The Adoption of Point-of-Care Testing in Primary Care:

Economic Evidence and Organizational Factors

Deon Lingervelder

THE ADOPTION OF POINT-OF-CARE TESTING IN PRIMARY CARE:

HEALTH ECONOMIC EVIDENCE AND ORGANISATIONAL FACTORS

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Chapter 1:

General Introduction

GENERAL INTRODUCTION

Diagnostics are indispensable tools in disease management to improve patient outcomes and wellbeing through (better) informed patient management decisions. More broadly, diagnostics are beneficial for different applications such as monitoring, screening, and diagnosis in several settings. Accurate diagnostics can result in improved patient outcomes when it is used to guide clinical decision making [1]. Additionally, diagnostics may generally lead to economic benefits for the healthcare system by directing resources and care to patients who will benefit most [2]; however, it can also lead to overdiagnosis, resulting in unnecessary costs from unnecessary treatments [3]. There are two categories of diagnostics that stand out in medical practice due to their market size, namely medical imaging and in-vitro diagnostics (IVD) [4]. There is a wide variety of imaging tests available to healthcare providers, including X-rays, computed tomography (CT) scans, positron emission tomography (PET) scans and ultrasound that can be used to create images of the human body to guide clinical decision making. In contrast, IVD's are clinical tests that analyse samples taken from the human body, such as blood, tissue, or saliva. Although clinical judgement is crucial for decision making, these tests are fundamental in routine patient management and clinical decisions are often driven by the test results. In a 2016 survey of physicians in Germany and the United States, it was found that 66% of clinical decisions were based on IVD results [5]. There is a wide variety of IVD technologies available, ranging from complex tests performed in a laboratory, handheld tests used in healthcare facilities or general practice, and simple tests that can be used by the patient at home. Globally, the IVD market continues to grow rapidly. In 2020 the IVD market size was valued at US$ 84 billion and is expected to reach US$ 96 billion by 2025 [6]. This growth is fuelled by the ageing population, increased awareness of the benefits of preventive health care and increased prevalence of several diseases, including cancer and inflammatory conditions [7]. The early detection of diseases is essential to reduce the risk of serious complications, increase the effectiveness of treatment, and save valuable healthcare resources [8–10]. The recent COVID-19 pandemic has emphasised the significance of early detection and rapid, reliable diagnostics.

A type of diagnostic test that can potentially benefit the healthcare system, is point-of-care (POC) testing. Over the past few decades, enhanced manufacturing

processes and new scientific developments have led to several innovations in diagnostics, such as lab automation, single-cell sequencing, liquid biopsies and POC testing. POC testing, in short, can be defined as a diagnostic test that is performed nearby the patient and provides test results at the time of the clinical decision making [11,12]. A POC test implemented in general practice is usually a handheld device that can vary in size. There are also larger desktop devices, which generally include systems designed for clinics or laboratories, although they can also be implemented in general practice if space is available [13]. The tests often require only a small urine or blood sample and can provide test results within a few minutes. To date, there is a wide variety of POC tests available on the market, for several disease areas, such as cardiovascular disease, venous thromboembolism and respiratory tract infections. Examples of some POC tests and the clinical setting in which they are typically applied are provided in Table 1.

Table 1. Examples of POC tests and clinical settings.

Test	Clinical Setting
HbA1c	General practice, monitoring diabetes patients
INR	Coagulation clinics
Cardiac markers	Emergency rooms, Primary care health centres
Blood gases	Emergency rooms
Influenza	Hospitals, ambulatory care
STDs (Chlamydia & gonorrhoea)	General practice, STD testing centres
CRP	General practice

CRP C-Reactive Protein, HbA1c Hemoglobine A1c, INR International Normalized Ratio, STD Sexually Transmitted Disease,

When properly utilised, accurate POC tests can improve patient outcomes and efficiency of health care by providing rapid test results, resulting in earlier treatment decisions without having to wait for laboratory results [11]. POC testing has also been associated with additional benefits, such as preventing unnecessary referrals from primary care to specialised or secondary care, improved monitoring of patients [14], decreased length of stay in hospitals [15], and improved patient satisfaction [16]. POC tests can furthermore be used for different applications in several settings, ranging from general practice, emergency rooms, hospitals, and cruise ships [11]. The reasons for implementing a POC test will typically vary according to the setting in which it is implemented. For example, in intensive care units or emergency rooms, the rapid test results of POC tests are useful to help guide urgent life-saving decisions that need to be made in a short

amount of time. In resource-limited settings or areas with poor infrastructure, access to healthcare facilities such as hospitals or laboratories is typically limited. In these settings, POC tests are very beneficial, since they can be used independently from the physical presence of a laboratory [17]. The rapid analysis may also lead to improved patient satisfaction and clinical performance, since it eliminates the long intervals between the first consultation with a patient and the discussion of the test results [18]

While advantages are described, implementation of POC testing is also accompanied by some challenges. In general, POC tests may have a lower diagnostic performance when compared with traditional laboratory tests. Furthermore, POC testing is typically more expensive than laboratory testing since POC testing reagents are single-use tests while laboratories benefit from economies of scale [19]. Some of the POC tests that are less easy to use may provide misleading test results when performed by professionals with a limited technical background. This can cause risk to patients and increase costs (due to follow-up tests) [11]. A summary of some of the main advantages and disadvantages are provided in Table 2.

Table 2. Advantages and disadvantages of POC testing.

Perspective	Advantages	Disadvantages
Healthcare funder	Fewer referrals	Quality of results
Patient	Increased patient satisfaction and convenience	Errors could reduce patient trust
	Small sample size	Out-of-pocket costs*
Healthcare Provider	Portable & easy to use	More room for human error
	Rapid results	Higher cost*
	More FN test results	Overutilisation

*Only in some cases, depending on the country and its healthcare/insurance system.

In primary care, the diagnostic process is typically reliant on laboratory testing, where test results are considered to be accurate, reliable and reproducible. The large variation of the clinical background of personnel in primary care may result in less reliable and inconsistent outcomes of POC tests compared to in-house laboratories with qualified personnel. Moving testing away from the central laboratory to on-site testing, therefore, comes with additional challenges and an increased workload to the staff in charge of managing and using POC tests [11,19].

In particular, quality control, quality assurance, calibration, and maintenance of POC tests may be less well developed in primary care [11,20].

The number of POC tests available on the market is quite extensive and is expected to grow even more due to the increasing demand for rapid tests and at-home testing. It is likely, that with this growth, issues surrounding the quality control of POC tests will increase as well. It is therefore important that the necessary steps (and instructions) regarding quality control, calibration, maintenance, cleaning, and quality assurance of the POC testing devices are strictly followed by healthcare providers. The growth of the POC market is also evident in large manufacturers such as Roche Diagnostics and Abbott Laboratories who continue to commercialise new and improve on existing POC tests [6]. Key factors driving this growth, have been attributed to new government initiatives and regulations, as well as the increasing geriatric population and patient awareness toward the value of IVDs [6,7]. However, when taking into account the rapid growth of available POC tests, it is interesting to note the relatively slow pace of wide-scale POC testing implementation in routine clinical practice in primary care [21]. With the exception of POC pregnancy and blood glucose tests, it seems that POC tests are, overall, mainly implemented in central laboratories, emergency rooms, critical care centres and intensive care units [6,7,22] POC tests are generally more widely implemented in primary care in areas with limited healthcare resources as opposed to in countries with a more established healthcare and laboratory network [22]. A survey published in 2014 looked at the usage of POC tests by primary care clinicians in five countries [23]. Even though some POC tests, such as urine pregnancy tests, urine leucocytes nitrite tests and blood glucose tests, were being used by 80% of the respondents (all general practitioners), the survey showed that other POC tests, including INR, heamoglobin, faecal occult blood, c-reactive protein and group A streptococci were used by less than 31% of overall respondents.

The barriers to the wide-scale implementation of POC tests is not a new subject and has been discussed before [24–26]. The main barriers to adoption have been identified as a lack of reliable health economic evidence, concerns around quality control and quality assurance, costs and reimbursements, and the high workload and complicated processes associated with the implementation [24–26]. The adoption of any innovation, such as POC tests, are typically focused on how the end-user experiences the technology. In the case of POC tests, the end-user,

technically, is not the patient, but the healthcare provider. It has been suggested that healthcare providers are not always aware of existing or new POC tests, which could also contribute to the slow adoption in primary care [27].

Extensive implementation of POC testing in primary care will have a large impact across the healthcare system. As mentioned previously, the implementation would involve shifting testing from the centralised laboratory to primary care, resulting in a higher workload for healthcare providers in primary care and new processes to be introduced into the primary care system [28]. These new processes are also correlated with the barrier of cost, due to the unclear (or lack of) standardised reimbursement rates of the up-front costs of purchasing the POC device and reagents and the costs of set-up, training and general organisation and management. Furthermore, while traditional laboratory staff are purely focused on generating quality test results, without the distraction of responsibilities related to patient care; healthcare providers in primary care need to ensure the quality assurance of POC testing devices next to their main care responsibilities.

This thesis aims to study health economic evidence and organisational factors explaining the slow adoption of POC testing in primary care and to improve the potential use and impact of POC testing using the insights generated. Briefly, it will seek to answer the following three concrete questions.

1) Is there a lack of evidence supporting the implementation of POC testing?

Chapters 2 and 3 will discuss the available health and economic evidence of POC testing. More specifically, in Chapter 2, a summary of POC tests used in primary care will be provided. Additionally, the evidence provided by POC test evaluations was investigated to determine whether it reflects previously established factors that are important for general practitioners in the decision to implement a POC test. Chapter 3 summarises the available evidence on the health economic impact of implementing POC testing to assess whether the slow uptake of POC tests may be related to a lack of evidence.

2) Is the current organisation of healthcare systems capable of supporting the implementation of POC testing?

Chapter 4 describes the healthcare system of the Netherlands, England, Australia and Norway, with a specific focus on primary care. To identify factors that could

explain the differences in uptake of POCT by general practitioners in the four countries, the healthcare systems are also compared in terms of seven, previously published factors that support the successful implementation, sustainability and scale-up of innovations.

3) What is the perception of end-users (regarding convenience) and the potential health and economic impact of novel diagnostic devices in primary care?

In Chapter 5, the societal impact of an at-home blood-sampling device is investigated. The chapter describes the blood-sampling preferences of chronically ill patients as well as a cost-analysis of a novel at-home blood-sampling device.

Lastly, Chapter 6 discusses the overall findings and conclusions of this thesis and presents directions for further research.

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Chapter 2:

Point-of-Care Testing in Primary Care: A Systematic Review on Implementation Aspects Addressed in Test Evaluations.

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ABSTRACT

OBJECTIVES: There are numerous point-of-care tests (POCTs) available on the market, but many of these are not used. This study reviewed literature pertaining to the evaluation/usage of POCTs in primary care, to investigate whether outcomes being reported reflect aspects previously demonstrated to be important for general practitioners (GPs) in the decision to implement a POCT in practice.

METHODS: Scopus and Medline were searched to identify studies that evaluated a POCT in primary care. We identified abstracts and full-texts consisting of applied studies (e.g., trials, simulations, observational studies) and qualitative studies (e.g., interviews, surveys). Data was extracted from the included studies, such as the type of study, the extent to which manufacturers were involved in the study, and the biomarker/assay measured by the test(s). Studies were evaluated to summarize the extent to which they reported on, amongst others, clinical utility, user-friendliness, turnaround-time, and technical performance (aspects previously identified as important).

RESULTS: The initial search resulted in 1,398 publications, of which 125 met the inclusion criteria. From these studies, 83 POCTs across several disease areas (including cardiovascular disease, venous thromboembolism and respiratory-tract-infections) were identified. There was an inconsistency between what is reported in the studies and what GPs consider important. GPs perceive clinical utility as the most important aspect, yet this was rarely included explicitly in test evaluations in the literature, with only 8% of evaluations incorporating it in their analysis/discussion.

CONCLUSIONS: This review showed that, despite the growing market and development of new POCTs, studies evaluating such tests fail to report on aspects that GPs find important. To ensure that an evaluation of a POCT is useful to primary care clinicians, future evaluations should not only focus on the technical performance aspects of a test, but also report on the aspects relating to the clinical utility and risks.

INTRODUCTION

Diagnostic testing plays a vital part in primary healthcare, providing valuable insight to support decisions regarding treatment and referral to secondary care [1]. Patient outcomes can be greatly improved with diagnostic testing when it is used to exclude a disease and identify those patients that will benefit the most from downstream actions, such as initiating, modifying, stopping or withholding treatment [2]. In primary care, the diagnostic process traditionally relies on laboratory testing. Laboratory information must therefore be accurate, reliable and reproducible. Although in some diagnostic questions rapid delivery of the test results is important, traditional centralized laboratories tend to highlight the quality and reliability of tests above the turn-around-time [3]. For many diseases, care providers and patients increasingly expect patient-focused, specialized diagnostic tests that can be performed quickly, easily and provide results within minutes [4]. This has led to the development of easy-to-use analyzers that can be performed at the point of care, more commonly known as point-of-care (POC) testing or near-patient testing [1].

The reason for implementing a POCT will vary according to the setting. In emergency departments or intensive care units, POCTs are used to find test results immediately to help guide life-saving decisions. In resource-limited settings, access to healthcare facilities is typically limited. In such settings, POCTs are beneficial in terms of their ease of use independent from the physical presence of a laboratory [5]. In primary care settings, POCTs are typically used to prevent unnecessary referrals to specialized or secondary care, to guide diagnostic and treatment decisions, and to provide reassurance to patients, e.g. by excluding an illness. The rapid analysis can also lead to improved clinical performance, since it eliminates the potentially long intervals between the patient's initial examination and the discussion of the test results [4].

The first major systematic review of POCTs in primary care was published more than 20 years ago by Hobbs et al. [6], who concluded that evidence in support of the general introduction of POCTs in general practice was low. Since then, the POC diagnostic market has grown substantially and continues to do so due to the increasing development of new (supporting) technologies such as novel biomarkers, wireless connectivity, nanoparticle techniques, and information sharing capabilities [7]. It is expected that the global POC diagnostics market will

reach $40.50 billion by 2022 [8]. Despite this growing market, primary care clinicians generally are hesitant to implement POCTs in their practice. According to a study on POC blood tests by Jones et al. [9], this is mainly due to concerns about accuracy, over-reliance on tests and limited usefulness.

A recent survey of general practitioners (GPs) in the UK [10], identified several themes regarding what GPs perceive as facilitators and barriers to the implementation of a POCT. Some of these themes were the workload, clinical utility, patient satisfaction, reimbursement, legislations, technical performance, connectivity, training, and maintenance. A similar survey study in the Netherlands found comparable results, with Dutch GPs believing the proven effect on clinical management and the tests' reliability to be among the most important aspects of POCTs [11]. This study aims to systematically review recent literature pertaining to the evaluation and usage of POCTs in primary care and to investigate whether the outcomes and evidence reported in the literature, reflect previously established factors [12] that are important for GPs in the decision to implement a POCT.

MATERIALS AND METHODS

Literature Search

The PRISMA guidelines were followed while carrying out this systematic review of available POCTs for primary care. Since this review aims to identify any POCTs that can be implemented in primary care, all types of primary research studies were included in the initial search. For this reason, it was not required that any specific outcome measure was reported in the initial search and no specific study characteristics or PICO-statement was used as part of the inclusion criteria. The review protocol for this systematic review is provided in Appendix 1 as a series of steps that were followed.

Two databases (Scopus and PubMed) were searched for relevant English or Dutch publications between 2007 and 2017. The initial search was performed in September 2017. The search included all terms and text words related to the intervention (POC diagnostics) and the setting (Primary Care). The search query used was (Scopus format):

TITLE-ABS-KEY ("POCT" OR "Point of care" OR "Point of care testing" OR "rapid testing" OR "bedside testing" OR "laboratory-independent" OR "near patient

testing") AND TITLE-ABS-KEY (diagnos*) AND ALL ("Primary Care" OR "General Pract*" OR "GP" OR "Primary Healthcare" OR "Primary Health Care")

Study Selection

Only publications that met the following inclusion criteria were selected for the review:

- Publications should focus on POC diagnostic technologies only. Publications reporting on, for example, scorecards or methodologies to diagnose patients at the point of care, decision support tools or online (cloud) systems, results sharing, electronic health records, etc. were excluded.
- Publications should focus on specific POC diagnostic technologies and not only provide a general summary of POCTs.
- Publications should focus on primary care only. Publications focusing on secondary care or self-monitoring were excluded.
- Publications should focus on high-income countries only. Publications that explicitly stated that their focus is on remote or rural areas were excluded, even if within a developed country.
- Publications should be an applied study that evaluates a POCT in terms of its effectiveness, performance, usage or application. This includes qualitative studies (such as surveys and interviews) and modeling studies. Reviews were excluded.

After removing duplicate publications from the initial search results, the abstracts were screened to determine whether publications met the inclusion criteria. Publications that undoubtedly failed to meet all of the inclusion criteria, based on the abstract screening, were excluded from the full-text assessment. If there was any doubt on whether or not a publication met the inclusion criteria, it was included for full-text assessment. The abstract screening was performed by one reviewer (DL), and potential issues were discussed with a second reviewer (HK) when required. The full-text assessment of all included publications was performed by one reviewer (DL).

