition to collect data in this area<br>Patient benefit often unclear<br>Limited expertise (interest) to produce data | Focus group FR |
| | Methodological problems in assessing the value of tests or Dx, which is uncommon and knowledge on interpretation is missing | Focus group FR |
| | No uniformly defined HTA process for in vitro diagnostics; depends on regions whether HTA is conducted -> differences between regions and additional effort due to assessment by several regions in parallel | Expert interview SE |
| **Pricing** | MoH defines fixed price dependent on products already on the market<br>-> Raised costs for developing Dx are not considered | Expert interview PL |
| | Price regulation in terms of a reference price system (RPS) in which the Third-Party Payer (social health insurance or national health service) determines a maximum amount; increased development costs for POCT are not compensated. | Focus group FR |
| | Expensive set-up, maintenance, and consumables | Expert survey AT |
| **Funding** | No consequences to physicians if POCT are not performed or if physicians must bear the cost of POCT<br>-> disadvantage by using POCT | Expert interview PL |
| | Long-term funding for local groups involved in national strategic programme against AMR (STRAMA)<br>Major hurdles and funding problems until the STRAMA program was implemented and financed. | Expert interview SE/STRAMA |
| | Separate reimbursement schemes (for procedures and not individual products) as funding of the products is included in the remuneration of health care professionals | Focus group FR |
| | Reimbursement of diagnostic tests would require an adaptation of the reimbursement system Lack of dedicated diagnostics budget | Focus group FR, Plun-Favreau et al. [95] |
| **Procurement** | Regions negotiate individually with manufacturers on pricing, reimbursement and procurement<br>-> untapped potential for collaboration | Expert interview SE |
| | Usually the MoH is responsible for procuring, storing, and paying machines and Dx<br>-> Expectations also for POCT on antibiotic susceptibility | Expert interview PL |
| | Tedious tenders necessary for procurement | Expert survey AT |

| | BARRIERS | SOURCE |
|---|---|---|
| **Other dimensions** | | |
| **Budget Impact** | Antibiotics are comparatively cheap, and diagnostics are relatively expensive | Hillock et al. [96] |
| **Awareness and knowledge on AMR and antibiotics** | Knowledge gaps on the ineffectiveness of antibiotics in viral infections. (not directly related to POCT but missing awareness is a barrier to the perceived need for the use of POCT prior to antibiotic prescribing) | Focus group FR |
| | Limited knowledge of physicians on AMR and Dx | Focus group FR |
| | Culture and decision support tools required for treatment and to confirm results. | Expert survey AT |
| **Treatment guidelines** | Testing before antibiotic use is not included in the guideline as mandatory but an option | Expert interview PL |
| | AMR topic is situated between diagnosis and treatment – no clear specification and thus not an attractive area for GPs and motivation for a guideline update is not there | Expert interview PL |
| | Not a barrier per se, but there were indications of a variety of Dx, with possibly varying usefulness, being available. Thus, there is potential for selecting the most useful Dx and guiding GPs decision to use those. | Expert interview EE |
| | Useful for viral infections, limits the use of antibiotics | Expert survey AT |
| **Responsibility for the topic** | No responsible institution on a national level to push the topic in health policy, Area not interesting for GPs | Expert interview PL |
| | Specialist association leads updates of clinical guidelines (clearly defined responsibility) | Expert interview EE |
| **Acceptance of POCT and its use** | Acceptance of patients and physicians to apply POCT is low if patients have no symptoms | Fuller et al. (2019) (other disease area) |
| | Especially in publicly funded practices in rural areas low acceptance by healthcare providers to apply POCT due to extra effort and there is no need to use Dx for funding of antibiotic therapy | Expert interview PL |
| | No motivation for GPs to apply POCT due to a lack of financial incentives and GPs are remunerated through a capitation fee. | Expert interview PL |
| | Highest acceptance among healthcare providers with POCT with very little hands on time | Expert survey AT |
| **Infrastructure** | Perceived low number of GPs and too many patients per physician. GPs do not have sufficient time for separate services (e.g., testing – only done by few outstanding GPs) | Expert interview PL |
| | SHI would need to equip all public practices with machines and IVD needed for testing (as common in Poland) | Expert interview PL |
| | Potential for use in emergency rooms, paediatric outpatient clinic | Expert survey AT |
| **Access and extra effort for physicians/users** | Space and cost for storage are a problem, especially for small practices | Expert interview PL |
| | Easy POCT with rapid and reliable results would be appreciated by doctors | Expert survey AT |

