Making Informed Decisions

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CHAPTER

11

General Discussion

Principle findings of this thesis

Part I: aspects of tests in practice

In part I of this thesis I considered economic aspects of three different settings where tests play an important role. The School Health System (SHS) provides an important framework to reach children from a young age and screen them for various illnesses, as well as to educate them on health-related matters. Although the tasks of the SHS vary between countries, in almost all European countries school doctors and nurses screen for height, weight, vision, hearing and dental problems. The majority of countries also include vaccinations, infection control and hygiene[56]. In a recent survey on the SHS, many professionals in this field indicated that a shortage of staff is a problem[56]. In chapter 2, a survey was sent out to professionals in 31 countries to estimate the number of staff and their salaries, which were expected to be the main driver of SHS expenditure. Additionally, I looked at various online sources, such as published literature and online sources such as the system of health accounts[60]. However, I was able to make an estimation on SHS expenditure on workforce for only five countries. Per 1,000 pupils, I estimated this to range from €43,000 in Estonia to €195,300 in Norway (corrected for purchasing power parities). This constitutes a minor part in total spending on healthcare: 0.16% - 0.69%. I conclude in chapter 2 that there is the major gap in knowledge regarding the spending on SHS in Europe, which may be problematic in light of the maintenance and further development of SHSs across Europe. Chapter 3 focusses on the costs associated with two outbreaks of vancomycin-resistant *Enterococci* (VRE) in the University Medical Center Groningen (UMCG). I used data from various sources in the hospital as well as interviews, to identify and quantify the costs resulting from tests, closed beds (opportunity costs), cleaning, additional personnel, and patient isolation. During the first outbreak, in 2017, tests were the major driver of the outbreak-related costs, constituting almost two thirds of the total costs. However, the second outbreak in 2018 was much shorter than the first: due to an early and aggressive screening, the outbreak was detected in an early stage and quickly controlled, reducing the clinical impact of the outbreak and the total costs. This illustrates the importance of using tests to have a good overview of the pathogens carried by patients. In chapter 4, I looked at a very specific case: periprocedural management for patients on vitamin K antagonists (VKAs). I combined various data sources in one model: INR changes, which are monitored intensively in these patients, and various risk scores for bleeding and strokes. These risk scores are applied commonly in clinical practice and combine data from various tests, such as blood pressure, INR and renal function, but also patient characteristics such as age and sex[111,411]. Around five days before a surgical procedure, VKA treatment is interrupted if the procedure-related bleeding risk is high. Bridging therapy may aid in this period of interrupted treatment to prevent strokes, but also significantly increases the bleeding risk[109]. I developed an easily interpretable matrix which can guide clinicians in their decision to bridge or not to bridge, considering the quality-adjusted life expectancy. The results predict that for patients at high risk of bleeding, bridging therapy is highly unlikely to be beneficial. For patients with a low risk of bleeding and a very high risk of strokes, I found a significant benefit of bridging. However, these patients are expected to be very rare, as most patients at a high risk of stroke will also have a high risk of bleeding. This modelling study is an example on how data gathered using various tests can be combined to optimize patient management.

Part II: methods to assess the value of diagnostics

The value of diagnostics, primarily of respiratory-tract infections, was the focus of part II. This includes the value for money, or the cost-effectiveness, but very specifically also