Data Extraction and Management

The data was extracted manually by one reviewer (DL) from the studies into Microsoft Excel (version 2016) in pre-defined and labeled columns. The following information was extracted from each of the included publications:

- The study design, classified according to one of three categories; namely, empirical study (trials, cohort studies, etc.), qualitative study (interviews, surveys, etc.), or modeling study.
- If relevant, the country where the study was performed. For multi-country studies, each individual country was counted separately.
- If applicable, the role that the manufacturer played in the study. This was classified in one of seven categories; namely, 1) manufacturer provided some financial support to the study, 2) manufacturer funded the study, 3) manufacturer provided the analyzer/test, 4) manufacturer funded the study and provided the analyzer/test, 5) one or more authors are employed by the manufacturer, 6) manufacturer played no part in the study or 7) nothing specified about funding or manufacturer involvement.
- The name of the POC device/test that was evaluated.
- The biomarker/assay that was measured by the POCT.

If a study evaluated more than one POCT, a separate data entry (row) was added for each individual test evaluation. During the full-text assessment, each test evaluation study was assessed to summarize the extent to which pre-defined determinants were being reported on. These determinants were identified previously [12] as key factors that affect the decision to implement a POCT in primary care. All 20 of these determinants are listed in Table 1.

Some of these determinants are not applicable to a POCT specifically, but rather to the disease prevalence and the GP and his practice (Frequency of use, Room for innovation, Risks). For example, Frequency of use and Room for innovation are both determinants that are associated directly with the GP's practice, while the impact and Risks of tests would differ between diseases. It is expected that these determinants will not be reported in the evaluations as frequently as some of the others. If there was any uncertainty to the first reviewer (DL) about whether a publication discussed a certain determinant, it was examined by a second reviewer (HK). On occasions when these two reviewers could not agree on a decision, a third reviewer was involved in making a final decision (either RK or MJIJ).

The data extracted from the included publications was summarized in both text and table format, before providing a descriptive synthesis of findings. Results were divided according to the biomarker/assay that the test measures.

Table 1. List of determinants and their description (Reproduced from Kip et al., 2019)

	Determinant	Description
1	Satisfaction patient	Extent to which the use of the POC test is expected to improve service for the patient.
2	Clarity of procedure	Extent to which the procedures for using the POC test are clearly described in protocols and/or manuals.
3	User-friendliness	Extent to which the POC test is easy to perform by the layman.
4	Test interpretation	Extent to which the POC test result is easy to read and the various test results are easy to interpret.
5	Turn-around-time (TAT)	Extent to which the POC test results are instantly available.
6	Frequency of use	Extent to which the test is used sufficiently with respect to the indication and the size of the general practice.
7	Room for innovation	The extent to which the pressure of daily practice leaves room for innovation and a mind-set for change.
8	Workload	Extent to which the POC test can be implemented without dramatic changes in the current way of working and user's workload.
9	Support, training and quality control	Extent to which the introduction, maintenance, and quality control of the POC test, as well as the training of personnel is sufficient and supported by a coordinator from the laboratory, manufacturer and general practice.
10	Connectivity	Extent to which the POC test results and errors are registered in an information system (HIS)
11	Clinical utility	Extent to which a correct (treatment) decision, as based on the point-of-care (POC) test result, has added value in clinical outcomes.
12	Technical performance	The extent to which the POC test is exact, precise, reliable and robust in the hands of the user.
13	Negative Predictive Value	Negative predictive value: Proportion of negative results that are true negative, which enhances the user's ability to reliably rule out a condition.
14	Positive Predictive Value	Positive predictive value: Proportion of positive results that are true positive, which enhances the user's ability to reliably diagnose a condition.
15	Risks	The impact of a (wrong) treatment/advice based on a (wrong) test result.
16	Clinical guidelines	Extent to which the POC test is implemented in national guidelines.
17	Scientific evidence	Extent to which the added value of the POC test is demonstrated (as compared with current practice) in scientific literature, in the right patient population and for a specific clinical pathway.
18	Reimbursement	Is the POC test reimbursed for the general practitioner?
19	Overall costs	Extent to which the POC test is expected to decrease costs of the health care system.
20	Legislations	Extent to which the innovation fits into existing legislations.

RESULTS

Search Results

A total of 1398 studies were obtained from the initial search of the Medline and Scopus database. To ensure that the search resulted in a comprehensive set of relevant publications, the selected search query was broad. This did, however, result in a large number of publications being excluded during the abstract screening, mostly due to publications focusing on something other than a (specific) POC diagnostic. After a screening of all abstracts, 286 studies were included in the full-text assessment.

After the full-text assessment, 125 studies were included in the final review. Studies were mostly excluded based on full-text assessment because they did not focus on POC diagnostics (n = 81), but instead described a tool, strategy or guideline to support POC testing. The PRISMA flow diagram of the search is presented in Appendix 1.

Characteristics of Included Publications

The 125 included studies consisted of 112 applied studies, 7 qualitative studies, 5 simulation studies and 1 study that used both applied and qualitative methods. The majority of the studies were applied in The Netherlands (n = 25; 20.0%), United States (n = 17; 13.6%) and United Kingdom (n = 13; 10.4%), followed by Spain (n = 6; 4.8%), Finland (n = 6; 4.8%), Australia (n = 5; 4%) and Canada (n = 5; 4%). In 35 studies (28%), the manufacturer(s) of the test(s) being evaluated provided support by either funding the study in full (n = 10) or partially (n = 8), by providing the analyzer(s)/test(s) (n = 14), or by both funding the study and providing the analyzer(s)/test(s) (n = 3). There was a single study where one of the authors was an employee of the manufacturer. For the majority of studies (n = 62; 49.6%) the manufacturer(s) had no involvement, whereas in 24 (19.2%) of the studies nothing was specified about funding or manufacturer involvement.

Overall Results

From the 125 studies in the synthesis set, 195 test evaluations were identified. The percentage that each determinant was reported in the test evaluations are provided in Figure 1, together with the overall weight of each determinant as found by [12]. The four determinants that were reported the most were turn-around-time

(n = 105; 52.2%), technical performance (n = 97; 48.3%), positive predictive value (n = 91; 45.3%), and negative predictive value (n = 89; 44.3%). The determinants reported the least in the evaluations were room for innovation (n = 0; 0%) and risks (n = 1; 0.5%), followed by reimbursement (n = 2; 1.0%), legislations (n = 3; 1.5%) and scientific evidence (n = 3; 1.5%).
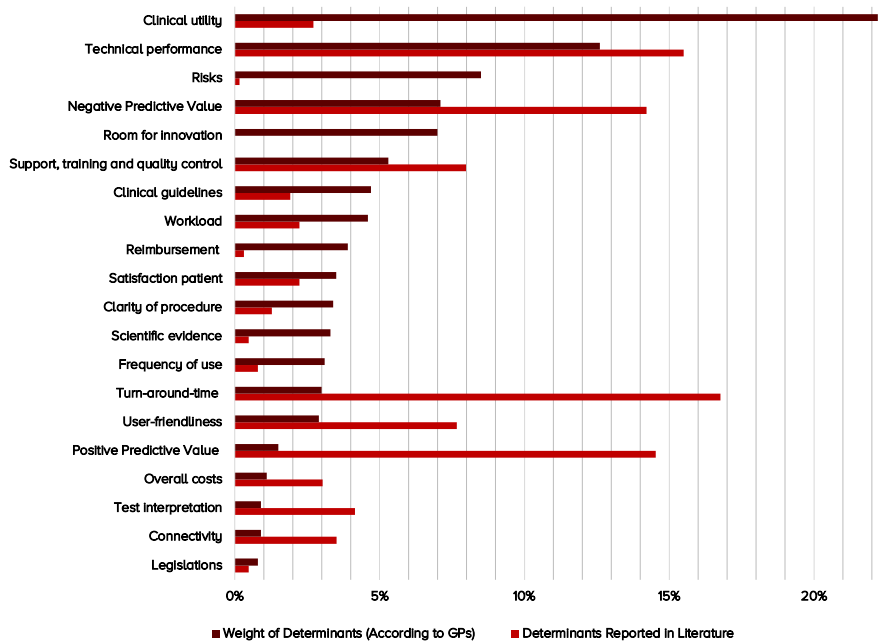
Figure 1. Comparison of determinant weights according to GPs and the percentage of times that each determinant was reported in the literature.

POCTs per Measurement

In 20 of the 195 evaluations (10.26%), the exact test(s) could not be recognized, since no identifiable information (such as the name of the device or the manufacturer) were provided. There were also 12 POCTs, occurring in 24 test evaluations, of which no information could be found on the official manufacturer or partner websites. It is expected that these tests are either discontinued/recalled (such as the Clearview Simplify D-Dimer device) or that the names of these tests have been changed. In cases where it could be confirmed that a device name has been changed (for example, the DCA 2000 has been renamed the DCA Vantage) the evaluations were included and categorized under the new device name. If no confirmation could be found, the device was excluded from the final list of tests.

After excluding the above-mentioned 20 + 24 = 44 evaluations, a total of 83 POCTs were identified with a total of 151 test evaluations. Each of these POCTs has at least one test evaluation. The most frequently evaluated tests were those measuring HbA1c (n = 14; 16.9%), CRP (n = 6; 7.2%), D-Dimer (n = 6; 7.2%) and Influenza and/or RSV (n = 6; 7.2%).

Hemoglobin A1c

A hemoglobin A1c (HbA1c) test measures glycated haemoglobin that gives an indication of the average blood glucose level of the past 60 to 120 days. Seeing as the prevalence of diabetes continues to rise each year, the timely management of HbA1c is particularly important in the primary care pathways of both patients with diabetes and those that remained undiagnosed [13]. In Appendix 2, Table 2.1, a list of the 14 HbA1c POCTs that were identified during the review is provided, in no particular order. The three most evaluated tests were the DCA Vantage Analyzer (n = 8), the Alere Afininion AS100 Analyzer (n = 6) and the A1CNow system (n = 5).

C-Reactive Protein

C-reactive protein (CRP) is an acute phase protein produced by the liver when inflammation occurs. Measuring CRP levels can help identify patients that are at high risk of having respiratory tract infections, inflammatory diseases or cardiovascular disease. To support the early detection of serious infections and diseases, CRP testing is increasingly being introduced in primary care [14]. A list of the 8 CRP POCTs that were identified during the review is provided in Appendix 2, Table 2.2. The Nycocard™ Reader II (n = 7) and the Alere Afininion AS100 Analyzer (n = 6), both manufactured by Alere, had the most evaluations in the literature.

D-Dimer

D-dimer is a protein fragment produced when a blood clot dissolves in the body. High levels of d-dimer are therefore typically used to assess the risk of thrombotic episodes and to exclude conditions such as deep vein thrombosis and pulmonary embolism [15]. In Appendix 2, Table 2.3, a list of the 6 D-Dimer POCTs that were identified during the review is provided.

Influenza and Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) is a common virus that causes lower respiratory tract infections, especially in infants and toddlers. Since reinfection occurs throughout life, specifically during fall and winter, GPs and emergency departments are typically met with a surge of patient visits during these colder months [16]. Influenza, more commonly known as the flu, is also particularly prevalent in children during winter months, causing a similar seasonal overflow of patients. Influenza is an infectious disease that causes febrile and respiratory illnesses, but typically remains undiagnosed since symptoms overlap significantly with other viral or bacterial infections [17]. POC devices for RSV and influenza can have a major positive impact on patient care by reducing both unnecessary diagnostic testing and antibiotic prescriptions [17]. A list of 6 POCTs for Influenza and RSV, that were identified during the review is provided in Appendix 2, Table 2.4.

Other Frequently Evaluated POCTs

In addition to the above-listed POCTs, there were also tests measuring calprotectin, streptococcus pyogenes, BNP and NT-proBNP, bladder carcinoma, uric acid, INR, IgA deficiency and chlamydia, among others. The majority of these tests had only one evaluation. A list of tests that have been evaluated more than once is provided in Appendix 2, Table 2.5.

DISCUSSION

There was a clear inconsistency between what is reported on in the identified evaluations and what GPs consider important. Certain determinants of the published list used in this review are not relevant to a POCT, but rather to the disease prevalence and the GP and his practice (frequency of use, room for innovation, risks). These determinants were, as expected, underreported. None of the evaluations addressed any aspect related to room for innovation whereas only one evaluation assessed the risk aspect of the test. Frequency of use was addressed in five of the test evaluations. Reimbursement (n = 2) and legislations (n = 3) were also rarely reported on in the evaluations. This could be since the impact of these determinants will vary between countries and were therefore purposefully excluded from the evaluations. The most relevant inconsistency was with clinical utility. Although GPs perceive clinical utility as the most important

aspect when it comes to POCT, it was rarely explicitly included in the test evaluations found in the review. Only 8% of evaluations incorporated some aspect of clinical utility in their analysis and/or discussion. Although the definition of clinical utility used in this paper was broad to ensure that it encompasses all aspects of clinical utility, it could be that certain aspects described in the test evaluations were not accounted for. One reason for the clinical utility of a test only rarely being mentioned, could be the fact that clinical utility is often implied rather than being described. For example, by pointing out that current testing and decision making is sub-optimal without explicitly indicating how POCT would improve this. Furthermore, the turn-around-time of the test was reported in more than half of the evaluations (52.5%) even though it is not among the ten most important determinants according to GPs. This could possibly be due to GPs expectations that user friendliness and short turn-around-time are evident properties of a POCT; which is why these properties are considered a high priority in the evaluation of POCTs. Technical performance is considered the second most important determinant among GPs and it was addressed by almost half of the evaluations (48.3%).

In a study by Huddy et al. [18], clinicians stated during interviews that POC devices with the ability to perform multiple tests (such as HbA1c combined with lipids) was seen as an additional incentive for purchasing. This could explain the high number of evaluations found in this review for the Nycocard™ Reader II (Seven evaluations for CRP, two for HbA1c and one for D-Dimer) and the Alere Afininion AS100 Analyzer (Six evaluations for CRP and six for HbA1c). However, not all of the multiple-test devices had a high amount of evaluations. For example, the AQT90 FLEX immunoassay analyzer can perform six tests (D-dimer, Procalcitonin, CRP, NT-proBNP, Troponin T and Troponin I), yet only one evaluation, in this case of its D-Dimer test, was identified in the review. However, since this instrument requires a large volume of blood, and therefore a venipuncture instead of a fingerpick, it may not be considered as a POCT [19]. Therefore, studies investigating this multiple-test device (or similar devices) without using POCT terminology may have been missed.

Care should be taken when interpreting the absolute number of evaluations per test, as some tests may have been available on the market longer than others, and could, therefore, have been evaluated more over the years. With respect to the aforementioned tests, the earliest year that information regarding the AQT90

FLEX was found, was in 2010, with the one test evaluation in this review being from 2015. For the Nycocard™ Reader II, the earliest information about the test is from 2008, with the 11 test evaluations in this review being from 2009 (n = 2), 2010 (n = 2), 2011 (n = 1), 2013 (n = 3), 2015 (n =2).

There are some POCTs that did not have as many evaluations in this review, for example, INR testing. Although POC INR testing is used in some outpatient labs and anticoagulation clinics, the reference standard remains clinical laboratory testing [20]. The use of POC INR testing has become popular for at-home testing, where patients can easily use the device to monitor their INR and report their results to a clinician (either in person or via telephone) who would then adjust their anticoagulant dose, if necessary. Another use is for patient self-management, where patients not only tests their INR themselves but can self-adjust their dose using a predetermined algorithm or protocol [21,22]. While some of the POCTs may also be applied by patients themselves, the focus of this review was related to the application of these tests in general practice. If an evaluation was on self-testing, it was not included.

It is worth mentioning, that a large number (n = 33; 39.2%) of the 84 identified tests are manufactured by only four companies, namely Alere (n = 13), Roche (n = 11), Quidel (n = 5) and pts Diagnostics (n = 4), whereas the remainder of the tests (n = 51) are manufactured by a total of 44 different companies. The POCTs manufactured by these four companies, also have the most test evaluations. In total, almost half (n = 71; 47.0%) of the 151 evaluations in this review were of tests manufactured by them, with 34, 19, 9 and 9 evaluations of tests manufactured by Alere, Roche, Quidel and pts Diagnostics, respectively. Although test evaluation studies are, in most cases, performed to collect (additional) evidence on test performance and added value, they may also serve the purpose to increase awareness of test availability amongst care professionals.

The biggest limitation of this review was missing studies due to not reporting the names or manufacturer of the POCT being evaluated. Furthermore, devices that have been discontinued or renamed provided further reduced the evidence base. Both of these factors could cause bias in the conclusions. Additional bias could also be caused due to the limited test selection (only applied studies in primary care). It is possible that by excluding evaluations of devices in secondary care, some tests applicable to primary as well were missed. However, if a POCT is truly

relevant to primary care, it is expected that at least one study evaluating it in a primary care setting would have been found. Some of the identified tests have, presumably, been available on the market for a longer period of time that others. This makes the absolute number of evaluations per test hard to interpret. The determinants investigated in this review was identified by [12] based on a review of existing literature. The relative importance of each determinant, however, could be specific to Dutch GPs and two specific POCTs were used as reference when assigning weights. It is therefore uncertain whether the determinants and their relative importance can be transferred to other POCTs and settings.

This review showed that, despite the growing market and rapid development of new POCTs, studies evaluating such tests fail to report on some of the key factors in the adoption of important innovative diagnostics in primary care. To ensure that an evaluation of a point-of-care test is useful to primary care clinicians, future evaluations should not only focus on the technical performance aspects of a test, but also report on the aspects relating to the clinical utility and risks.