| | BARRIERS | SOURCE |
|---|---|---|
| **Surveillance and Feedback to clinicians** | Current existing international and national surveillance systems do not meet all the needs and expectations of policymakers, public health workers and researchers related to POCT. Large heterogeneity across countries in the levels of surveillance systems with respect to:<br>• quality and nature of data collections<br>• data source and sampling frame<br>• state-of-the-art microbiological diagnostics and the ability for early detection<br>• quality of antimicrobial susceptibility testing<br>• availability and quality of national reporting systems.<br>Systems do not cover all components of One Health - only a few surveillance systems contain molecular and genotyping analyses or details on patient outcome. | JPIAMR [97], p. 23 |
| | Raise awareness on need for robust data | Focus group FR |
| | No feedback from national institutions monitoring surveillance and prescribing behaviour of antibiotics to GPs on their own performance in comparison to peers at all | Expert interview PL |
| | No systematic documentation in outpatient sector | Expert interview PL |
| | There are no resources in the health system provided by the Ministry of Health to finance antimicrobial stewardship and surveillance in the outpatient sector | Expert interview PL |
| | There is a negative impact on participation in national and European surveillance activities if there is no compatibility with either laboratory information system or documentation system in hospitals or documentation software in the outpatient sector | Expert survey AT |
| **Veterinary and agriculture** | Exclusion of the area for the application of diagnostics since spread of AMR via animals and food is also part of AMR transmission | STRAMA [98] |

**Abbreviations:** AMR: antimicrobial resistance; CA-ARTI: Community-acquired respiratory tract infections; Dx: diagnostics; HTA: Health Technology Assessment; POCT: Point of care test; SHI: Social health insurance; STRAMA: the Swedish strategic programme against antibiotic resistance; AT: Austria; EE: Estonia, FR: France; SE: Sweden; PL: Poland.

*Table 3: Facilitators for the uptake of CA-ARTI POCT in the outpatient sector*

| | FACILITATORS | SOURCE |
|---|---|---|
| **Key dimensions** | | |
| **HTA / Benefit assessment** | Push for Coverage with Evidence Development (CED) schemes ("forfait innovation", RIHN) in recent 5 years to grants early access to innovative devices (including diagnostics) while generating clinical data. At the end of the CED period a definite reimbursement decision is made. | Focus group FR |
| | No HTA for antibiotic susceptibility POCT necessary<br>-> enables fast market access | Expert interview PL |
| | Encourage and support Dx manufacturers in producing clinical data (capacity-building, supported by pharmaceutical manufacturers;<br>new EU regulations will trigger a push towards new clinical studies for Dx to solve the challenge of limited availability and access to robust (comparative) clinical data for diagnostics | Focus group FR, IVD Medical Devices Regulation (EU) 2017/746 (IVDR) [22] |

| | FACILITATORS | SOURCE |
|---|---|---|
| | Challenges in the assessment of the real impact on patient improvement or the assessment of a multiplex PCR that screens for multiple pathogens at the same time | Focus group FR |
| | Importance of actions on a national level:<br>France has initiatives (by HAS in 2022) to focus on the assessment of different Dx and by involving all stakeholders, inter alia a strategic plan to reduce AMR | Focus group FR |
| | Stakeholder involvement at an early stage in HTA and, where applicable, in research and development of new tests, e.g., by consulting physicians on practical issues related to Dx application | Focus group FR |
| | Early Scientific Advice for manufacturers:<br>HAS offers Early Scientific Advice for MD, including diagnostics, if requested by manufacturers ask for it. Aim is to support manufacturers in the HTA by giving feedback if the health technology is mature enough and clinical evidence is sufficient for HTA.<br>-> Time and cost savings | Focus group FR |
| | Availability of high-level evidence on the effectiveness and cost-effectiveness of CA-ARTI POCTs application prior to antibiotic use would be beneficial if evidence can be implemented in clinical guideline recommendations (e.g., S3 guideline) | Expert survey AT |
| | HTA has not been addressed as challenge but most Dx are imported from other countries, and, therefore, the POCT have already been assessed in other countries. | Expert interview EE |
| | Industry collaborations:<br>Maybe potential in liaising diagnostics manufacturers with pharmaceutical manufacturers (e.g., for companion diagnostics), who have experience in this field. | Focus group FR |
| | Best practice: Joint Rapid Effectiveness Assessment on EU-level according to EUnetHTA standards conducted by HIQA (Ireland) with collaboration of Austria. Short version of HTA on POCT for CA-ARTI has been published in German | Expert survey AT [48] |
| **Pricing** | National price negotiations within the scope of the reimbursed amount; possibly even at European level | Expert interview SE |
| | Price cap for Dx<br>-> no price increases by wholesalers possible | Expert interview PL |
| | No separate pricing negotiations since most Dx are imported and prices are regulated by the European market. No need for specific pricing policies. | Expert interview EE |
| **Reimbursement** | No reimbursement eligibility for treatment of respiratory tract infections if no diagnostic test performed | Expert interview SE |
| | “Subscription-style” payment model (test phase in the UK) | NICE [73] |
| | SHI reimburses defined fixed price for POCT, which are included in a list of registered medical devices, to GPs. | Expert interview PL |
| | Significant impact on health care costs | Expert survey AT |
| | Well-designed process of inclusion of Dx into reimbursement (including remuneration for services to use Dx offered by the health care provider) | Expert interview EE |
| | Funding for Dx and its use (reimbursement list) | Expert interview EE |
| | Possibility to evaluate MD (including (CA-ARTI)-Dx) before including them into reimbursement | Expert interview EE |
| | Stakeholder involvement in the reimbursement process | Expert interview EE |
| | Possible facilitator: not only the Dx per se is reimbursed but the GPs / health professionals are remunerated for providing the service | Expert interview EE |