the value in containing, or even reducing, antimicrobial resistance (AMR). In chapter 5 I reviewed 70 health-economic analyses of diagnostics for infections of the respiratory tract, covering influenza, pneumonia, pharyngitis, and tuberculosis, among others. Most included studies used relatively simple models to assess the cost effectiveness, such as decision trees, with short time horizons and non-generalizable outcome measures, instead of quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs). AMR is also an important aspect in this area that was only included in a minority of the papers, mainly three approaches were used for this: adding a 'societal cost' to all antibiotic prescriptions; assuming a fixed percentage of infections were resistant; or dynamic resistance, varying over the modelled time horizon, e.g., using antibiotic consumption. Considering health-economic guidelines, there is room for improvements in the model design and reporting of CEAs of diagnostics[50]. To aid in this process, I provided eight recommendations in chapter 6, which were linked to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist and reference case for economic evaluation[50,238]. The symptoms patients experience, the clinical setting, locations of test sampling and analysis, and diagnostic algorithms should be clearly reported. The used time horizon should reflect the time horizon used to model the treatment after the diagnostic pathway. QALYs or DALYs should be used as the clinical outcomes, but may be combined with other relevant outcomes, such as real options value. If the number of tests using the same equipment can vary, the economy of scale should be considered. An understandable graphical representation of the various diagnostic algorithms should be provided to understand the results, such as an efficiency frontier. Finally, the budget impact and affordability should be considered. Many of these recommendations were applied in chapter 7, where I assessed the value of hypothetical POC tests in primary care in the Netherlands. Even though bacteria are estimated to cause a minority of community-acquired acute respiratory tract infections (CA-ARTI) cases in Europe, CA-ARTI are a major driver of antibiotic consumption in primary care, accounting for around 40% of all antibiotic prescriptions by general practitioners (GPs)[262]. We aimed to quantify the investments required for a large-scale rollout of improved point-of-care diagnostics in Dutch primary care effective at reducing antibiotic prescriptions. We developed a model that simulates consultations for CA-ARTI at GP practices in the Netherlands and compared a scenario where GPs test all CA-ARTI patients with a hypothetical diagnostic strategy to continuing the current standard of care for the years 2020-2030. The simulation was run in the newly developed Modelling the Economics of Respiratory tract Infections and AMR (MERIAM) model, an individual-based simulation model for CA-ARTI. MERIAM is an innovative model which enabled forecasts of AMR, focussing specifically on predicting resistance of *Streptococcus pneumoniae* to penicillins, which are the most prevalent cause of bacterial CA-ARTI and most prescribed antibiotic[17,263,266]. The diagnostic algorithm increased the total costs of GP consultations for CA-ARTI with 7.7% or with 18% over 10 years, at price points of €5 or €10 per consulting patient, respectively. In these simulations, the forecast increase in resistance of *S. pneumoniae* resistance against penicillins would be partly contained.

Part III: improving development, assessment, and financing

In part III, I considered the development, assessment, and financing of tests in the healthcare system, partly by looking to other fields. Chapter 8 concerns a memorandum of initiative, which was submitted to the Dutch *Tweede Kamer* (Parliament) and minister of health by a member of parliament. This memorandum promoted the application of real option analysis (ROA) for strategies used to counter infectious diseases. Its primary focus was on new vaccines and antibiotics, but the proposed framework could be used to consider the development, assessment, and implementation of various microbiological