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APPENDIX 1. REVIEW PROTOCOL AND PRISMA FLOW DIAGRAM.
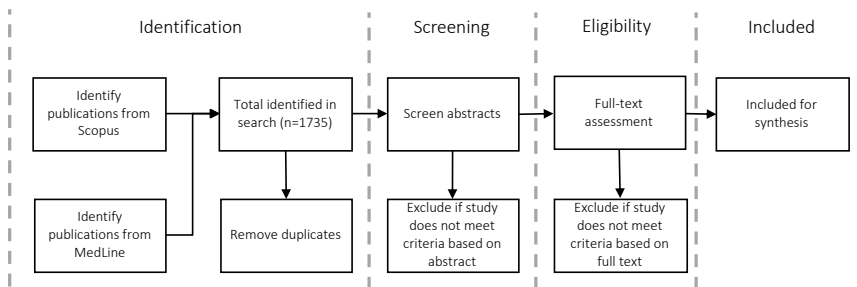
Figure 1.1. Review protocol.
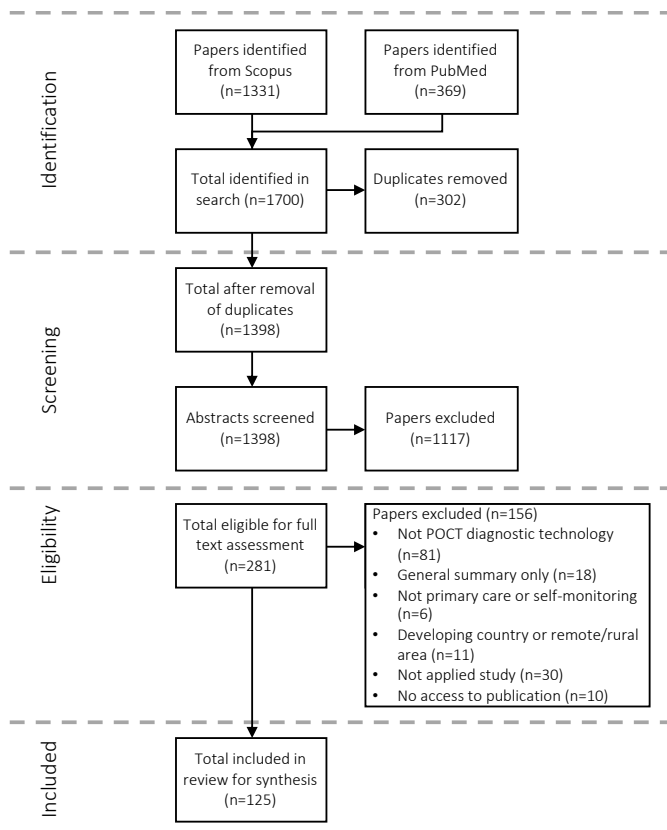
Figure 1.2. PRISMA flow diagram.

APPENDIX 2. LISTS OF POINT-OF-CARE TESTS, PER MEASUREMENT, THAT WERE IDENTIFIED DURING THE REVIEW.

Table 2.1. List of HbA1c POCTs identified from the review.

Name of Device/Analyzer/Test	Number of Studies	Manufacturer	Measurement Used in Study	Other Available Measurements
A1CNow System	5	pts Diagnostics	HbA1c	N/A
Cobas b 101 POC system	1	Roche	HbA1c	HbA1c & Lipid Panel
Cobas b 101 POC system	1	Roche	HbA1c & Lipid Panel	HbA1c
Nycocard™ Reader II	2	Abbott/Alere	HbA1c	D-Dimer, U-Albumin, CRP
B-analyst	1	Menarini Diagnostics	HbA1c	hsCRP, CRP
A1c EZ 2.0	1	BioHermes	HbA1c	N/A
SAKAE's A1c Gear	1	SAKAE Corporation	HbA1c	N/A
Alere Afininion AS100 Analyzer	6	Abbott/Alere	HbA1c	Albumin/Creatinine Ratio, CRP, Lipid Panel
DCA Vantage Analyzer	8*	Siemens	HbA1c	Albumin/Creatinine Ratio
Quo-Test® HbA1c Analyzer	1	EKF Diagnostics Holdings	HbA1c	N/A
Clover A1c Analyser	1	EuroMedix	HbA1c	N/A
in2it™ A1C	2	Bio Rad	HbA1c	N/A
InnovaStar®	1	DiaSys Diagnostic Systems	HbA1c	CRP, Glucose
LABGEO PT10	2	Samsung	HbA1c	Several

Table 2.2. List of CRP POCTs identified from the review.

Name of Device/Analyzer/Test	Number of Studies	Manufacturer	Measurement Used in Study	Other Available Measurements
ABX Micros CRP 200	1	ABX Diagnostics (Horiba Medical)	CRP	N/A
Alere Afininion AS100 Analyzer	6	Abbott/Alere	CRP	Albumin/Creatinine Ratio, HbA1c, Lipid Panel

Nycocard™ Reader II	7	Abbott/Alere	CRP	D-Dimer, U-Albumin, HbA1c
QuikRead 101	4	Orion Diagnostica	CRP	Faecal Occult Blood, U-Albumin
QuikRead Go	3	Orion Diagnostica	CRP	CRP & HbA1c, Streptococcus pyogenes
Eurolyser Smart 700l340	2	EuroLyser Diagnostika	CRP	15 of them

Table 2.3. List of D-Dimer POCTs identified from the review.

Name of Device/Analyzer/Test	Number of Studies	Manufacturer	Measurement Used in Study	Other Available Measurements
Roche CARDIAC® D-Dimer (D-Dimer assay) on the cobas h 232 POC system	2	Roche	D-Dimer	CK-MB, Troponin T, Myoglobin, NT-proBNP
Nycocard™ Reader II	1	Abbott/Alere	D-Dimer	D-Dimer, U-Albumin, CRP
AQT90 FLEX immunoassay analyzer	1	Radiometer	D-dimer	Procalcitonin (PCT), CRP, NT-proBNP, Troponin T, Troponin I
Triage D-Dimer Test	2	Quidel	D-Dimer	N/A
PATHFAST	2	Mitsubishi Chemical Europe GmbH	D-Dimer	Troponin I, NT-proBNP, hsCRP, Myoglobin, HCG and CK-MB mass
LABGEO IB10	1	Samsung	D-Dimer	Troponin I, NT-ProBNP, Troponin I & NT-ProBNP, Troponin I & CK-MB & myoglobin, Troponin I & NT-ProBNP & D-Dimer, beta-hCG, Thyroid-stimulating hormone, Procalcitonin

Table 2.4. List of Influenza and RSV POCTs identified from the review.

Name of Device/Analyzer/Test	Number of Studies	Manufacturer	Measurement Used in Study	Other Available Measurements
cobas® Liat® PCR System	1	Roche	Influenza A & Influenza B	Streptococcus pyogenes group A, Influenza A & Influenza B & RSV, Cdiff, MRSA/SA
cobas® Liat® PCR System	1	Roche	Influenza A & Influenza B & RSV	Streptococcus pyogenes group A, Influenza A & Influenza B, Cdiff, MRSA/SA

mariPOC® (Respi test)	4	ArcDia	Influenza A & Influenza B	Influenza A virus & Influenza B virus & Respiratory syncytial virus & Human Coronavirus OC43 & Human metapneumovirus & Human bocavirus & Parainfluenza virus type 1 & Parainfluenza virus type 2 & Parainfluenza virus type 3 & Adenovirus & Streptococcus pneumoniae
Alere™ i	1	Abbott/Alere	Influenza A & Influenza B	RSV, Streptococcus pyogenes group A
BD Veritor™ Plus system	1	Becton, Dickinson and Company (BD)	RSV	Influenza A & Influenza B
QuickVue Influenza A+B Test	2	Quidel	Influenza A+B	N/A

Table 2.5. List of other frequently evaluated POCTs identified from the review.

Name of Device/Analyzer/Test	Number of Studies	Manufacturer	Measurement Used in Study	Other Available Measurements
AUTION ELEVEN AE-4020	3	Arkray/A.Menarini Diagnostics	Urine Analysis	N/A
Urisys 1100®	2	Roche	Urine Analysis	N/A
Quantum Blue® fCAL	3	Buhlmann Labs	fCAL	Adalimumab, CRP, Infliximab
Triage BNP Test used with the Quidel Triage MeterPro	3	Quidel	BNP	CK-MB & Myoglobin & Troponin I, Troponin I & BNP, CK-MB & Troponin I & BNP, Troponin I & CK-MB & myoglobin & BNP & D-dimer, Troponin I
CoaguChek® XS system	5	Roche	INR	N/A
Alere Cholestech LDX® Analyzer	5	Abbott/Alere	Lipid Panel	N/A
CardioChek® PA Analyzer	2	pts Diagnostics	High Density Lipoprotein (HDL)	Glucose, Total Cholesterol, Triglycerides
Biocard™ Celiac Test	3	Labsystems Diagnostics	IgA deficiency	N/A

Xpert® MTB/RIF	2	Cepheid	MTB and Rifampin-Resistance Mutations	N/A
CardioDetect med	2	rennesens GmbH	Fatty-Acid-Binding Proteins	N/A
Roche CARDIAC® POC Troponin T (Troponin T assay) on the cobas h 232 POC system	3	Roche	Troponin T	CK-MB, D-Dimer, Myoglobin, NT-proBNP

Chapter 3:

Health Economic Evidence of Point-of-Care Testing: A Systematic Review.

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ABSTRACT

OBJECTIVE: Point-of-care testing (POCT) has become an essential diagnostic technology for optimal patient care. Its implementation, however, still falls behind. This paper reviews the available evidence on the health economic impact of introducing POCT to assess if poor POCT uptake may be related to lacking evidence.

STUDY DESIGN: The Scopus and PubMed databases were searched to identify publications describing a health economic evaluation of a of point-of-care (POC) test. Data were extracted from the included publications, including general and methodological characteristics as well as the study results summarized in either cost, effects or an incremental cost-effectiveness ratio. Results were sorted in 6 groups according to the POC test's purpose (diagnosis, screening or monitoring) and care setting (primary care or secondary care). The reporting quality of the publications was determined using the CHEERS checklist.

RESULTS: The initial search resulted in 396 publications, of which 44 met the inclusion criteria. Most of the evaluations were performed in a primary care setting (n = 31; 70.5%) compared to a secondary care setting (n = 13; 29.5%). About two thirds of the evaluations were on POC tests implemented with a diagnostic purpose (n = 28; 63.6%),. More than 75% of evaluations concluded that POCT is recommended for implementation, although in some cases only under specific circumstances and conditions. Compliance with the CHEERS checklist items ranged from 20.8% to 100%, with an average reporting quality of 72.0%.

CONCLUSION: There were very few evaluations in this review that advised against the implementation of POCT. However, the uptake of POCT in many countries remains low. Even though the evaluations included in this review did not always include the full long-term benefits of POCT, it is clear that health economic evidence across a few dimensions of value already indicate the benefits of POCT. This suggests that the lack of evidence on POCT is not the primary barrier to its implementation and that the low uptake of these tests in clinical practice is due to (a combination of) other barriers. In this context, aspects around organization of care, support of clinicians and quality management may be crucial in the widespread implementation of POCT.

INTRODUCTION

Diagnostic testing plays a pivotal part in guiding disease management to improve patient outcomes and wellbeing. Accurate diagnostics can result in both clinical benefits for patients and economic benefits for the healthcare system [1]. Patient outcomes can be improved significantly with diagnostic testing when it is used to identify those patients that will benefit the most from downstream actions, such as initiating, modifying, stopping, or withholding treatment [2]. Furthermore, it can also help to decrease the related healthcare costs by directing resources and care to those that will benefit the most [1].

Early detection of diseases is often cited for being of crucial importance for a patient's survival and to reduce the risk of serious complications [3–5]. To benefit from earlier detection, the diagnostic and therapeutic processes need to be accelerated [6–9]. One way to do this is with the use of point-of-care testing (POCT), a test that supports clinical decision making, which can be performed nearby the patient. It is typically performed during or very close to the time of consultation with results available in minutes [10]. When appropriately utilized, POCT can improve healthcare delivery by providing test results more rapidly, allowing treatment decisions to be made earlier and eliminates the need for individuals to transfer to another location for (laboratory) testing.

POCT has been proven to be beneficial for different applications (monitoring, screening, diagnosis) in several settings. In primary care, GPs can make medical decisions almost immediately, without having to wait for test results from a laboratory [11]. It also makes monitoring patients easier, allowing GPs to change medication on the spot [12]. In countries where the distance to and between medical facilities are quite large, POCT can prevent delay and discomfort. In secondary care, POCT has resulted in shorter waiting time for results, earlier discharge, and a decreased length of stay, which is especially useful in hospitals running over capacity [13]. In low-resource countries with poor infrastructure, the low cost, ease of use and swiftness of POCT has been especially beneficial to allow diagnosis, screening and monitoring of infectious diseases, since access to hospitals and laboraties are limited [14]. Furthermore, it has also been showed that patient satisfaction increases when POCT is used [15].

There are a wide variety of POCTs available for the diagnosis, screening and monitoring of several diseases and health problems, such as cardiovascular disease, sexually transmitted diseases, venous thromboembolism, diabetes and respiratory-tract-infections [16]. The uptake of different POCTs can vary across devices and diseases areas. Variation in uptake can be explained by several factors, such as the number of eligible patients, the perceived clinical utility or the pricing as well as organizational aspects [17]. POC tests may, in some cases, be relatively expensive compared to central laboratory testing. Even for POC tests with proven acceptable accuracy and effectiveness, concerns remain about the cost-effectiveness of the tests. One of the first systematic reviews on POCT in primary care [18], reported on the lack of economic analyses on POC tests and claimed conclusions about its cost-effectiveness could not be drawn due to "insufficient data." Almost a decade later, the National Academy of Clinical Biochemistry published another systematic review of POCT [19], and again, it was reported that there was a lack of reliable evidence regarding the cost-effectiveness of POC tests. This lack of evidence may limit support of policy makers regarding implementation strategies for POCT.

This paper presents a systematic review on the available evidence on the health economic impact of introducing POCT and thereby updates previous research in this area [18,20].

MATERIALS AND METHODS

Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed while carrying out this systematic review [21]. The review aimed to identify publications that evaluated the use of POCT compared with traditional methods (i.e., where no POC tests are used) in terms of health economic outcomes. The publication had to describe any of the following health economic analyses [22]: cost minimization, cost-effectiveness, cost consequence, cost-utility, cost-benefit, budget impact. The study could include any population, time-horizon, and perspective and could be based on real-world data, trial data, experimental data or simulation modelling.

Scopus and PubMed was searched for relevant publications in the English or Dutch language, between 2007 and 2019. The search was performed in

December 2019 and included all terms and text words related to the intervention (POCT) and the type of analysis (health economic evaluations). To ensure that a wide-ranging set of relevant publications were included in the search, the selected search query was kept broad. The review protocol for this systematic review is illustrated in Appendix 1 as a series of steps that were followed.

The search protocol used (in Scopus format) was:

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( TITLE ( "POCT" OR "Point of care" OR "Point of care testing" OR "rapid testing"
OR "bedside testing" OR "laboratory-independent" OR "near patient testing" )
AND  TITLE-ABS-KEY ( "Health effect*" OR "Economic effect*" OR "health
economic" OR "cost minimization" OR "cost-effectiveness" OR "cost
consequence" OR "cost-utility" OR "cost-benefit" OR "budget impact" ) )  AND
PUBYEAR > 2006
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Publications were included based on the following criteria:

- Patients: any human patient population.
- Intervention: an existing POC test that is used to diagnose, screen, or monitor disease. Hypothetical (non-existent) POC tests were excluded.
- Comparator: the publication should compare the usage or implementation of POC testing with one or more strategies, not including POC testing. For example, if a publication compared different POC testing guidelines without also comparing these to a strategy that did not including POC testing, it was excluded from further analysis.
- Study design: publications had to compare POC testing with non-POC (for example laboratory testing) in terms of health and/or cost outcomes. The publication had to describe a health economic evaluation, and report on its methods, data, and results. The evaluation could either be trial-based or model-based cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-consequence analysis (CCA), cost-utility analysis (CUA), cost-benefit analysis (CBA) or budget impact analysis (BIA). Publications not mentioning or performing such analyses but still investigating economic and/or health aspects and comparing POC testing with an alternative without POC testing, were also included (if they met the other criteria). Editorials, letters, methodological/protocol articles, and reviews were excluded.
- Setting: the intervention could be evaluated in any country, as long as it was applied in a primary care or secondary care setting. Publications describing a POC test evaluation in an at-home or self-monitoring setting were excluded.

Study Selection

After collecting publications from Scopus, the titles and abstracts of identified studies were screened for relevance by one reviewer (DL) and discussed with a second reviewer (HK) when required. Any disagreements during the screening were resolved through discussion with a third and fourth reviewer (MIJ; RK).

If there was any doubt on whether or not a publication met the criteria based on the abstract, it was included for full-text assessment. The full-text assessment of all included publications was performed by one reviewer (DL).

Data Extraction and Management

The data was extracted manually by one reviewer (DL) from the publications into Microsoft Excel (version 2016) in pre-defined and labeled columns. General publication characteristics that were extracted, consisted of the country where the evaluation was performed, how the POCT was applied (disease and purpose), whether the POC test was evaluated in a primary care or secondary care setting, the specific setting (for example, hospital or general practice), the purpose of the POC test (diagnosis, monitoring or screening), the comparator and the population. Furthermore, some methodological characteristics were also extracted, namely whether the evaluation was model- or trial-based, the type of health economic evaluation performed, the chosen time horizon, the perspective from which the costs and effects were evaluated, and the type of sensitivity analysis. Outcomes of interest extracted were the impact of POCT on costs (overall costs and cost per patient), the impact on health outcomes (e.g., QALYs/DALYs, prescriptions avoided, life-years saved), and the balance between the two (e.g., Incremental Cost Effectiveness Ratio). The conclusions of each evaluation were also extracted. The extracted data was summarized in both text and table format before providing a descriptive synthesis of findings.