| | FACILITATORS | SOURCE |
|---|---|---|
| | In case of tariffs (reimbursement) that are considered to be too low, health care professionals can address the third-party payer to negotiate updates tariffs – close interaction between health care providers and public payer (why? Investment of EHIF into good communication culture, small country?) | Expert interview EE |
| | Reimbursement is not a challenge since funding is adapted continuously to actual costs via feedback interviews from physicians and health care system can afford it. An idea for the future is to limit reimbursement to the more useful test. | Expert interview EE |
| **Procurement** | Easy accessibility of Dx via wholesalers | Expert interview PL |
| **Other dimensions** | | |
| **Budget Impact** | National procurement and framework contracts for diagnostics that cap costs and do not create a budgetary disadvantage for frequent users of Dx | Hint from expert interviews SE, EE, and other sources |
| **Awareness and knowledge on AMR and antibiotics** | Informed patients and physicians, who know about risks related to unnecessary antibiotics use<br>Overcome behavioural and socioeconomic barriers | [97] |
| | Improving public awareness and knowledge, e.g., by online accessible treatment recommendations, regular press releases to the general public on consumption and resistance, information leaflets in different languages (also for immigrants), web-based educational materials on antibiotic use for clinicians, the public, and parents of new born children; targeted information on a local level for pre-school children and elderly | [98] |
| | Previous crises that have caused a shift in public thinking<br>Presence of AMR and overuse of antibiotics in the media and in public spaces<br>Awareness campaigns on the European antibiotic awareness day | STRAMA [98] |
| | Small country, but excellent health care because quality standards and treatment guidelines are followed by physicians. | Expert interview EE |
| | High awareness in the society and among practitioners for the risk of AMR and the importance of reducing antibiotic use | Expert interview SE |
| | Raise awareness with health professional on the benefits of tests | Focus group FR |
| | Implementation of National Reference Centre for AMR<br>Increase knowledge and awareness of physicians by improving education | Expert interview PL |
| **Treatment guidelines** | Strong recommendation to use point of care diagnostics prior to antibiotic prescribing as part of treatment guidelines | Expert interview SE |
| | A statement by SHI that that correct antibiotic prescribing is required | Expert interview PL |
| **Responsibility for the topic** | Institutionalization of accountability: STRAMA program; advocacy group consistently places the issue of AMR reduction in professional circles and in the media; Great commitment by volunteers to give voice to the issue of AMR | Expert interview SE |
| | Importance of national targets, e.g., regarding number of prescriptions in outpatient care.<br>-> Quality indicator must be based on treatment guidelines | STRAMA [98] |
| **Acceptance** | Acceptance is higher if it is explained to patients why they have to wait for the result | Fuller et al. (2019) [99] |
| | Affordability (defined as funding higher or equal to costs) of consumables increases the acceptance of healthcare providers to use POCT | Expert survey AT |
| | High readiness in the medical community and among patients for pre-diagnostics | Expert interview SE |
| | Early dialogue, early scientific advice, and involvement of all stakeholders | Focus group FR |

| | FACILITATORS | SOURCE |
|---|---|---|
| | "Premium" practices use POCT prior to antibiotic prescriptions to apply good practice for receiving ISO certificate as competitive advantage | Expert interview PL |
| **Infrastructure** | Sufficient infrastructure for testing, e.g., laboratory capacity and staff capacity for testing, for which there is adequate funding | Expert interview SE |
| **Access and extra effort for physicians/users** | Incentives: bonus payment for the treating person if few antibiotic prescriptions are issued | Expert interview SE |
| **Surveillance and Feedback to clinicians** | The use of diagnostics and detection of drug susceptibility will support rational clinical decision algorithms leading to a targeted, more sustainable use of antimicrobials and improved tracking of AMR. | JPIAMR [97], p. 22 |
| | "stewardship programmes" and monitoring antibiotic prescriptions on a national level and on county level (mainly voluntary reporting on local level via laboratories) | STRAMA [98] |
| | Regular feedback or reporting to care providers (e.g., monthly) on their performance so that they can compare their prescription numbers with peers and see their own numbers in perspective; operationalized outcomes can be used for financial incentives for good performance | Expert interview SE, STRAMA [98]; Juszczyk et al. [100], Gulliford et al. [101] |
| **Veterinary and agriculture** | Establishment of POCT in other areas where antibiotics are used, e.g., factory farming | STRAMA [98] |
| **Miscellaneous** | Resistant germs keep entering the country via travellers. AMR control would have to be intensified in other countries to reduce this risk. -> Potential for European approach | Expert interview SE |
| | Additional monitoring of travel, trade, food, and animal transmissions | STRAMA [98] |

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