tests as well. ROA can aid decision makers in considering time and scenarios. Decisions in healthcare are rarely 'yes' or 'no' questions, they can be regarded as 'right now' or 'maybe later' questions. ROA can be used to value specific investments, even if they are not used or needed immediately. A common (and very Dutch) example would be a dike: dikes are not built for common water levels measured every year, they are built for extreme floods, which may occur once every millennium or even less frequently[412]. I argued that a similar perspective is required for the inherent uncertainty regarding infectious disease outbreaks, whether this concerns a pandemic or the development of multi-drug-resistant bacteria. For vaccines this means we should invest in the development of platform technologies which can be tailored to new diseases, regarding the assessment, we need to consider various scenarios regarding the incidence of the disease against which a vaccine protects, and regarding the procurement, we need to consider the availability of various types of vaccines during outbreaks. For novel antibiotics, we should incentivize the pharmaceutical industry to invest in research by offering subscription services to antibiotics that are 'saved' for when we need them. Finally, for our testing infrastructure, ROA can be used to assess the value of an AMR monitoring programme, an early-warning system for potential pandemic diseases or the value of being able to screen the whole population in case of a pandemic. In chapter 9, I considered the EF methodology, using a model for a novel drug to treat heart failure: sacubitril/valsartan. The EF approach is a method to assess the cost effectiveness of interventions; in Germany the EF is the primary method to decide whether a new intervention is cost effective[323,324]. The EF has the advantage that, next to QALYs, many different types of outcomes can be used, and that the willingness-to-pay threshold is derived directly from the frontier, which means decision makers do not need to set a threshold. A major disadvantage of this technique was also illustrated in this chapter, which is the difficulty to compare a novel, innovative strategy (such as sacubitril/valsartan) to established, much less expensive, strategies. In this case, an EF could not be created, and the willingness-to-pay threshold could not be established. The main advantage of this method in the field of diagnostics is to compare and visualize various diagnostic algorithms, using various outcomes relevant to the decision problem. I believe this approach can be used in addition to the standard methods in health economics, such as the incremental cost-effectiveness ratio (ICER) and cost-effectiveness acceptability curves (CEACs). In Chapter 10, I proposed a tripartite insurance model (TIM) to create incentives to prevent outbreaks of resistant infections in the hospital setting, by connecting the hospitals, laboratories, and a casualty insurer. If the TIM is applied, the hospital negotiates a lump-sum contract with a laboratory to run the microbiological tests in the hospitals, including screening and diagnostics. This removes a barrier to run a test for clinicians, as they do not have to pay for each individual test. At the same time, the hospital acquires an insurance for the risk of outbreaks, so that part of the costs discussed in chapter 2, such as the opportunity costs of closed beds, are reimbursed in case of an outbreak. This introduces an incentive for the insurer to minimize this risk: the insurer contracts the laboratory to audit the hospital regarding the implementation of infection prevention measures. In this model, the laboratory is not just analysing the test samples, it also provides expertise regarding the interpretation of the results. As discussed in the chapter, many questions remain to be answered and an implementation trial would be beneficial to further develop the TIM.

Key messages

This thesis uses examples from a broad collection of tests to research the health-economic aspects of testing strategies: from simple tests at primary schools to advanced genetic tests

used in the hospital, to clinical algorithms used by clinicians which are basically free to implement. Screening can be used for the whole population, as is the case for the various tests included in the SHS, or for very specific groups, for example to prevent the spread of VRE through the hospital. When antibiotics are considered, diagnostic tests offer value as they can lead to more appropriate prescriptions[267] and, in time, reduce AMR[275,288]. Finally, monitoring can be done to optimise treatment for an individual patient, but also for the benefit of the whole population, where tests can inform public health decisions, for example related to AMR or infectious diseases capable of causing large-scale outbreaks. The testing infrastructure and organisation is an essential part of our healthcare system. To prioritize decisions and further improve this area, it is critical to have a better overview of these organisational aspects, regardless of whether this is performed within the SHS, at POC or within a large-scale laboratory.

As testing does not provide direct improvements for patient health in most cases, different ways to assess its value may be required. When considering the economic value of diagnostic testing using CEAs, there are some specific issues to be addressed. CEAs are usually used to assess mutually exclusive strategies; however, diagnostic algorithms offer a lot of flexibility not applicable to many other strategies in healthcare. Diagnostics within these algorithms can be combined in various ways, either sequentially or simultaneously, they can be sampled and analysed at various locations, e.g., at POC or within a large-scale laboratory, and they can be followed by several treatment options. The specifics of these algorithms can affect both the costs and the outcomes of the CEA and therefore, the characteristics should be reported in a transparent manner. To compare various diagnostic algorithms, the EF approach can be helpful.