Methodological assessment

The reporting quality of the publications included in the synthesis set was determined by assessing how many of the 24 key criteria contained in the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist were met [23]. This checklist was selected based on its endorsement by several journals as a guideline on how to report a health economic evaluation. The 24 criteria items are divided according to title and abstract (2 items);

introduction (1 item); methods (14 items); results (4 items), and discussion (3 items). When scoring publications against the CHEERS checklist, items that completely met the criteria were given a score of 1, while a score of 0 was given to items that did not meet the criteria. If an item only partially met the criteria, it was also given a score of 0. In individual studies, some of the criteria items were deemed as not applicable. For example, if the evaluation was performed alongside a trial without the use of a model, aspects such as choice of model (item 15), and assumptions underlying the model (item 16), was not applicable. Furthermore, if the evaluation was a cost analysis only, the measure of effectiveness (item 11) was not applicable. Therefore, only criteria items relevant to the publication counted towards the calculation of its overall compliance. To assess the overall compliance of a publication with the checklist, the proportion of criteria items that were met were calculated, based on a total number of applicable criteria items in the checklist. If more than 75% of the criteria items were met, publications were classified as high quality; if between 50% and 75% of the items were met, they were classified as medium quality; and if less than 50% of the items were met, they were classified as low quality.

The reporting quality did not play any role in the inclusion or exclusion of publications; all publications meeting the inclusion criteria had their quality assessed as described above.

RESULTS

Search Results

A total of 540 publications were obtained from the initial search of the Scopus and PubMed database, of which 144 were duplicates. A further 300 of publications were excluded during the abstract screening. The main reason for excluding publications was because they did not describe a health economic evaluation or did not compare with non-POCT. After screening all abstracts, 96 publications were included in the full-text assessment. Based on the full-text assessment, 52 publications were excluded, with the main reasons for exclusion being publications did not describe a health economic evaluation (n = 21) or did describe a comparison of POCT with a method that did not include POCT (n = 18). Ultimately, 44 publications were included in the final review for synthesis. The PRISMA flow diagram of the search is presented in Figure 1.
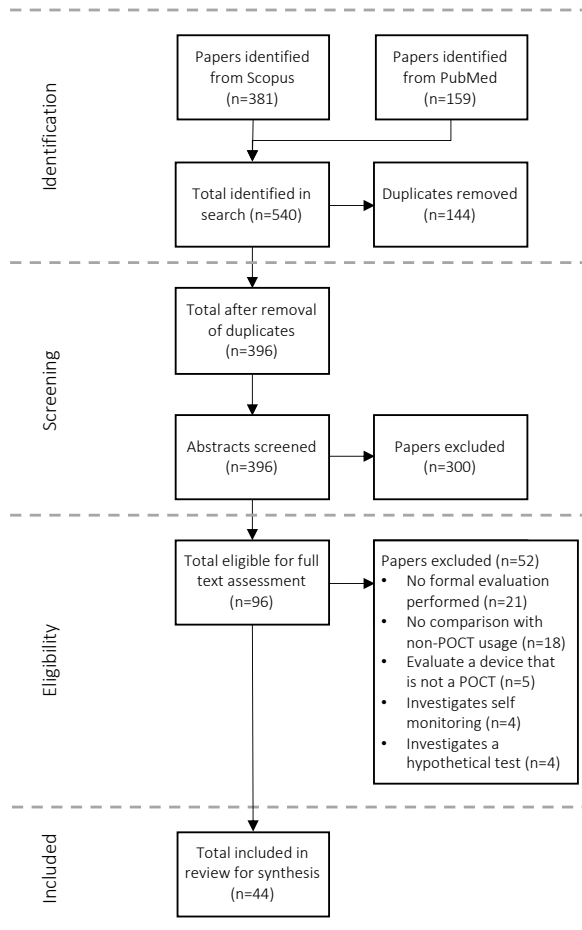
Figure 1. PRISMA flow diagram

General Characteristics

An overview of the general characteristics of the publications that were included for synthesis is provided in Table 1. Publications with a score of more than 75%, based on the CHEERS checklist, are shaded green. Nearly 60% (n = 26) of the 44 publications were published since 2015, with countries of origin being the United States (n = 9) and the United Kingdom (n = 7), followed by the Netherlands (n = 5) and Australia (n = 4). There were also several publications focusing on Sub-Saharan Africa (n = 10), of which four were specific to South Africa and two to Mozambique.

Table 1. General Characteristics of Included Publications

Publication	Country	Setting	Purpose	Health Problem	Comparator	Population
Frank et al. 2019 [41]	Zimbabwe	Primary care, clinics	Diagnosis	HIV	POCT & usual care (conventional assays)	HIV-exposed infants
Goldstein et al. 2019 [42]	South Africa	Secondary care, emergency centre	Diagnosis	Symptom specific	Laboratory testing & POCT with CBC & POCT without CBC	Adult patients with abdominal/chest symptoms or generalised body pain/weakness
Gout-Zwart et al. 2019 [43]	The Netherlands	Primary care, community pharmacies	Screening	Decreased renal function	POCT & standard care	Patients (>65 years) presenting with antibiotic prescriptions in community Pharmacies
Lee et al. 2019 [44]	India	Primary care, health centres & clinics	Diagnosis	Tuberculosis	Sputum smear microscopy in DMCs & Xpert MTB/RIF in DMCs & Truenat in DMCs & Truenat for POC	HIV-negative adult patients with a suspicion of tuberculosis
Pooran et al. 2019 [45]	South Africa, Zambia, Zimbabwe, and Tanzania	Primary care, clinics	Diagnosis	Tuberculosis	POC Xpert & smear microscopy	Patients presenting at the clinics with symptoms suggestive of tuberculosis
Rahamat-Langendoen et al. 2019 [46]	The Netherlands	Secondary care, hospital	Diagnosis	Influenza and respiratory syncytial virus	POCT & laboratory testing	Adult patients with suspicion of respiratory viral infection
Rajasingham et al. 2019 [47]	South Africa	Primary care, clinics	Monitoring	HIV-TB co-infection	POCT (≥120 threshold) & POCT (≥200 threshold) & POCT (bin placement) & automated testing & current standard of care	HIV/TB co-infected adults on antiretroviral therapy who were initiating TB therapy
Spaeth et al. 2019 [27]	Australia	Primary care, health clinics	Diagnosis	Sepsis, respiratory infection and appendicitis	POCT & clinical judgement (without POCT)	Patients presenting with fever and symptoms suggestive of sepsis, respiratory infection or appendicitis
Esteve et al., 2018 [48]	Spain	Primary care; primary care centers	Diagnosis	Coeliac disease	POCT followed by biopsy & POCT followed by blood analysis and biopsy & standard diagnosis followed by blood analysis and biopsy	Adult patients (following a gluten containing diet with clinical manifestations of coeliac disease)
Holmes et al., 2018 [49]	United Kingdom	Primary care; general practice	Diagnosis	Respiratory tract infection	POCT & immediate antibiotic prescription	Adult patients (with symptoms of respiratory tract infection)
Lubell et al., 2018 [50]	Viet Nam	Primary care; primary care healthcare setting	Diagnosis	Respiratory infections	POCT & clinical judgement (without POCT)	Patients (with non-severe acute respiratory infection)

Study	Country	Setting	Type	Condition	Intervention	Population
Spaeth et al., 2018 [51]	Australia	Primary care; health centers	Diagnosis	Acute coronary syndrome	POCT & clinical judgement (without POCT) and review of clinical record	Patients (presenting with chest pain)
				Renal failure		Patients (presenting with chronic renal failure - missed dialysis)
				Diarrhea/dehydration		Patients (presenting with acute diarrhea)
El-Osta et al., 2017 [52]	United Kingdom	Primary care; 9 general practices (7 using POCT; 2 not using POCT)	Screening	Cardiovascular disease	POCT & laboratory testing	Patients aged 40-74 years (eligible for NHS Health Check)
Hyle et al., 2017 [53]	Mozambique	Primary care; rural setting clinics	Monitoring	HIV	Clinical antiretroviral therapy monitoring strategy with POCT & clinical antiretroviral therapy monitoring strategy without POCT	Adult patients (initiating ART)
		Primary care; urban setting clinics			Biannual POCT or Viral load monitoring & laboratory testing	
Kip et al., 2017 [54]	The Netherlands	Primary care; general practice	Diagnosis	Acute coronary syndrome	POCT & clinical judgement (without POCT)	Patients older than 35 (presenting with chest complaints)
Lewandrowski et al., 2017 [55]	United States	Primary care; general practice	Diagnosis	Not specified – Applied HbA1c test and Lipid Panel	POCT & laboratory testing	Patients (for who tests were deemed medically indicated by the physician)
You et al., 2017 [56]	Hong Kong	Secondary care; ambulatory care	Diagnosis	Influenza	POCT & clinical judgement (without POCT)	Patients (elderly, presenting with influenza symptoms)
Heffernan et al., 2016 [57]	South Africa	Primary care; clinic (representative of current care)	Diagnosis	HIV	POCT & laboratory testing	Patients (heterosexual adults aged 15-49 years from the start of the HIV epidemic)
		Primary care; clinic (enhanced counselling and testing context)				
		Primary care; clinic (universal test and treat context)				
Janković et al., 2016 [58]	Serbia	Primary care; general practice	Diagnosis	Acute coronary syndrome	POCT & the standard diagnostic procedure, physical examination, and electrocardiogram monitoring	Patients (presenting with nontraumatic chest pain)
Ward et al., 2016 [59]	United States	Secondary care; emergency department	Screening	Sepsis	A POC lactate program & Usual Care Strategy	Older patients (suspected sepsis)
Whitney et al., 2016 [60]	United States	Secondary care; pediatric emergency department	Diagnosis	Acute gastroenteritis	POC electrolyte testing & traditional serum chemistry testing	Patients (children with acute gastroenteritis)

Study	Country	Setting	Purpose	Condition	Intervention & Comparator	Population
Challen et al., 2015 [61]	United States	Secondary care; pharmacist-run anticoagulation clinics within a community-owned health system	Monitoring	Anticoagulant therapy	POCT & laboratory testing	Adult patients (indication for anticoagulation that had been taking warfarin for at least 1 year)
Ciaranello et al., 2015 [62]	South Africa	Primary care; general antenatal clinic	Monitoring	HIV	POCT & laboratory testing	Adult patients & their infants (HIV-infected, pregnant women)
Hendriksen et al., 2015 [63]	The Netherlands	Primary care; general practice	Diagnosis	Deep venous thrombosis	POCT & laboratory testing & referral to hospital for further testing	Adult patients (suspected lower extremity deep venous thrombosis)
Hunter et al., 2015 [25]	United Kingdom	Primary care; general practice	Diagnosis	Respiratory tract infection	GP or practice nurse with POCT & GP with POCT and communication training & clinical judgement (w/o POCT)	Patients (with respiratory tract infection)
Whiting et al., 2015 [26]	United Kingdom	Secondary care; hospital	Diagnosis & Screening	Haemostasis	POCT & laboratory testing	Adult patients (undergoing cardiac surgery with high risk of bleeding) Adult patients (trauma patients with high risk of bleeding)
Asha et al., 2014 [64]	Australia	Secondary care; emergency department	Diagnosis	Acute coronary syndrome	POCT & laboratory testing	Adult patients (suspected acute coronary syndrome)
Crocker et al., 2014 [65]	United States	Primary care; ambulatory care	Monitoring & Screening	Hypertension, dyslipidemia & diabetes	POCT & laboratory testing	Adult patients (requiring HbA1c, fasting lipid, or comprehensive metabolic panel testing)
Chadee et al., 2014 [66]	Canada	Primary care; clinic	Monitoring	Diabetes	POCT & laboratory testing	Patients (with diabetes)
Henson et al., 2014 [28]	United States	Secondary care; hospital	Screening	Methicillin-resistant Staphylococcus Aureus	POCT & laboratory testing	Patients (admitted to the intensive care unit)
Hyle et al., 2014 [67]	Mozambique	Secondary care; outpatient voluntary testing and counseling clinics	Diagnosis	HIV	POCT & laboratory testing	Adult patients (newly diagnosed with HIV)
Nilsson et al., 2014 [68]	Sweden	Primary care; healthcare centres	Diagnosis	Acute myocardial infarction & unstable angina	POCT & clinical judgement (without POCT)	Patients older than 35 (presenting with chest pain, dyspnoea on exertion, unexplained weakness and/or fatigue)
Turner et al., 2014 [69]	United Kingdom	Primary care; genitourinary medicine clinics	Diagnosis	Chlamydia & gonorrhoea	POC NAAT & standard pathways of management for chlamydia and gonorrhoea (w/o POCT)	Adult patients (visiting the clinic)

Study	Country	Setting	Type	Condition	Comparison	Population
Huang et al., 2013 [70]	United States	Primary care; sexually transmitted disease clinic	Screening	Chlamydia	POCT & traditional nucleic acid amplification testing	Patients (sexually active women)
Oppong et al., 2013 [7]	Norway & Sweden	Primary care; clinic	Diagnosis	Acute cough & lower respiratory tract infections	POCT & clinical judgement (without POCT)	Patients (presenting with acute or worsened cough)
Van Dyck et al., 2012 [72]	United Kingdom	Primary care; general practice	Diagnosis	Acute coronary syndrome	POCT & primary care prevention (cardio-vascular exercise programme) & telemonitoring adherence tools & current care	Patients (at risk of developing acute coronary syndrome)
Cats et al., 2011 [73]	The Netherlands	Primary care; general practice	Diagnosis	Respiratory Tract Infection	POCT & POCT with communications training & usual care	Adult patients (with lower respiratory tract infection)
Fitzgerald et al., 2011 [74]	United Kingdom	Secondary care; emergency department	Diagnosis	Cardiovascular disease	POC biomarker panel & usual care without the POC panel	Adult patients (suspected myocardial infarction)
Owusu-Edusei Jr. et al., 2011 [75]	Sub-Saharan Africa	Primary care; clinic	Screening	Syphilis	A Dual-POC test & laboratory testing & POC RPR testing & POC treponemal immunochromato-graphic strip testing & no testing	Patients (pregnant woman in high syphilis prevalence population)
Golden et al., 2010 [76]	United States	Secondary care; hospital	Diagnosis	Cardiovascular disease	POCT & laboratory testing	Child patients undergoing cardiac catheterization
Laurence et al., 2010 [77]	Australia	Primary care; general practice	Monitoring	Diabetes / Hyperlipidaemia / Anticoagulant therapy / Acute coronary syndrome	POCT & laboratory testing	Adult patients (with diabetes, hyperlipidaemia and/or being on anticoagulant therapy)
Kong et al., 2008 [29]	Singapore	Secondary care; hospital-based anticoagulation clinic	Monitoring	Anticoagulant therapy	POCT & laboratory testing	Adult patients (admitted to the anticoagulation clinic)
Rydzak et al., 2008 [78]	Sub-Saharan Africa	Primary care; prenatal health clinic	Screening	Syphilis	POCT RPR screening & POC immunochromatographic strip screening & standard laboratory screening & no screening	Patients & their infants (pregnant women older than 15)
Udeh et al., 2008 [79]	United States	Primary care; general practice	Diagnosis	Adenoviral conjunctivitis	POCT & clinical judgement (without POCT)	Patients (with a conjunctivitis diagnosis)

Green shaded cells indicate that the publication received a score of more than 75%, based on the CHEERS checklist.
ART Antiretroviral therapy, CBC complete blood count, CD4 cluster of differentiation 4, DMC designated microscopy centers, HIV Human Immunodeficiency virus, NHS National Health Service.

Most of the evaluations were described in a primary care setting (n = 31; 70.5%) compared to a secondary care setting (n = 13; 29.5%). More than half of the evaluations were on POC tests implemented with a diagnostic purpose (n = 28; 63.6%), whereas the number of evaluations on monitoring (n = 7; 15.9%) and screening tests (n = 7; 15.9%) were evenly divided. In one publication, the POC test being evaluated was implemented for both monitoring and screening purposes, whereas in another, the test was implemented with both a diagnostic and monitoring purpose.

The POC tests being evaluated, cover several health problems. Some publications evaluated a POC test for more than one health problem, resulting in a total of 57 entries. Among these, acute coronary syndrome and cardiovascular diseases were the most covered disease (n = 9), followed by respiratory infections (n = 6), HIV/Aids (n = 6), sexually transmitted diseases (n = 5), including chlamydia, gonorrhea and syphilis, diabetes (n = 4), and anticoagulant therapy and haemostasis (n = 4).

Overall, a total of 61 effectiveness measures were reported across all publications. The measure of effectiveness that was reported on the most was QALYs (n = 12), followed by antibiotic prescriptions (n = 6), length of stay (n = 5), life expectancy (n = 5) and hospitalization/referrals (n = 4). The length of stay measure (n = 5) was unique to evaluations in a secondary care setting, and measures related to antibiotic prescriptions (n = 6) were only used in evaluations in primary care.