New European regulations: risks and opportunities

In the next few years, we may see the effects of the new regulations from the European Union (EU) for market entry of non-pharmaceutical medical innovations: the medical device regulation (MDR) and in-vitro diagnostics regulation (IVDR). They aim to improve patient safety by requiring more robust clinical evidence before a new product can be brought to market. Patient safety is important - most would agree that the example in the introduction of this thesis should be avoided[45] - but these new barriers may also limit patient access to new technologies. The collection of clinical data can be expensive and takes time. During crises, adapting to new situations quickly is essential. An example is the PCR test developed by the University Medical Center Groningen during the VRE outbreak of 2017, as discussed in chapter 2. Initially, a commercial PCR device was used to sequence patient and environmental samples, however, this device only had 16 slots and required a lot of manual labour. During the outbreak, an alternative approach was developed, which could be analysed on regular PCR devices using an automated approach. Although the IVDR has an exception for diagnostics used solely within health institutions[413], whether this approach would still be feasible under the IVDR remains to be seen - this legal question certainly is outside of the scope of this thesis. For the COVID-19 pandemic, EU countries could approve the use of specific tests for use within their country as an emergency response[414]. Very early in the COVID-19 pandemic, PCR tests were able to identify infected patients, but of course these methods had not gained market entry under the IVDR. Additionally, there was a global shortage of reagents required to perform the recommended tests, so various experimental, alternative approaches were developed to deal with the shortages and to be able to adequately treat patients presenting with respiratory complaints in hospitals[4,415,416]. Later during the pandemic rapid antigen tests to detect

SARS-CoV-2 could enter the market before gaining EU market authorization, using national emergency procedures.

However, patient access regarding tests is broader than gaining market access: they should also be implemented in clinical practice. As the clinical evidence supporting the introduction of novel tests will be more extensive under the new regulations, this may be used to inform the implementation. As discussed in chapter 5, the long-term clinical evidence supporting economic evaluations of diagnostics is lacking. After the IVDR comes into effect, I expect more evidence to be available for decision makers regarding the benefits for clinical patient outcomes, as opposed to only technical evidence such as the sensitivity and specificity of tests. Using standard health-economic methods, the clinical effects can subsequently be extrapolated to longer time horizons[330]. In chapter 5, I also recommend companies to collect quality-of-life data during clinical trials to be able to calculate the costs per QALY. Just as in the market for pharmaceuticals, this enables policy makers and clinicians to compare the various available tests using CEAs and to implement the most cost-effective options. Additionally, the use of CEAs also enables comparisons between tests and other technologies, whether these are pharmaceuticals, medical implants, surgical procedures, or any other health technology.

Further considerations linked to health technology assessment

This thesis covered most topics that should be included in an health technology assessment (HTA) according to the domains of the HTA Core Model, as discussed in the introduction of this thesis (see Box 11.1 for a summary)[38]. The first two points are rather straightforward; as described above, the technical characteristics have traditionally been the focus for new tests. Due to the beforementioned introduction of the IVDR, I expect the quality of safety and clinical effectiveness data to improve. The clinical effectiveness data should increasingly include relevant clinical outcomes for patients, such as QALYs. Chapter 4 focussed exclusively on optimizing clinical effectiveness, in this case using quality-adjusted life expectancy as an outcome measure. In chapter 6, several recommendations regarding the costs and economic evaluation are provided. Ethical aspects are highly relevant for the SHS, as described in chapter 2, where providing access to basic health care for all pupils, regardless the financial situation or health literacy of their parents, can aid in providing a more equitable start[53]. Another ethical aspect is AMR[20,417]. As mentioned in the introduction, AMR is both an inter-generational and a global issue[20]. An inter-generational issue as AMR develops on the long term, I would argue current generations have a responsibility to not leave future generations with a plethora of multi-resistant bacteria which are difficult to treat. And also a global issue as resistant bacteria cross borders, carried by people, also countries that are doing relatively well, such as the Netherlands, should not ignore the resistance rates in other countries[85]. Related to the availability of antibiotics, there needs to be a right balance between excess and access: still many people die globally because they do not have access to antibiotics[14]. I elaborate further on the inclusion of AMR in economic analyses below.