Health Economic Evaluations of POCT

Screening

The outcomes for POC tests that were evaluated in the screening of patients are summarized in Table 2.1 in Appendix 1. This category has the least amount of publications (n = 8), with six publications in a primary care context and two publications in a secondary care context, each with one evaluation. Only three of the evaluations reported a ratio== of the costs and effectiveness. In all of these evaluations, POCT resulted in favorable cost-effectiveness compared to usual care and the implementation of POCT is recommended. Of the remaining five evaluations not reporting a ratio, four found that POCT is less expensive and increases effectiveness while one reported an increase in both costs and

effectiveness. All but one of these evaluations concluded that the implementation of POCT is a cost-effective option. Owusu-Edusei, Gift, & Ballard (2011) concluded in their evaluation of primary care syphilis screening in Sub-Saharan Africa, that some POC tests could lead to overtreatment and would generally only be cost-effective in resource-poor settings with high disease prevalence.

Diagnostics

A summary of the outcomes for POC tests that were evaluated as a diagnostic (or for diagnostic support) is provided in Table 2.2 in Appendix 2. About two-thirds of the publications in this review, evaluated POCT as a diagnostic (or for diagnostic support). Twenty-three of the 34 evaluations reported a ratio of the costs and effectiveness. Of these, 20 concluded in favor of implementing POCT, while one concluded against its implementation based on a high probability that POCT is dominated by standard care. One evaluation noted that the ratio changes according to adherence to clinical guidelines and concluded that POCT becomes considerably less cost-effective when deviating from clinical guidelines, that is, when the test outcome does not always affect the subsequent patient management decision. Of the 11 evaluations that did not report a ratio, all found an increase in effectiveness due to POCT, two found an increase in costs, while the rest reported cost savings.

Monitoring

A summary of the outcomes for POC tests that were evaluated for the monitoring of patients is provided in Table 2.3 in Appendix 2. In total ten evaluations considered a primary care context and 4 evaluations a secondary care context. Nine of the evaluations reported a ratio of the costs and effectiveness. Of these evaluations, three evaluations concluded in favor of the implementation of POCT, while 1 concluded against its implementation since POCT was both more expensive and less effective. The remaining five evaluations could not conclude with certainty whether or not POC should be implemented for monitoring in primary care. Two of these evaluations concluded that even though POCT dominated usual care, POCT is only likely to be cost-effective in settings without access to laboratory services. The remaining three evaluations did find that POCT has a chance of being cost-effective, but that this chance depends (heavily) on the value society would place on the effectiveness outcome or that more precision

in their estimations is required. The five evaluations that only reported costs and a measure of effectiveness (without an associated ratio) all concluded in favor of POCT, with four of the five reporting reduced costs due to POCT and all five reporting increased effectiveness.

Methodological Characteristics

An overview of the methodological characteristics of the publications is provided in Table 2. Most of the health economic evaluations were labelled by the publications in the title, abstract, or methods section as a cost-effectiveness analysis (n = 27; 61.4%). Additionally, two publications described both a cost-effectiveness analysis and cost-benefit analysis, and two publications described both a cost-effectiveness and budget-impact analysis. The time horizon applied in evaluations ranged from 28-days to a lifelong time horizon. There were 10 publications that failed to indicate the selected time horizon. This would mean their results cannot be interpreted nor compared with those of other studies investigating the same POC test. A 6-month and lifelong time horizon were applied the most (both n = 5; 11.4%) followed by a 28-day period (n = 3; 6.8%).

The majority of the publications (n = 26; 59.1%) were classified as model-based and used a decision-analytic model to describe the health economic evaluation. The remaining publications (n = 18; 40.9%) were classified as trial based. The most popular choice of model was a decision tree (n = 15) followed by a Markov model (n = 7). There were also two studies combining these modelling methods. Only three of the 18 trial-based evaluations made use of a simulation model. One of these publications used data collected during a trial as input for a decision tree model and one as input for a Markov model. The other used a regression model to analyze trial data.

The evaluations were mostly performed from a healthcare system perspective (n = 14; 31.8%), societal perspective (n = 7; 15.9%) and healthcare provider perspective (n = 4; 9.1%). The healthcare system perspective relates to the perspective of the entire (nationwide) healthcare organization whereas the healthcare provider perspective relates to the perspective of a single type of provider, such as GPs. Nine (20.5%) of the publications failed to indicate the perspective of the study. More than 60% of publications (n = 28; 63.6%) made use of a sensitivity analysis to assess the uncertainty of results. Of these, 15 performed a deterministic analysis

only (5 trial based; 10 model-based), 8 performed a probabilistic analysis only (1 trial-based evaluation including bootstrapping; 7 model-based evaluations including a probabilistic analysis), and five evaluations applied both deterministic and probabilistic analyses (all model-based). The remaining 16 publications did not apply any sensitivity analysis and mainly concerned trial-based evaluations (n = 9).

Table 2. Methodological Characteristics of Included Publications

Publication	Type	Model	Perspective	Evaluation	Time Horizon	Reported (CP/OC/E/R)	DSA	PSA
Frank et al. 2019 [41]	Model based	State-transition model	Health system	CEA	HIV programme	CP/E/R	X	
Goldstein et al. 2019 [42]	Trial based	NA	Emergency centre perspective	CEA	± 4 months	CP/E/R		
Gout-Zwart et al. 2019 [43]	Model based	Decision tree	Healthcare payers	BIA	1 year	CP		
Lee et al. 2019 [44]	Model based	Microsimulation model	Health system	CEA & BIA	5 years	CP/OC/E/R	X	
Pooran et al. 2019 [45]	Trial based	NA	Healthcare provider	CEA	1 year	OC/E/R	X	
Rahamat-Langendoen et al. 2019 [46]	Trial based	Markov model	Health economic	CBA	5 months	CP/E/R		
Rajasingham et al. 2019 [47]	Model based	Markov model	Health sector	CEA	6 months	OC/E/R	X	X
Spaeth et al. 2019 [27]	Trial based	NA	Not specified	CBA	6 months	OC/E		
Esteve et al., 2018 [48]	Trial based	NA	Not specified	CEA	18 months	CP		
Holmes et al., 2018 [49]	Model based	Decision tree	Healthcare system (NHS)	CEA	28 days	OC/E/R	X	X
Lubell et al., 2018 [50]	Trial based	NA	Societal	CBA	Not specified	CP/E	X	
Spaeth et al., 2018 [51]	Trial based	Decision tree	Healthcare system	CEA	6 months	CP/OC/E		X
El-Osta et al., 2017 [52]	Model based	Decision tree	Healthcare system (NHS)	CMA	< 1year	CP/E		X
Hyle et al., 2017 [53]	Model based	Markov model*	Societal	CEA & BIA	Lifelong	CP/E/R	X	
Kip et al., 2017 [54]	Model based	Decision tree	Societal	CUA	Lifelong	CP/E/R		X
Lewandrowski et al., 2017 [55]	Trial based	NA	Not specified	CRA	Not specified	CP/E		
You et al., 2017 [56]	Model based	Decision tree	Healthcare provider	CEA	Season of influenza	CP/E/R		X
Heffernan et al., 2016 [57]	Model based	Dynamic, transmission model	Not specified	CEA	1 - 3 years	OC/E/R		
Janković et al., 2016 [58]	Model based	Decision tree	Healthcare services purchaser	CEA	ACS treatment episode	CP/E/R		X
Ward et al., 2016 [59]	Model based	Decision tree	Societal	CEA	Not specified	CP/E/R	X	
Whitney et al., 2016 [60]	Model based	Decision tree	Payer and provider (hospital system)	CEA	Not specified	CP	X	

Study	Type	Model	Perspective	Analysis	Time horizon	Outcome	DSA	PSA
Challen et al., 2015 [61]	Trial based	NA	Not specified	CEA	2 years	OC/E		
Ciaranello et al., 2015 [62]	Model based	Decision tree	Healthcare system	CBA	Lifelong	CP/E	X	
Hendriksen et al., 2015 [63]	Model based	Markov model	Health economic	CEA	10 years	CP/E/R		X
Hunter et al., 2015 [25]	Model based	Decision tree & Markov model	Healthcare system (NHS)	CEA	3 years	CP/E/R		X
Whiting et al., 2015 [26]	Model based	Decision tree	Healthcare system (NHS)	CEA	1 year	CP/E/R		X
Asha et al., 2014 [64]	Trial based	NA	Healthcare system	CEA	6 months	CP/E/R		
Crocker et al., 2014 [65]	Trial based	NA	Healthcare provider	CRA	Not specified	CP/E		
Chadee et al., 2014 [66]	Model based	Not specified	Healthcare system	BIA	Not specified	OC	X	
Henson et al., 2014 [28]	Model based	Outcomes tree	Not specified	CBA & CEA	3 months	CP/OC/E		
Hyle et al., 2014 [67]	Model based	Markov model*	Healthcare system	CBA & CEA	Not specified	CP/E/R	X	X
Nilsson et al., 2014 [68]	Trial Based	NA	Societal	CEA	30 days	CP/E/R		
Turner et al., 2014 [69]	Model based	Decision tree	Healthcare system (NHS)	CEA	28 days	OC/E/R	X	
Huang et al., 2013 [70]	Model based	Decision tree	Healthcare system	CEA	2 – 10 years	OC/E/R	X	X
Oppong et al., 2013 [71]	Trial based	Regression model	Health service	CEA	Not specified	CP/E/R		
Van Dyck et al., 2012 [72]	Model based	Decision tree	Not specified	CEA	Not specified	CP/E		
Cals et al., 2011 [73]	Trial based	NA	Healthcare provider	CEA	28 days	CP/E/R	X	
Fitzgerald et al., 2011 [74]	Trial based	NA	Healthcare system (NHS)	CUA	3 months	CP/E/R	X	
Owusu-Edusei Jr. et al., 2011 [75]	Model based	Decision tree & Markov model	Societal & healthcare provider	CEA	Lifelong time horizon	OC/E	X	X
Golden et al., 2010 [76]	Trial Based	NA	Not Specified	CBA	3 months	CP/E		
Laurence et al., 2010 [77]	Trial based	NA	Societal	CEA	18 months	OC/E/R	X	
Kong et al., 2008 [29]	Trial based	NA	Not specified	CIA	6 months	CP/E		
Rydzak et al., 2008 [78]	Model based	Markov model	Not specified	CEA	Lifelong	OC/E/R	X	
Udeh et al., 2008 [79]	Model based	Decision tree	Societal	CEA	Not specified	CP/E/R	X	

BIA Budget impact analysis, *CBA* Cost-benefit analysis, *CEA* Cost-effectiveness analysis, *CIA* Cost-identification analysis, *CMA* Cost-minimization analysis, *CP/OC/E/R* Cost Per Patient/Overall Cost/Effectiveness/Ratio *CRA* Cost-revenue analysis, *CUA* Cost-utility analysis, D*SA* Deterministic Sensitivity Analysis, *PSA* Probabilistic Sensitivity Analysis
*Not specified in study, but derived from text

Quality of Publications

Two of the publications [25,26] reported all of the applicable items in the CHEERS checklist. Compliance with the checklist items ranged from 20.8% to 100%, with an average of 72.0%. There were three publications [27–29] that were classified as being of low reporting quality, with a score of less than 50%. Almost half of the publications (n = 21; 47.7%) were considered of high reporting quality with a score of more than 75%, the remainder of the publications (n = 20; 45.5%) were medium quality. The worst scoring criteria items were time horizon, discount rate, target

population and subgroups, and study perspective. Publications focusing on primary care had an average score of 75.2%, whereas publications focusing on secondary care had an average score of 65.7%. Generally, publications evaluating POC tests as a diagnostic tool scored slightly higher (75.35% for primary care, 72.2% for secondary care) compared to monitoring (74.8% for primary care, 64.0% for secondary care) and screening (74.5% for primary care, 58.5% for secondary care).

DISCUSSION

The heath economic benefits of POCT reported most often by evaluations in this review was that it allows early diagnosis, a decrease in the number of hospitalizations and referrals to specialized care, reduced risks of infection and antibiotic prescription, and a decrease in additional burden and costs associated with referrals and additional testing. Some of the evaluations, specifically those incorporating a longer time horizon, even found that the costs continue to decrease over time when POCT is implemented. There were very few evaluations that recommended against the implementation of POCT. Three evaluations found that the benefits of implementing POCT do not outweigh the increase in cost. One evaluation found during the implementation of POCT in a trial, that clinicians choose not to adhere to the results of the test. They concluded from a sensitivity analysis that only with higher adherence to test results, would POCT be cost-effective. Similarly, a few publications mentioned that POCT is more effective with closer adherence to clinical guidelines.

Although the publications included were, on average, considered to be of medium reporting quality, there are some important criteria items that were generally not reported on. Firstly, although most of the publications described the health economic assessment within a specific timeframe, it was rarely explained why the selected timeframe was chosen. Secondly, the cost-effectiveness of an intervention is conditional to the target population [30]; therefore, it is important providing a sufficient description or reference of the considered population is essential for the correct interpretation of results. In several of the publications, however, the target population and subgroups were poorly described. The lack of reporting on these items might limit the usefulness of these evaluations to policy and decision makers. However, it is important to note that the CHEERS checklist only reflects the way evaluations are reported and communicated, and not

necessarily the quality of how they were conducted. Furthermore, the overall reporting quality of publications evaluating POC tests implemented as a diagnostic is slightly higher than that of publications evaluating POC tests for screening and monitoring. However, there are not enough publications evaluating screening and monitoring POC tests to draw robust conclusions about purpose-related quality.

Three common limitations observed in the evaluations in this review were, firstly, that the whole healthcare system and clinical pathways were not always considered, but only a specific cohort in a generally small setting. Secondly, only a few specific outcome measures were selected to evaluate the impact that POCT could have, omitting other outcome measures that could be relevant [31]. A third observed limitation was the limited evidence available to populate models, which often leads to assumptions having to be made [32], especially regarding prescribing behavior related to PCT test results and adherence to treatment. When properly accounted for, such assumptions or limited evidence, lead to substantial uncertainty in the results. Regarding adherence and behavior data from protocolized randomized trials may also not be optimal to use in models, as these data may not reflect actual real-world use and interpretation of POC test outcomes.

This review confirmed the wide range and applicability of POCT. Evaluations ranged from POC tests used by general practitioners to prevent unnecessary treatment and referrals to the emergency room where the rapid diagnosis allows patients to be discharged more quickly. Further value is added by POCT through increased patient satisfaction and overall improvement in care provision [1,15]. In addition to these benefits, the implementation of POCT may also have negative impact, for example, an increase in costs, increased labor requirements, and alterations to the processes and workflow [33,34]. These aspects could discourage GPs and care providers from implementing POCT in their practice [35].

Considering that POCT is accompanied by both potential benefits and potential burdens, it is necessary to establish that the implementation of POCT in practice will have sufficient benefits to justify the burdens. From this review, it is apparent that many publications find POCT to be a valuable counterpart to traditional laboratory testing or usual care. However, POCT should not always be perceived as cost-saving. Some publications indicated that implementing POCT would result

in higher costs, but this was justified by the long-term gains such as increased life expectancy, reduced unnecessary referrals to specialists, unnecessary antibiotic prescriptions and decreased length of stay. It is important to recognize that the cost-effectiveness of POCT, in general, will likely vary according to the target disease, and the cost-effectiveness of specific POC tests can vary according to the population and setting [36].

The implementation and utilization of POC tests will not be reliant on technical advancements alone, but also on the changes in costing systems and reimbursement practices. Health system resources are limited, and it is essential to ensure that the resources allocated to diagnostics, such as POC tests are optimized. Health economic evaluations are often conducted to contribute to and inform on such decisions. This review showed that high-quality health economic evaluations on POCT are limited. It is highly recommended that future health economic evaluations follow a formal checklist, such as the CHEERS [23] or AGREEDT [37] checklist when reporting to ensure that all of the important criteria are included in the final evaluation report. This might also, indirectly, increase the quality of the evaluations themselves, if such checklists are considered during the evaluation process itself rather than when reporting results at the end.

In general, the results of the health economic evaluations that were included in this review are somewhat limited or non-transferrable. In most cases, the evaluations are described and set up to meet the local needs and requirements, which resulted in studies that are cohort-specific and have a limited scope. Consequently, the evidence generated from these evaluations is not as comprehensive as it could have been. In a study using HbA1c as an exemplar, it has also been suggested that the benefits of POCT are not realized, in part, because it is not measured in studies [38]. While dimensions of value and relevant impact elements for POCTs have been defined in literature [31,37], including all of these is very challenging [39] foremost due to a common lack of evidence on the expected benefits in certain dimensions.

Even though the evaluations included in this review did not always include the full long-term benefits of POCT, it is clear that health economic evidence across a few dimensions of value already indicate the benefits of POCT. Previous systematic reviews [18,19] reported that more health economic evidence is necessary to guide the expansion of the use of POCT. As seen in this review, the health economic

evidence has increased and provides promising evidence, with about 77% of the health economic evaluations included in this review, concluding in favor of implementing POCT. However, regardless of the increase in health economic evidence, the overall uptake of POCT remains slow [17,38,40]. This suggests that the lack of health economic evidence on POCT is not the primary barrier to the expansion of POCT and that the slow uptake of these tests in clinical practice is due to (a combination of) other barriers. It is also possible that the system-level evidence provided in health economic evaluations, is irrelevant to the local stakeholders in charge of the implementation of POCT [22]. In this context, aspects around organization of care, support of clinicians and quality management may be crucial in the widespread implementation of POCT.