The organizational aspects of tests are rather complicated, and they should be explained well in CEAs, as recommended in chapter 6. In chapter 2 the economic aspects of one of the most important systems for screening and early diagnosis is the focus: the SHS[56]. The data availability regarding SHS staff and remuneration was lacking in most European countries, which I consider to be a risk for informed decision-making as these aspects need to be clear when performing an HTA. In chapter 10 I suggest how the organisation of tests in the hospital setting can be tailored to deal with AMR more adequately by incen-

Box 11.1. Domains HTA Core Model

1. Health problem and current use of technology
2. Description and technical characteristics
3. Safety
4. Clinical effectiveness
5. Costs and economic evaluation
6. Ethical analysis
7. Organizational aspects
8. Patient and social aspects

tivizing collaboration on this topic between various stakeholders.

The information gathered when testing is used to inform clinical decision-making. To maximize the impact, both the clinician and the patient need to be able to interpret the test result and to use the information to decide on the consecutive steps. Especially clinical studies focussed on the adequate prescription of antibiotics consider this and, in some cases, combine the diagnostic intervention with professional training for clinicians[137]. How does diagnostic-driven antibiotic prescribing affect care-seeking behaviour by patients on the long term? Does the additional information on the aetiology of a patient's complaints increase the likelihood to consult a physician in the future? Or will patients be less likely to seek care when the probability of being prescribed an antibiotic is lower? Decision making based on more informative diagnostics may have improve patient adherence to the treatment that follows: a specific element of value described elsewhere, but inconsistently used in CEAs[105]. The final HTA domain, legal aspects, was discussed previously.

Eventually, the aim of HTA should be to decide on the implementation of certain tests. By definition, this requires input from various scientific fields and as discussed above, there are various barriers and uncertainties to consider[37]. The currently-running, EU-funded VALUE-Dx research project may set the stage for HTAs of diagnostics into the future[418]. Within the consortium all factors of value are considered for various diagnostics used for patients with respiratory tract infections and are expected to reduce antibiotic prescribing. The technical characteristics of all relevant diagnostics are thoroughly reviewed. Two clinical trials assess the value for patients seeking care in the community setting, with adequate follow-up to include the major elements of value, such as health outcomes, productivity losses and adherence[105]. A trial-based health-economic model closely follows the costs incurred during the trial, while a broader health-economic framework is used to calculate the cost effectiveness from the long-term, societal perspective. The organizational, patient, and social aspects related to changing clinical practice are thoroughly assessed using qualitative research methods and the regulatory issues are investigated using interviews with national authorities. MERIAM, the model described in chapter 7 of this thesis will form the basis of the health-economic framework of VALUE-Dx and can be used to assess patient outcomes, such as QALYs, and public-health outcomes, such as the development of AMR. In further research also the social aspects, such as future care-seeking behaviour, can be included in the model to inform decision makers and make strategic decisions to transform clinical practice[418].

Towards tailored testing

More frequent testing requires significant investments, as described in chapters 3 and 7. Especially when screening, testing more will result in more positive findings and even more costs, which negatively impact the cost effectiveness. Additionally, as discussed in

chapter 5, the cost-effectiveness of a diagnostic strategy is highly dependent on the disease incidence. To construct cost-effective testing strategies, it may be vital to look towards improved predictive models that aid in testing tailored populations that benefit from the test result, i.e., a population at increased risk of a certain condition. For example, the risk scores for stroke and bleeding used in chapter 4 are very inexpensive to apply and are used frequently in clinical decision-making to improve patient outcomes. Little *et al*, compared care-as-usual, a clinical score and an antigen test combined with a clinical score for patients consulting a GP for acute sore throat in England. They found that the clinical score reduced antibiotic prescribing with 29%, but did not find an additional benefit related to the use of the antigen test[271]. Deciding whom to test may be very important for the testing strategy to remain cost-effective. In essence, testing is all about probabilities: test results change the probability of a patient having a specific condition, which in turn guides treatment decisions. Combining epidemiological data and patient characteristics may enable testing algorithms more tailored to the individual, and, as less tests need to be performed, improved cost effectiveness. As more health data become available and accessible, for example through large-scale cohort studies such as Lifelines[419] and data infrastructure such as Health-RI[420], data scientists gain the tools to build better models to predict diseases. These models can be used to quantify the added value of specific tests for individual patients; using tests to fill in missing data points will change the probability of having the disease and be informative to estimate the effectiveness of specific treatment options.