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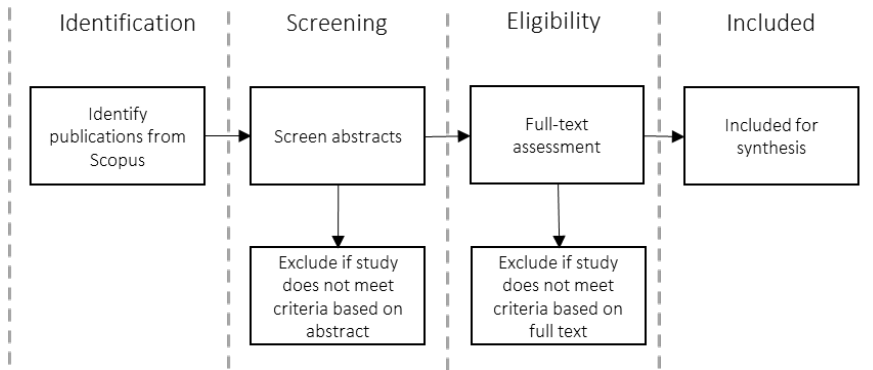
APPENDIX 1. REVIEW PROTOCOL.

Figure 2.1. Review protocol

APPENDIX 2. SUMMARY OF THE OUTCOMES FOR POC TESTS THAT WERE EVALUATED FOR THE SCREENING, DIAGNOSIS AND MONITORING OF PATIENTS.

Table 2.1. Outcomes of POCT for Screening

Primary Care					
Author, Year	Cost per patient	Overall cost	Effectiveness	Ratio	Conclusion
Gout-Zwart et al. 2019 [43]	Standard care: €264.20; POCT: €178.12; Cost savings of €86.08				In favor of POCT
El-Osta et al., 2017 [52]	POCT: £5.28 less (not taking into account patients that did not respond or show up) OR £7 less (taking into account patients that did not respond or show up).		Number of NHS Health Checks completed - POCT: 8.74; laboratory testing: 7.50.		In favor of POCT
Crocker et al., 2014* [65]	Financial benefit due to POCT was $31.26 per patient		Total number of tests ordered per patient - 21% decrease due to POCT. Letters and phone calls to patients - 89% decrease due to POCT. Revisits due to abnormal test results - 61% decrease due to POCT.		In favor of POCT
Huang et al., 2013 [70]		POCT: $711,508; NAAT: $782,214; Savings of $70,706 due to POCT.	Cases of pelvic inflammatory disease averted - POCT: 14; NAAT: 0.	ICER: -$5050 per disease averted	In favor of POCT
Owusu-Edusei Jr. et al., 2011 [75]		Dual-POC test: $79,000; Laboratory testing: $86,000; POC RPR testing: $84,000; POC ICS testing: $76,000; No testing: $106,000.	DALYs averted - Dual-POC test: 299; Laboratory testing: 234; POC RPR testing: 247; POC ICS testing: 326; No testing: 0. Overtreatment rates – Dual-POC test: 0.18; Laboratory testing: 0; POC RPR testing: 0.32; POC ICS testing: 1.42; No testing: 0.		Neither against nor in favor of POCT: will only be cost-effective in resource-poor settings with high prevalence
Rydzak et al., 2008 [78]		Per 1000 women compared with no screening - POC RPR screening: cost savings of $161,310; POC ICS Screening: cost savings of $170,030; standard laboratory screening: cost savings of $110,220.	Life years gained (per 1000 women) - POCT RPR screening: 250; POC ICS screening: 270; standard laboratory screening: 200; no screening: NA. Life years gained (for Children Per 1000 Women) - POCT RPR screening: 6114; POC ICS screening: 6611; standard laboratory screening: 4396; no screening: NA.	POC ICS Screening dominates	In favor of POCT

Secondary Care

Author, Year	Cost per patient	Overall cost	Effectiveness	Ratio	Conclusion
Ward et al., 2016 [59]	POCT Program: $39.53 per patient; Usual Care: $33.20 per patient. POCT Program cost an additional $6.33 per patient.		QALYs - POCT program: 9.7384 QALYs per patient; Usual Care: 9.7382 QALYs per patient. POCT resulted in an additional 0.0002 QALYs per patient.	Extrapolated to an ED with 30 000 annual patient visits, the POCT Program would equate to $33 318 paid per additional QALY gained.	In favor of POCT
Henson et al., 2014 [28]	POCT: $602.95/positive detected; Laboratory testing: $364.30/positive detected.	Total costs - POCT: $37,383; Laboratory testing: $22,586.70	POCT results in decreased length of stay		In favor of POCT

* also in primary care monitoring

DALY Disability-Adjusted Life Year, *ED* Emergency Department, *ICER* Incremental Cost Effectiveness Ratio, *ICS* Immunochromographic Strip, *NAAT* Nucleic Acid Amplification Testing, *NHS* National Health Service, *POCT* Point of Care Test(ing), *QALY* Quality-Adjusted Life Year, *RPR* Rapid Plasma Reagin.

Table 2.2. Outcomes of POCT for Diagnosis

Primary care

Author, Year	Cost per patient	Overall cost	Effectiveness	Ratio	Conclusion
Frank et al. 2019 [41]	Usual care: $610; POCT: $690		Life expectancy – Usual care: 22.7 years; POCT: 25.5 years. Survival at 12 weeks – Usual care: 76.1%; POCT: 83.5%.	ICER: $680/YLS	In favor of POCT
Lee et al. 2019 [44]	Sputum smear microscopy: $80; Xpert MTB/RIF: $120; Truenat in DMCs: $120; Truenat for POCT: $120	Truenat POCT instead of Xpert increased 5-year expenditures by $270 million	Life expectancy – Truenat POCT compared to sputum smear microscopy: +0.39 years; Truenat POCT compared to Xpert MTB/RIF: +0.08 years; Truenat POCT compared to Truenat at DMCs: + 0.09	Truenat POCT compared to sputum smear microscopy: $210/YLS; Truenat POCT compared to Xpert MTB/RIF: $120/YLS;	In favor of POCT
Pooran et al. 2019 [45]		POCT cost an additional $35 529	Initiated on treatment – an additional 24.3 due to POCT; Same day treatment initiations – an addition 63.4 due to POCT; Completing treatment – an additional 29.4 due to POCT	POCT has 90% chance of being cost-effective in settings willing to pay $9450 per culture positive patient diagnosed, $4450 per patient starting treatment on the same day as diagnosis, $3820 per patient completing treatment, or $5840 per patient with improved morbidity.	In favor of POCT

Study				Conclusion
Spaeth et al. 2019 [27]	POCT + biopsy: €7,360.63/case; POCT + blood analysis and biopsy: €8,929.84/case; standard diagnosis + blood analysis and biopsy: €13,033.33/case	AU$481,440 across 6 months	Unnecessary medical retrieval prevented: 34% of patients	In favor of POCT
Esteve et al., 2018 [48]				In favor of POCT
Holmes et al., 2018 [49]	1) Routine practice. POCT: £52.35; usual care: £40.41. 2) Adherence to guidelines. POCT: £48.79; usual care: £39.48.	1) Routine practice. QALYs - POCT: 0.0615 QALYs; Usual care: 0.0609 QALYs. Antibiotic prescription avoided - POCT: 0.74; Usual care: 0.00. 2) Adherence to guidelines. QALYs - POCT: 0.0577 QALYs; Usual care: 0.0556 QALYs. Antibiotic prescription avoided - POCT: 1.00; Usual care: 0.00.	ICER (routine practice): £19,705 per QALY gained & £16.07 per antibiotic prescription avoided; ICER (adherence to guidelines): £4390 per QALY gained and £9.31 per antibiotic prescription avoided.	Neither against nor in favor of POCT: is more effective with closer adherence to clinical guidelines
Lubell et al., 2018 [50]	POCT: $1.24 (SD:1.53); clinical judgement: $1.31 (SD:1.52).		Antibiotic prescribing on first attendance - POCT: 43%; Clinical judgement: 63%.	Against POCT
Spaeth et al., 2018 [51][1]	POCT: $84 more expensive per patient; (95%CI: $81–$86) but would lead to cost savings (due to unnecessary medical evacuations avoided) of $4,674 per patient.	POCT: cost savings of $13.72 million per annum.	Unnecessary medical evacuations avoided - 0.2109 per patient (95% CI: 0.2106–0.2112)	In favor of POCT
Spaeth et al., 2018 [51][2]	POCT: $34 more expensive per patient; (95%CI: $32-$36) but would lead to cost savings (due to unnecessary medical evacuations avoided) of $8,035 per patient.	POCT: cost savings of $6.45 million per annum	Unnecessary medical evacuations avoided: 0.3577 per patient (95% CI: 0.3572–0.3582)	In favor of POCT
Spaeth et al., 2018 [51][3]	POCT: $102 more expensive per patient (95% CI: $100–$103) but would lead to cost savings (due to unnecessary medical evacuations avoided) of $786 per patient.	POCT: cost savings of $1.157 million per annum	Unnecessary medical evacuations avoided: 0.04 per patient (95% CI: 0.0384–0.0403)	In favor of POCT

Study	Costs	Outcomes	Cost-effectiveness result	Conclusion
Kip et al., 2017 [54]	POCT: €1144 (95% CI €892 to €1145); clinical judgement: €1221 (95% CI €955 to €1154); cost savings of €77 [95% CI €-127 to €-33].	QALYs - change in QALYs is negligible (−0.0004); Hospital referrals - decrease referrals in non-ACS patients from 38.46% to 31.85%; increase non-referral among ACS patients from 0.22% to 0.27%.	Not calculated due to negligible impact on health outcomes	In favor of POCT
Lewandrowski et al., 2017 [55]	Financial benefit of $11.90–14.74 per patient visit due to POCT.	Follow-up tests – 50% reduction due to POCT; Patient letters – 99% reduction due to POCT; Patient calls – 75% reduction due to POCT; Follow-up appointments – 39% reduction due to POCT.	In favor of POCT	In favor of POCT
Heffernan et al., 2016 [57]4	POCT: $0.11 billion (only the additional costs from introducing POCT)	DALYs averted were 0.02m DALYs (0.01 million —0.04 million DALYs)	$4,468/DALY averted	In favor of POCT
Heffernan et al., 2016 [57]5	POCT: $0.22 billion (only the additional costs from introducing POCT)	DALYs averted were 0.03m DALYs (0.02 million —0.05 million DALYs)	$6,986/DALY averted	In favor of POCT
Heffernan et al., 2016 [57]6	POCT: $0.29 billion (only the additional costs from introducing POCT)	DALYs averted were 0.03m DALYs (0.02 million —0.05 million DALYs)	$9,215/DALY averted	In favor of POCT
J Janković et al., 2016 [58]	POCT: 24,653.53 ± 4,121.40 RSD (99%CI); Standard procedure: 30,269.25 ± 4,834.17 RSD (99%CI); POCT results in a saving of 5,615.72 Serbian dinar per treatment episode	Number of patients who survived per 1000 treatment episodes – POCT: 981 ± 11 (99%CI), Standard procedure: 971 ± 3 (99%CI). Number of hospitalizations per 1000 treatment episodes – POCT: 160 ± 30 (99%CI), Standard procedure: 270 ± 40 (99%CI). Number of performed coronarographies per 1000 treatment episodes: POCT: 16 ± 10 (99%CI), Standard procedure: 32 ± 14 (99%CI).	The cost per hospitalization avoided: 120,620.27 RSD; cost per coronarography avoided was 110,351.83 RSD	In favor of POCT
Hendriksen et al., 2015 [63]	Laboratory testing: €8354; POCT Nycocard: €8297.57; POCT Simplify: €8198.63; POCT Cardiac: €8270.80; POCT Triage: €8370.87; Referral to hospital: €8467.59.	Laboratory testing: 6.986 QALYs per patient; POCT Nycocard: 6.9845 QALYs; POCT Simplify: 6.982 QALYs; POCT Cardiac: 6.987QALYs; POCT Triage: 6.988QALYs; Referral to hospital: 6.989 QALYs.	Not calculated due to marginal differences in health outcomes	In favor of POCT

Study	Costs	Results	ICER	Conclusion
Hunter et al., 2015 [25]	Per 100 patients - Clinical judgement: £18,081; GP + POCT: £18,039; Nurse + POCT: £17,401; GP + POCT + Communications training: £18,431.	QALYs (per 100 patients) – Clinical judgement: 255.630 QALYs; GP + POCT: 255.764 QALYs; Nurse + POCT: 255.761 QALYs; GP + POCT + Communications training: 255.588 QALYs. Antibiotic courses prescribed (per 100 patients) – Clinical judgement: 184; GP + POCT: 136; Nurse + POCT: 167; GP + POCT + Communications training: 137. Infections (per 100 patients) – Clinical judgement: 217.89; GP + POCT: 202.97; Nurse + POCT: 202.97; GP + POCT + Communications training: 199.98.	GP + POCT and practice nurse + POCT both dominate compared to current practice over 3 years. GP + POCT + communications training is dominated by current practice as it costs more and results in fewer QALYs.	In favor of POCT
Nilsson et al., 2014 [68]	POCT: SKr 11 247; No POCT: Skr 16 010.	Emergency referrals – POCT: 25% of patients; No POCT: 43% of patients. Diagnosed patients – POCT: 6.2% of patients; No POCT: 8.8% of patients. Missed cases – POCT: 2 missed cases; No POCT: 0 missed cases.	Skr 290 000 was saved per missed case of AMI or UA.	Neither against nor in favor of POCT: may be cost saving but at the expense of missed cases.
Turner et al., 2014 [69]	POC NAAT: £103.9 million; Standard care: £115.6 million; POCT cost £11.7 million less.	QALYs - POCT: increase of 46 QALYs. Inappropriate treatments - POCT: 95 000 avoided. Onward transmissions - POCT: 17 561 avoided.	POCT pathway dominates, the ICER is not meaningful and is not presented.	In favor of POCT
Oppong et al., 2013 [71]	POCT: increases costs by €11.27	QALY - POCT: QALY gain of 0.002 (95% CI – 0.001 to 0.004). Antibiotic prescribing - POCT: reduces probability of prescribing by 10% per patient but relationship was not statistically significant at the 5% level.	POCT: cost per QALY gain of €9391 and cost per patient prescription avoided of €112.70.	In favor of POCT
Van Dyck et al., 2012 [72]	All three interventions simultaneously: -€3164; Primary Prevention: increased costs by €292; POCT: increased costs by €480; Telemonitoring for adherence: -€3008.	All three interventions simultaneously: +0.036 QALYs; Primary Prevention: +0.018 QALYs; POCT: +0.006 QALYs; Tele monitoring for adherence: +0.019 QALYs.		Neither against nor in favor of POCT: it is cost-effective, but keeping people out of the system has larger benefit
Cals et al., 2011 [73]	Usual care: €35.96 (SD 58.12); POCT: €37.58 (SD 45.24); POCT with Communications training: €37.78 (SD 42.08)	Antibiotic prescribing - Usual care: 68%; POCT: 39%; POCT with communications training: 23%.	POCT & usual care: €5.79 for every 1% reduction in antibiotic prescribing; POCT with communications training & usual care: €4.15 for every 1% reduction in antibiotic prescribing.	In favor of POCT

Author, Year	Cost per patient	Overall cost	Effectiveness	Ratio	Conclusion
Udeh et al., 2008 [79]	Clinical judgement: $111.56; POCT: $40.25		Inappropriate antibiotic use – Clinical judgement: no cases avoided; POCT: 0.1786 cases of inappropriate antibiotic use avoided.	POCT: of $225.40 per case of inappropriate antibiotic treatment avoided; Clinical judgement: more costly and less effective	In favor of POCT
Secondary care					
Goldstein et al. 2019 [42]	Laboratory testing: $10.53; POCT with complete blood count: $18.79; POCT without complete blood count: $29.37.		Time saved using POCT – POCT with complete blood count: 31min; POCT without complete blood count: 21min.	POCT with complete blood count: 0.27 US$/min; POCT without complete blood count: 0.90 US$/min.	In favor of POCT (in a LMIC resource-constrained environment)
Rahamat-Langendoen et al. 2019 [46]	Laboratory testing: € 5243; POCT: €4206 – €4904		POCT reduced time-to-diagnosis and hospital stay		In favor of POCT
You et al., 2017 [56]	POCT: $116.6; Clinical judgement: $83.4		QALYs - Clinical judgement: -0.00251 QALYs; POCT: -0.00139 QALYs. Hospitalization - clinical judgement: 2.85% ; POCT: 1.38%. Mortality rate - clinical judgement: 0.16%; POCT: 0.08%.	ICER: $29,582 per QALY saved.	In favor of POCT
Whitney et al., 2016 [60]	POCT: $784.48; Serum electrolytes: $1087.78. POCT results in a cost savings of $303.30 per patient. Time saved with POCT factored by average nursing salary shows a mean cost savings of $33.60 per patient.		.		In favor of POCT
Whiting et al., 2015 [26]*	POCTs - ROTEM: £139; TEG: £103; SLTs: £78; and Sonoclot £50. Laboratory tests: £182. Cost-saving was slightly smaller for ROTEM (£43) than for TEG (£79) or Sonoclot (£132).		QALYs - Laboratory test: 0.8762 QALYs; All POCTs: 0.8773 QALYs.	POCT dominates standard laboratory tests (in all three cases)	In favor of POCT
Whiting et al., 2015 [26]*	POCTs - ROTEM: £203; TEG: £170; SLTs: £130; and Sonoclot: £73. Laboratory tests: £891. Cost-saving were £688 for ROTEM, £721 for TEG and £818 for Sonoclot.		QALYs -Laboratory test: 0.5644 QALYs; All POCTs: 0.5713 QALYs	POCT dominates standard laboratory tests (in all three cases)	In favor of POCT

Author, Year	Cost per patient	Overall cost	Effectiveness	Ratio	Conclusion
Asha et al., 2014 [64]	POCT: $174+/-$157; Laboratory testing: $150+/-$129; net difference: $24 (95%CI $4–$44).		Time to disposition decision - POCT: 3.24 hours; laboratory testing: 3.50 hours. Emergency department length-of-stay - POCT: 4.32 hours; laboratory testing: 4.52 hours.	ICER: $113 per hour saved in time to disposition decision	In favor of POCT
Hyle et al., 2014 [67]	POCT: $2,800 (95% CI, $2,790–$2,800); Laboratory testing: $2,440 (95% CI, $2,440–$2,450).		5-year survival - laboratory testing: 60.9% (95% CI, 60.9%–61.0%); POCT: 65.0% (95% CI, 64.9%–65.1%). Life expectancy - laboratory testing: 9.6 years (95% CI, 9.6–9.6); POCT: 10.3 years (95% CI, 10.3–10.3).	ICER: $500/YLS (95% confidence interval: $480–$520/YLS)	In favor of POCT
Fitzgerald et al., 2011 [74]	POCT: £1217.14 (standard deviation [SD] ± 3164.93); Standard care: £1005.91 (SD ± £1907.55).		QALYs – Standard care: 0.161(SD ± 0.052) QALYs; POCT: 0.158 (SD ± 0.056); Difference: -0.003.	High probability that POC strategy is dominated by standard care (empirical probability = 0.888). Probability of POCT being cost effective at £20,000 / QALY ($31,229) is very low (0.004).	Against POCT
Golden et al., 2010 [76]	POCT: $37; Laboratory testing: $4		TAT – POCT: 2.5; Laboratory testing: 10min. Total anesthesia time: no difference. Physician satisfaction: improved satisfaction when using POCT.		Neither against nor in favor of POCT: did not improve patient outcomes, but can improve patient care

[1] Acute coronary syndrome
[2] Renal failure
[3] Diarrhea/dehydration
[4] Current care
[5] Enhanced counselling and testing context
[6] Universal test and treat context
[7] Cardiac surgery patients with high risk of bleeding
[8] Trauma patients with high risk of bleeding
* also in monitoring

CI Confidence Interval, DALY Disability-Adjusted Life Year, GP General Practice, ICER Incremental Cost Effectiveness Ratio, NAAT Nucleic Acid Amplification Testing, POCT Point of Care Test(ing), QALY Quality-Adjusted Life Year, RSD Serbian Dinar, SD Standard Deviation, SKr Swedish Krona, TAT Turnaround time, YLS Year of Life Saved.

Table 2.3. Outcomes of POCT for Monitoring

Primary Care

Author, Year	Cost per patient	Overall cost	Effectiveness	Ratio	Conclusion
Rajasingham et al. 2019 [47]		POCT (≥200 threshold): $79154.36; POCT (bin placement): $79152.01; Automated testing: $79222.74; Current standard of care: $79151.65	POCT (≥200 threshold): 8.917; POCT (bin placement): 8.918; Automated testing: 8.921; Current standard of care: 8.903	POCT (bin placement) vs Current standard of care: $20/QALY; Automated testing vs Current standard of care: $5200/QALY	In favor of POCT

Study	Cost	Outcomes	ICER	Conclusion
Hyle et al., 2017 [53]1	POCT: US$3000; clinical strategy: US$2360	Life expectancy - POCT: 19.9 years; clinical strategy: 17.1 years. Time on failed treatment - reduced by 1.1 years with POCT.	ICER: POCT strategy dominates with an ICER of US$480/YLS	Neither against nor in favor of POCT: will only be cost-effective in settings without access to laboratory services
Hyle et al., 2017 [53]2	Laboratory testing: US$3120; viral load: POCT: US$3250; POCT: US$3380	Life expectancy - Laboratory testing: 19.8 years; viral load: POCT: 19.8 years. Time on failed treatment - reduced by 0.3 years with POCT and by 1.1 years with viral load.	ICER of POCT strategy not reported since it was dominated by the viral load strategy (ICER of US$440/YLS).	Neither against nor in favor of POCT: will only be cost-effective in settings without access to laboratory services
Ciaranello et al., 2015 [62]	POCT: combined cost of $24,900/mother-infant pair; laboratory testing; combined cost of $24,930/mother-infant pair.	Mother-to-child HIV transmission risk at weaning (age 6 months) - POCT: 5.3%; laboratory testing: 5.7%. Maternal and pediatric life expectancy - POCT: 53.4 pediatric life years, 21.2 maternal life years; laboratory testing: 53.2 pediatric life years, 21.2 maternal life years.		In favor of POCT
Crocker et al., 2014 [65]*	Total financial benefit to the practice due to POCT: $31.26 per patient	Total number of tests ordered per patient – 21% decrease due to POCT. Letters and phone calls to patients - 89% decrease due to POCT. Revisits due to abnormal test results - 61% decrease due to POCT.		In favor of POCT
Chadee et al., 2014 [66]	Laboratory testing: $91.5 million; POCT: $86.8 million; POCT would save approximately $4.7 million per year.			In favor of POCT
Laurence et al., 2010 [77]3	POCT: $3,676 (95% CI: $3,062, $4,191); laboratory testing: $3,672 (95% CI: $2,972, $4,628).	Proportion of patients in target range - POCT: 0.6548; Laboratory testing: 0.5618.	POCT had higher costs and was more effective (ICER = $40)	Neither against nor in favor of POCT: depends on WTP of society
Laurence et al., 2010 [77]4	POCT: $2,732 (95% CI: $1,994, $3,241); laboratory testing: $2,202 (95% CI: $1,875, $2,765).	Proportion of patients in target range - POCT: 0.1592; Laboratory testing: 0.1066.	POCT had higher costs and was more effective (ICER = $10,082)	Neither against nor in favor of POCT: depends on WTP of society
Laurence et al., 2010 [77]5	POCT: $3,297 (95% CI: $2,262, $4,197); laboratory testing: $3,150 (95% CI: $1,786, $3,853).	Proportion of patients in target range - POCT: 0.5701; Laboratory testing: 0.61477.	POCT was more expensive and less effective than laboratory testing	Against POCT
Laurence et al., 2010 [77]6	POCT: $1,727 (95% CI: $1,378, $2,309); laboratory testing: $1,954 (95% CI: $1,319, $2,712).	Proportion of patients in target range - POCT: 0.7739; Laboratory testing: 0.7418.	POCT dominates laboratory testing, being both less costly and more effective	Neither against nor in favor of POCT: depends on WTP of society

Secondary Care					
Author, Year	Cost per patient	Overall cost	Effectiveness	Ratio	Conclusion
Challen et al., 2015 [61]		Cost savings of $27,557 as a result of POCT (excluding initial equipment and training).	Time in therapeutic INR range - POCT: 60.4%; laboratory testing: 52.5%. Emergency room visits - POCT: 4; laboratory testing: 1. Hospitalizations - POCT: 0; laboratory testing: 2.		In favor of POCT
Whiting et al., 2015 [26][7]	POCTs - ROTEM: £139; TEG: £103; SLTs: £78; and Sonoclot: £50. Laboratory tests: £182. Cost-saving was slightly smaller for ROTEM (£43) than for TEG (£79) or Sonoclot (£132).		QALYs - Laboratory tests: 0.8762 QALYs; All POCTs: 0.8773 QALYs	POCT dominates standard laboratory tests (in all three cases)	In favor of POCT
Whiting et al., 2015 [26][8]	POCTs - ROTEM: £203; TEG: £170; SLTs: £130; and Sonoclot: £73. Laboratory tests: £891. Cost-saving were £688 for ROTEM, £721 for TEG and £818 for Sonoclot.		QALYs - Laboratory tests: 0.5644 QALYs; All POCTs: 0.5713 QALYs	POCT dominates standard laboratory tests (in all three cases)	In favor of POCT
Kong et al., 2008 [29]	POCT: 3.17 Singapore Dollars; Laboratory testing 3.07 Singapore Dollars.		Average time spent in laboratory and anticoagulation clinics (minutes) - POCT: 76; laboratory testing: 105. Average total time spent in hospital (minutes) - POCT: 105; laboratory testing: 140.		In favor of POCT

[1] Rural setting clinics
[2] Urban setting clinics
[3] Diabetes
[4] Hyperlipidaemia
[5] Anticoagulant therapy
[6] Acute coronary syndrome
[7] Cardiac surgery patients with high risk of bleeding
[8] Trauma patients with high risk of bleeding
* also in screening
' also in diagnostics

CI Confidence Interval, *POCT* Point of Care Test(ing), *ICER* Incremental Cost Effectiveness Ratio, *YLS* Year of Life Saved, *HIV* Human Immunodeficiency Virus, *WTP* Willingness to Pay.

Chapter 4:

How to Realize the Benefits of Point-of-Care Testing at the General Practice: A Comparison of Four High-Income Countries.

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ABSTRACT

BACKGROUND: In some countries, such as the Netherlands and Norway, point of care testing (POCT) is more widely implemented in general practice compared to countries such as England and Australia. To comprehend what is necessary to realize the benefits of POCT, regarding its integration in primary care, it would be beneficial to have an overview of the structure of healthcare operations and the transactions between stakeholders (also referred to as value networks). The aim of this paper is to identify the current value networks in place applying to POCT implementation at general practices (GPs) in England, Australia, Norway and the Netherlands and to compare these networks in terms of seven previously published factors that support the successful implementation, sustainability and scale-up of innovations.

METHODS: The value networks were described based on formal guidelines and standards published by the respective governments, organizational bodies and affiliates. The value network of each country was validated by at least two relevant stakeholders from the respective country.

RESULTS: The analysis revealed that the biggest challenge for countries with low POCT uptake was the lack of effective communication between the several organizations involved with POCT as well as the high workload for GPs aiming to implement POCT. It is observed that countries with a single national authority responsible for POCT have a better uptake as they can govern the task of POCT roll-out and management and reduce the workload for GPs by assisting with set-up, quality control, training and support.

CONCLUSION: Setting up a single national authority may be an effective step towards realizing the full benefits of POCT. Although it is possible for day-to-day operations to fall under the responsibility of the GP, this is only feasible if support and guidance are readily available to ensure that the workload associated with POCT is limited and as low as possible.

BACKGROUND

Diagnostics is an integral part of primary healthcare, as it provides valuable insight to support medical decisions to improve patient outcomes and wellbeing [1]. Accurate diagnostics can lead to clinical benefits for patients, but also economic benefits for the healthcare system [2]. For many diseases, both clinicians and patients continue to expect rapid and simple diagnostic tests that can provide results within minutes [3]. This has led to the development of innovative diagnostics, specifically, easy-to-use analyzers that can be performed at the point of care, more commonly known as point-of-care (POC) testing [1].

A POC test in primary care can be defined as an analytical test that is typically performed during or very close to the time of consultation by a healthcare professional near the point of care instead of a laboratory setting [4]. The tests often require only a small blood, urine, feces or sputum sample from a patient and can provide test results within a few minutes. This enables a real-time discussion of test results between the general practitioner (GP) and patient during the initial consultations and eliminates the need for a follow-up appointment or telephone discussion [5]. Subsequently, the consultation process is more convenient for patients and has previously been associated with an increase in patient satisfaction [6]. POCT has been proven to be cost-effective in areas with limited infrastructure and medical laboratories where it is typically used for easier and faster diagnosis of diseases and infections with high prevalence [7], including HIV [8], syphilis [9], and tuberculosis [10]. The usefulness of POCT is not only limited to resource-poor settings. It has been shown to be cost-effectiveness in several 1st world countries for a range of health problems and functions, such as screening for cardiovascular disease [11], monitoring patients' anticoagulant therapy [12] and diagnosing respiratory infections [13] and influenza [14]. While several studies have shown that POCTs can be cost-effective, ensure high-quality care and even show that outcomes may be better than if patients are monitored by laboratory tests [15], access to these tests in some countries is limited.

Over the past few years, enhanced manufacturing processes and new developments in microchip technology have led to the production of more robust and more accurate POC devices, compared to earlier generations [16]. Despite these improvements, the implementation of POC testing is still predominantly reliant on the active organization and management of clinicians using the tests,

including training and quality control [17]. The implementation of POCTs in primary care varies significantly between countries. A survey published in 2014 looked at the usage of POCTs by primary care clinicians in five countries [1]. They found that in Australia, for example, the only POCTs that are relatively widely implemented are urine pregnancy tests (68% of respondents), INR tests (48% of respondents), and blood glucose tests (74% of respondents). In comparison, POC tests seem to be much more prevalent in the Netherlands with respondents reporting the use of urine pregnancy tests (94%), urine leucocytes or nitrite tests (96%), blood glucose tests (96%), haemoglobin tests (58%), C-reactive protein tests (48%) and quantitative β-human chorionic gonadotropin tests (22%). The UK also has high usage of certain tests such as urine pregnancy tests (80%), urine leucocytes or nitrite tests (90%), blood glucose tests (69%) and INR tests (43%). In Norway, 99% of all GPs use POC tests in their practice, with urine strips, blood glucose tests, C-reactive protein tests, haemoglobin tests, INR tests, HbA1c, urine pregnancy tests, Urine albumin-creatinine ratio (ACR), streptococc, mononucleose tests and fecal occult blood tests being implemented by more than half of GPs [18].

The slow adoption and uptake of certain POC tests have been attributed to several issues, mainly relating to costs and the high workload associated with the implementation. Furthermore, the negative perception of physicians (due to concerns around accuracy and perceived higher workloads) may also contribute to the slow adoption. The recent COVID-19 pandemic has emphasised the significance of rapid, reliable diagnostics and proves that POCT can potentially help reduce the burden on healthcare systems, especially those that are already overwhelmed [19,20]. It has been shown that the use of COVID-19 POCT has positively affected healthcare providers through improved morale, and reduced worry associated with COVID-19 without disruption of workflow [21]. The acceptance of COVID-19 POC tests by both healthcare providers and patients will, optimistically, improve the way that POCT is perceived, and contribute to growing adoption rates. The successful implementation of POCTs proven to be cost-effective demands transformation and integration of services across healthcare organizations. There is a need for a better understanding of how POCT fits into the care pathway and how stakeholders influence the implementation [22]. Furthermore, implementing large-scale changes in a healthcare system successfully is a complicated task. The introduction of POCTs in general practice is not a single event but requires a series of interlinked processes involving

several stakeholders with different responsibilities. To comprehend what is necessary to realize the benefits offered by POCT, it is key to understand if differences between health systems can explain different uptake levels. Therefore, it is necessary to have an overview of the actors in the POCT value network, that are involved in the core aspects and the structure of healthcare operations and the transactions between them. A value network can be defined as a network of interconnected and interdependent relationships and activities between actors that determines the way an organization creates and delivers value [23]. It is merely the conceptualization of the complex relationships between different actors in the healthcare system.

In this paper, we will use the concepts of value networks to analyse if they can be used to identify factors explaining why some countries have and others have not routinely adopted cost-effective POCTs. This paper maps the value networks in four countries (England, Australia, Norway and the Netherlands) that can explain differences in uptake of POCT by GPs and compares these networks in terms of seven, previously published factors that support the successful implementation, sustainability and scale-up of innovations.

METHODS

Identification and Validation of Value Networks

The methodology applied to identify the value networks is based on a previously published theoretical framework for analyzing a healthcare system as a value network [23]. For each country, a literature review is conducted to identify each of the respective country's value network. An initial search of government websites was done for official reports and papers to gain an understanding of each country's health system as a whole and to identify the stakeholders that play a role in the implementation of POCT. Standards, clinical guidelines, and implementation guides of diagnostics and POCTs within primary care were reviewed to identify the process(es) and requirements of POCT implementation at general practice. Only official documents from governments and organizations affiliated with the government were reviewed. Any journal publications referred to in these documents were included as well if relevant.

From the full set of information that was gathered during the literature review, the actors that are involved in the value network and the relationships between these

actors (the way that actors are connected and communicates) were identified. A visual representation of the value network was developed to comprehend how the different actors connect. The relationships between actors were classified as information, value, and financial transactions or flows [24]. Information flow refers simply to the movement of information between the different actors, and financial flow encompasses the flow of funds, both receivables (e.g., reimbursements) and payables (e.g., investments and costs). The value flow refers to the added value between two actors that would drive their Willlingnes to Pay; for example, a POCT can create added value for the GP by providing earlier information of the diagnosis. These flows do not reflect any downstream effects or impacts, such as societal costs or patient benefits. Since the focus of this paper is on primary care, specifically GPs, the presented value networks are from the perspective of the general practice. However, each primary care practice can consist of any number of GPs, and the constructed value network is applicable to either single or multiple GP practices.

Health System Perspectives

If a country has public and private healthcare, the focus of the value network will be on the public system and the mechanism behind the implementation of POCT in the public system.

Validation of the Value Networks

Upon drafting the value networks, each value network was tested for consistency and exchangeability with the core investigators. The value network of each country was validated by the relevant investigators, namely JE and PF for Australia, CPP and HVM for England, SS and TBE for Norway and JTMD and JWLC for the Netherlands. Any uncertainties in the value networks that arose from a misapprehension of the official documents, guidelines, or standards were resolved during the validation process.

Comparison of Value Networks

Upon validation, each of the value networks was summarized in terms of seven key factors that support the successful adoption, implementation, sustainability, spread, and scale-up of service innovations, as identified by Nolte [25]. A brief description of the seven factors is provided in Appendix 1. Details of these factors

are published elsewhere [25]. Based on these seven factors, key differences between the countries were identified and discussed.

RESULTS

In all four countries, primary care is typically the first point of contact with the healthcare system and a patient has to be referred by a GP to receive specialist care. Therefore, GPs (as gatekeepers) play an essential part in containing costs. In all countries, if indicated, a consultation with the GP is followed by a sample being collected from the patient for the POC test, either by the GP or the practice assistant/nurse. The test result should be available within a few minutes and the results are discussed with the patient by either the practice assistant/nurse or the GP. GPs may also refer patients to secondary care based on the test results.