For infections, the probability that a disease is caused by a certain virus, bacterium or parasite changes depending on the incidence within the community. Incidence data of different infections in the population can be incorporated in predictive models and combined with patient symptoms and characteristics to estimate the disease aetiology before any tests. This approach was researched for febrile illness in South-East Asia, where regional surveillance data for diseases like dengue, scrub typhus, influenza and leptospirosis were collected using a relatively expensive multiplex PCR in the hospital setting to inform empirical treatment in rural areas[248]. Although the use of surveillance data only was not deemed to be cost-effective, combining surveillance data with CRP testing was considered to be highly cost-effective and was estimated to prevent hundreds of deaths while reducing antibiotic prescribing[248]. Further research could focus on the development and implementation of flexible diagnostic algorithms for infectious disease that recommend tests and treatment in clinical practice based on the real-time aetiology of infections, while considering the overall cost effectiveness. This approach could also allow for more flexible antibiotic treatment options, as local resistance rates could feed into the system, preventing the use of antibiotics a patient is likely to be or become resistant to. Privacy of patients remains an important issue to consider in the context of large-scale data collection but should not be a major barrier as aggregated test results should not be traceable to individuals. Of course, there are costs associated with gathering sufficient surveillance data as well, but these data may serve several purposes, as they are important in informing policies regarding AMR and pandemic preparedness, which are described in more detail below.

Preventing a post-antibiotic era

In chapter 1, I introduced warnings from experts on a post-antibiotic era[13,14]: a future which is difficult to predict, but would be detrimental to healthcare as we know it today. As can be seen from our forecasts of resistance of *pneumococci* to broad-spectrum penicil-

lins in chapter 6, this is not something that seems likely if only current trends are extrapolated in the Netherlands. Globally however, in some countries resistance rates for specific bacterium-antibiotic pairs exceed 90%[421]. Considering the low number of new antibiotics in development[422,423], the development and spread of these resistant bacteria needs to be prevented. In many cases, AMR develops by chance, as random mutations introduce a benefit to survival to resistant organisms[9]. This is the case for tuberculosis, caused by *Mycobacterium tuberculosis*, for which already variants exist that are resistant to all known antibiotics[9,424]. Surveillance of AMR is an important aspect to be able to act on changes in the population, e.g., by changing treatment guidelines. Looking at national resistance rates, the data used to support decision making currently is rather limited[425]: they are derived from a limited number of samples and primarily from the hospital setting. Implementing tests capable of detecting resistant organisms in a way where the collected data do not only benefit the individual patient but can also be used for AMR surveillance on the population level, can be highly beneficial. These data can be used to develop the personalized testing algorithms described earlier, to inform empirical treatment decisions, to develop improved AMR prediction models and to draft AMR-related policy.

In chapter 6 of this thesis, we discussed the value of diagnostics to combat AMR and advocated for a more strict adherence of CEAs of diagnostics to the reference case for economic evaluations[50]: including that the main outcome should be an ICER expressed as costs per QALY or DALY. Apparently contradictory to our own recommendation, chapter 7 is a study that uses costs and reductions of AMR as the main outcome of interest. Here we used previously detailed methods to build a model which forecasts the effects of CRP testing on AMR[12,284]. However, the assumption was made that there was no change in QALYs between the CRP-testing scenario and the current standard-of-care, meaning that an ICER is impossible to calculate as the denominator is zero. Two approaches could have worked to be able to enable the calculation of an ICER: firstly, previous research has shown that it is possible to express lost health due to AMR in DALYs[11,254] and cost-effectiveness outcomes[284], so this approach could be followed. However, as this approach is focussed on the hospital setting, it may not be a valid approach for the community setting. Secondly, clinical trials could show differences in QALYs, albeit marginal, which is an approach tried in the VALUE-Dx project, the results of which will be incorporated in the health-economic model in the future. Still, I would argue that the ethical considerations discussed in the part on HTA warrant the approach taken in chapter 7. There is inherent value in reducing AMR, as this contributes to preventing the worst-case scenario, a post-antibiotic era. Dorgali *et al*. previously estimated that the willingness to pay for containing AMR in the United Kingdom was around £8.35 billion annually[293]. To account for the uncertainty in the future development of AMR, I suggest the use of ROA. Performing a ROA for any new intervention that affects antibiotic consumption may not be a feasible approach for HTAs, hence I would suggest a two-step approach. Start with a ROA: consider scenario analyses regarding the long-term effects of AMR, quantify the associated costs, and use this to develop a long-term mission on AMR. Similar to the Paris climate agreement, where the international community agreed to limit global warming to 1.5 °C above pre-industrial levels[426], specific goals to contain AMR should be set. Within this mission-oriented approach, budgets should be structured in a way so that the long-term AMR goals can be reached[21]. Any innovative intervention that aids in reaching these goals should be assessed based on its relative contribution and investment, i.e., the AMR reduction in relation to the additional costs. The analysis performed in chapter 7 would fit in such a framework and similar methods could be incorporated in other CEAs without too much effort. Additionally, the EF approach as used in Germany, discussed in chapter

9, inherently considers outcome measures other than QALYs and could be used to relate costs to changes in AMR for various strategies.

Preparing for the next pandemic

This thesis started with the massive impact of the COVID-19 pandemic on health and the economy. Next to the recommendations related to ROA in chapter 8, what can the findings in this thesis contribute to preparing for the next pandemic? As mentioned, having an adequate testing infrastructure is an important aspect of pandemic preparedness, while this infrastructure can also be used during "inter-pandemic" times. In the coming years, the EU is expected to invest heavily in cross-border health and pandemic preparedness[427]. At the time of writing, the EU is working on the Health Emergency preparedness and Response Authority (HERA), an organization to "improve Europe's capacity and readiness to respond to cross-border health threats and emergencies"[428]. Although this plan is expected to have a broad scope, one of the aspects is expected to be an intensive collaboration with the European Centre for Disease Prevention and Control (ECDC) to improve surveillance of potential pandemic pathogens[427]. During the COVID-19 pandemic, the ECDC already played an important role in drafting guidelines[129] and sharing relevant data[429]. One of the ECDC's strategic goals for the coming years is to enhance surveillance and emergency preparedness by streamlining epidemiological information from existing systems[430]. If innovative, widely applied microbiological tests would feed into these surveillance systems, this can be used to identify potential threats faster, enabling authorities to hit hard and early to potentially prevent the next pandemic and related economic and health damage.

Concluding remarks

In this thesis, I covered many aspects related to the economics of testing strategies in healthcare, from the organization of screening tests to the use of diagnostics to combat AMR. It is important to consider the testing infrastructure: where should testing take place, close to the patient or in specialized laboratories; who should perform the test and how are these health professionals organized; and what value do the test results have for public health and how are these data shared? These are some of the issues to be considered for HTAs of tests. From a cost-effectiveness perspective, the underlying clinical data should be sufficient to compare the testing strategy to other health technologies, by using generalizable health outcomes, such as QALYs, and by using sufficiently long time horizons. In a CEA, the costs for society are related to the clinical benefits for patients, but for microbiological tests, the clinical value is broader than that, especially if tests can identify specific pathogens. The collected data can be used to make public health decisions, for example by updating treatment guidelines for infectious disease and by responding to AMR and potentially pandemic pathogens. These data could feed into decision models that are able to support clinical decision making by tailoring testing strategies to individual patients, thereby improving the cost-effectiveness.