Australia

A description of the overall health system of Australia is provided in Appendix 2. The value network demonstrating the implementation of POCT in general practice for Australia is illustrated in Figure 1. Australia has 31 Primary Health Networks that work directly with GPs and other primary care providers to improve the coordination of care to patients [26]. In Australia, GPs are typically considered self-employed and part of a practice with an average of four GPs per practice [27]. For specialist services, a patient can only receive an Medicare Benefits Scheme (MBS) benefit if referred by a GP.

Australia's leading professional general practice organization is the Royal Australian College of General Practitioners (RACGP) and provides support to GPs through education, training and developing resources, guidelines and standards that GPs can use to deliver high-quality healthcare [28]. The RACGP has stated that they believe POCT should be accessible by GPs and covered by MBS [29]. The Australian College of Rural and Remote Medicine (ACRRM) is the professional organisation for many rural GPs. The value network of Australia could potentially be slightly different from a rural perspective.

There are no mandatory standards or guidelines for GPs to follow when using POCT, and practices are responsible for developing their own quality framework; however, the use of POCTs under these conditions is not covered by MBS. For a GP to be eligible for MBS rebates, the practice must be accredited against the
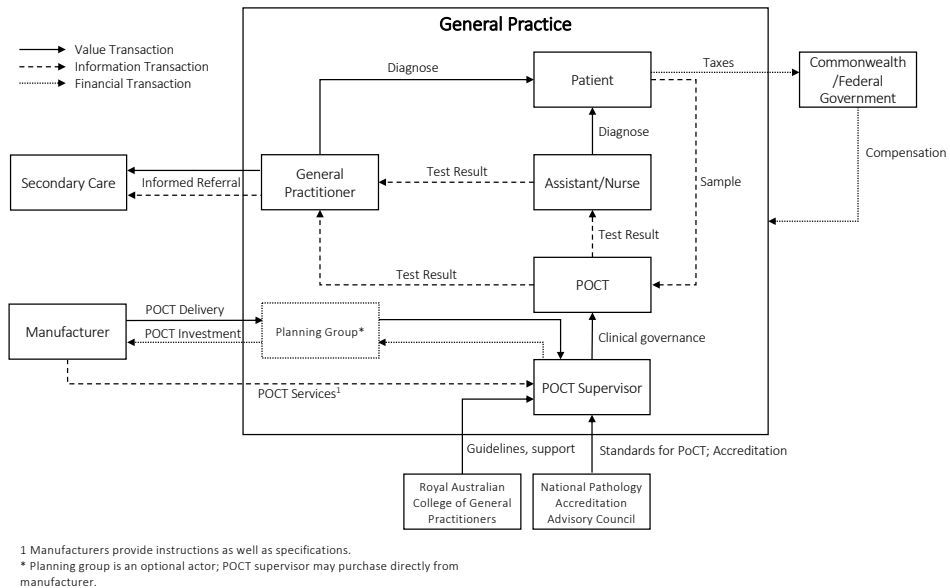
Figure 1. General practice point-of-care testing value network for Australia

standards for POCT. The standards for POCT (implemented at the general practice) fall under the National Pathology Accreditation Advisory Council (NPAAC), which requires GPs to uphold the same standards as pathology laboratories [29]. This means that GPs have to follow accreditation measures that were developed for pathology laboratories, which requires each GP to apply to become an approved pathology practitioner and an approved pathology authority. It also requires GPs to register their practice as an accredited pathology laboratory according to Australian Standards administered by the National Association of Testing Authorities (NATA), which can be time-consuming and costly as it includes site visits and strenuous administration work. The majority of POCT currently implemented at GPs are conducted without accreditation through NATA certified system. This means that there is no governance of the quality for these tests, nor can it be charged to MBS [30]. As of 2019, less than 20 GPs in Australia using POCTs in their practice have been accredited [30].

Currently, there are two sets of standards and guidelines for implementing POCT and ensuring appropriate use at the general practice; one is drafted by NPAAC [31] and the second by the RACGP [32]. Both documents set out the requirements when implementing POCT at the GP, such as clinical governance, quality frameworks, training and safety, and waste disposal. Before implementation,

practices are required to establish the clinical and diagnostic purpose of the POCTs they wish to implement, based on several reliable sources and provide evidence that the analytical performance of each test method has been evaluated. It is also required to prove that the POCTs will help in meeting the needs of patients in terms of local health infrastructure and other circumstances. The Australasian Association of Clinical Biochemists (AACB) recommends that any healthcare center wishing to implement POCT should set up a planning group consisting of all the staff that will be involved with the use of the POCTs, to share the planning responsibilities (before implementation) required by the standards and guidelines [30]. This planning group will ideally also decide on which POCTs to purchase and be responsible for the procurement of the devices from the manufacturer. If no planning group is set up, the POCT supervisor (a designated member of the practice who is ultimately responsible for POCT) will be responsible. The guidelines and standards require that each practice has a POCT supervisor (a designated and trained GP, nurse or practice assistant) that oversees the use and management of POCT in the practice, and that this person has a sufficient understanding of both POCT and the POCT standards [32].

The POCT supervisor must have completed appropriate POCT training and can delegate some of the responsibilities to another member of the practice, as long as that member has also received POCT training. The supervisor or delegate is also responsible for the quality assurance of POCT within the practice, and must regularly perform and review quality checks, investigate results and performance, and review trends in the quality check results [31].

Although the practice should be accredited as a pathology laboratory, the clinicians in the practice using the POCTs (for example, GPs, nurses or assistants) are considered non-laboratory trained personnel. Therefore, the POCT supervisors need to ensure that in addition to training, continuous support is provided to the users. Australia has introduced a regulation that requires POCT manufacturers to supply users with easy to understand instructions as well as specifications that ensures the devices are used correctly. It has been recommended by the AACB that POCT supervisors create active partnerships with manufacturers and other key stakeholders, including the AACB, to ensure continuous support, including additional training and assistance with maintenance and troubleshooting.

3.2 England

A description of the overall health system of England is provided in Appendix 2. The value network demonstrating the implementation of POCT in general practice for England is illustrated in Figure 2. Within primary care, general practices are owned and managed by an individual or groups of GPs or social enterprises of Community Interest Companies, with a board of directors (who has an APMS contract). They are viewed as independent contractors and are commissioned by Clinical Commissioning Groups (CCGs) to provide services to patients who need it. GPs receive payment from the global sum, to cover the cost of providing routine primary care services to the practice's registered list of patients. The amount that the practice receives is based on several factors, such as the patients' age, gender, levels of morbidity and mortality, the area's index of mean deprivation, the number of patients in nursing and residential homes, patient list turnover and local costs of staff. When a region has specific healthcare needs and priorities, the CCGs (on behalf of NHS England) may commission community-based services. These include any service that is required to meet the needs of the local population, such as screening for sexually transmitted diseases, weight management, stop smoking programs, etc. Practices can also benefit from financial rewards if certain indicators, as given in the Quality and Outcomes Framework, are met. The Quality and Outcomes Framework is a voluntary incentive scheme, and the majority of practices take part in it, although it is being slimmed down as it seems to lead to further fragmentation of care. The Care Quality Commision do inspections that regularly lead to practices closing. Furthermore, NHS England sets a prescribing budget for drugs and medication for each of the CCGs on an annual basis. The calculation of the budget is based on several factors, such as the historic spend of CCGs, the local level of deprivation for each GP in the CCG, recent changes in guidelines, new drugs and treatments, prevalence data and population size of the CCG. The CCGs are then responsible for setting a prescribing budget for each general practice within their organization. Typically, CCGs will also develop strategies, such as cost-effective prescribing measures, for GPs to apply. Local commissioners are often GPs.

Since the GPs are contracted by the NHS, but are not employed by them, they need to follow specific guidelines and quality frameworks. The Medicine and Healthcare Products Regulatory Agency (MHRA) has guided the implementation and management of POCT devices along with a quality framework that should be

followed to ensure that all requirements are met. One of the points raised by the MHRA is that a GP interested in adopting POCT within his practice should partake in close collaboration with a local hospital pathology laboratory. The pathology laboratory can give guidance on a diverse range of topics on the implementation and management of POCT. These may include the purchase of devices, quality control, and assessment, training, and safety provisions. For all issues regarding POCT, a close collaboration between the pathology laboratory and the GP using the test is of importance. In most cases, this should be formally defined through, for example, a service level agreement (SLM), specifying products, services, practical applications, and responsibilities from the relevant stakeholders. General practices are also strongly encouraged to assemble a POCT committee that represents all immediate stakeholders that will be influenced by the implementation, e.g., clinicians, nurses, pharmacists, IT, finance. These committees should also have a POCT manager that keeps track of their responsibilities towards clinical governance as well as the medico-legal implications of inaccurate results. On top of all their other tasks, this is not a simple consideration. In many practices, the role of the POCT committee is embedded in the local hospital POCT committee with links to the general practice.

1 Some manufacturers provide initial set-up and training (if required).
2 Purchasing, training, interpretation of results, troubleshooting, quality control.
3 Reports on the usage of POC tests, and shows how clinical governance is maintained.
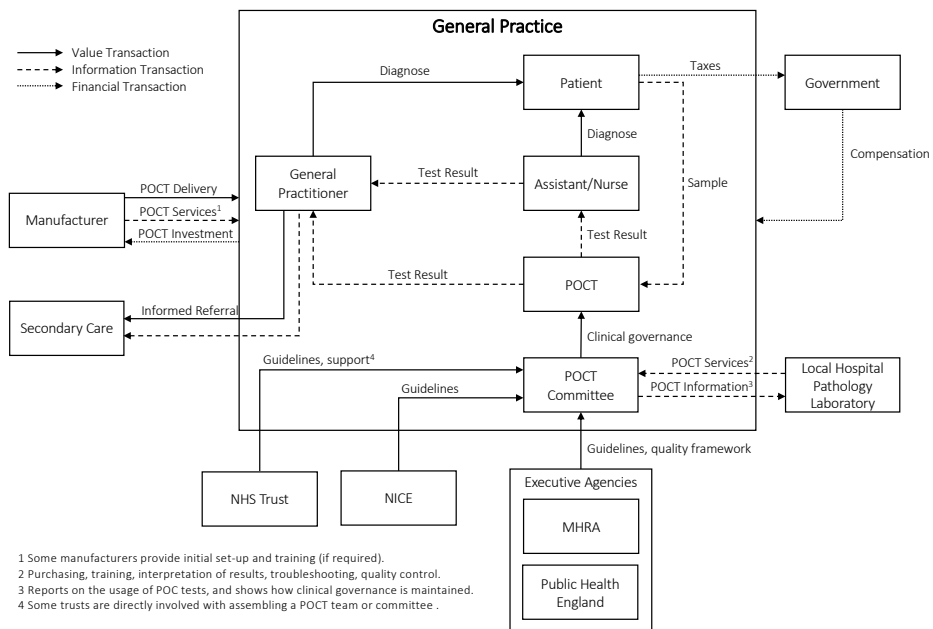4 Some trusts are directly involved with assembling a POCT team or committee .

Figure 2. General practice point-of-care testing value network for England

The National Institute for Health and Care Excellence (NICE) is one of the many organizations working with the NHS. They provide the NHS with guidance on how to promote high-quality healthcare and how to prevent and treat illness. Furthermore, they also support healthcare providers and commissioners in improving health outcomes for people using the NHS, public health, and social care services [33]. The guidance set up by NICE considers both clinical and cost-effectiveness. Technology appraisals performed by NICE is supported by mandate, and NHS England is legally required to provide funding for all medicines and treatments recommended by the institute. The POCT committee should ensure that all guidelines set by the MHRA, NICE, and (if applicable) NHS trusts are adhered to and should also keep track of adherence. Manufacturers can submit the details of their POC test to NICE for consideration and should include sufficient data and analyses proving the accuracy and effectiveness of the device [34].

3.3 Norway

A description of the overall health system of Norway is provided in Appendix 2. The value network demonstrating the implementation of POCT in general practice for Norway is illustrated in Figure 3. The majority of GPs are self-employed and part of a practice with two to six physicians. The GPs decide themselves which POCT they offer their patients. The practice forms part of the public system through contracts with the municipalities. GPs receive payment from the municipalities, a fee-for-service from the Norwegian Health Economics Administration (HELFO) and out-of-pocket payments from patients up to a about 250 Euros per year, after which there is no co-payment. The exact payment system is decided on a national level by the Ministry of Health after negotiations with the Norwegian Medical Association (NMA) [35,36]. Approximately 95% of Norwegian physicians are registered members of the NMA, a professional association and a trade union for physicians. The NMA plays an active part in the development of the healthcare system [37].

GPs are fairly widespread across the country, but specialist care is typically confined to urban areas [35]. Most GPs both in urban and rural settings make use of POCT. In 1992, the NMA, the Municipal Association of Local Authorities and the Ministry of Health and Care Services established The Norwegian Quality Improvement of Primary Care Laboratories (Noklus) [38] to ensure that all POCTs
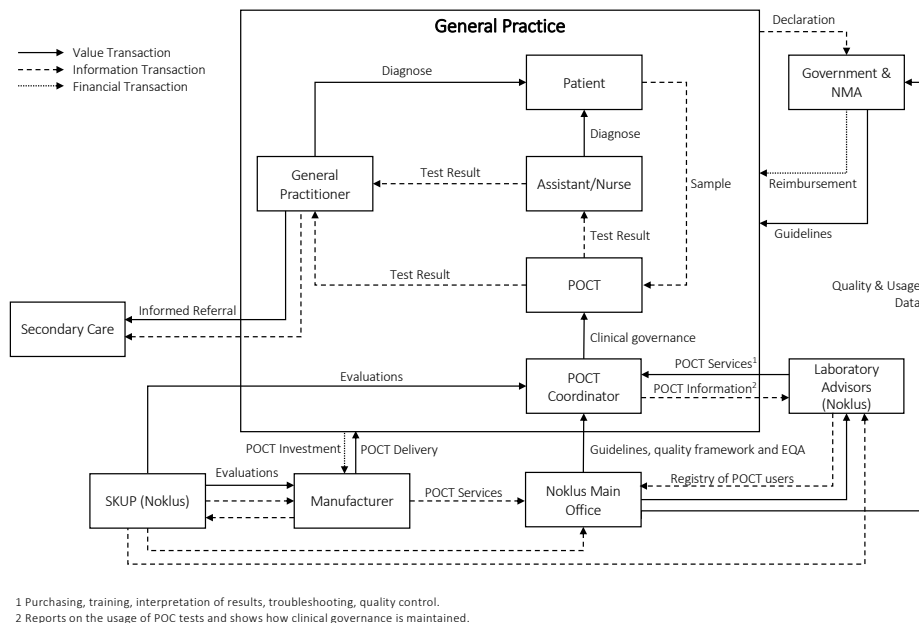
Figure 3. General practice point-of-care testing value network for Norway

are ordered, performed and interpreted correctly. In 2017, Noklus merged with the Norwegian Clinical Chemistry External Quality Assessment program to form the Norwegian Organization for Quality Improvement of Laboratory Examinations , which focuses on both primary and secondary care. Noklus is a non-profit organization (foundation) that aims to manage and improve the quality of the entire POCT process and covers the entire country. Noklus is also chairing the Scandinavian evaluation of laboratory equipment for point of care testing (SKUP), that was established in 1997 to improve the quality of POCT throughout Scandanavia. Suppliers and manufacturers of POCTs can pay to have SKUP evaluate their tests. Tests that fail to meet analytical or quality requirements are not recommended to be bought by GPs in Scandanavia [39].

Participation in Noklus is not compulsory, yet approximately 99% of all GPs participate willingly [18]. Noklus is managed by a team consisting of mainly biomedical laboratory scientists but also includes medical doctors, specialists in laboratory medicine, IT programmers, researchers and statisticians. Most of the biomedical scientists are trained as "laboratory advisors" and situated at 22 hospitals across Norway. These advisors supervise and guide the primary care laboratories in their region with regards to quality assurance and all laboratory

matters. The advisors are involved with every step of the POCT process, including acquisition, implementation and management [18]. Their responsibilities include giving individual advice on which POCTs are necessary, advising on maintenance programs, contributing to the protocols set up in terms of test usage, ensuring that quality control programs are followed and evaluated, providing support when problems might arise, and to arrange necessary training for GPs and assistants on the usage and quality control of POCTs. Each advisor has an overview of all POCT users in their region and a total register is maintained by the main office. The professional guidance of the laboratory advisors are done by the main office of Noklus who also runs the external quality assurance (EQA) system for all laboratory users in primary health care. Noklus constantly monitor and evaluate the users in terms of quality assurance, usage of tests and any problems that might arise. Noklus also advises the government and the NMA on which tests should be reimbursed, and the majority of tests recommended by Noklus for GPs are reimbursed by the government. Of Noklus´ 3300 participants, 1600 are GP offices. The remainining participants are nursing homes, home care units, oil platforms, prisons etc.

3.4 The Netherlands

A description of the overall health system of the Netherlands is provided in Appendix 2. The value network demonstrating the implementation of POCT in general practice for the Netherlands is illustrated in Figure 4. In the Netherlands, the GP plays a predominant role, and treats patients for basic health problems and also performs, for example, gynecological or pediatric examinations. Without a referral from your GP for further medical care, such as hospitalization or specialist care, access can be restricted and may not be covered by health insurance. The majority of Dutch GPs work independently or in a partnership, typically in a group practice with two or more GPs. As of 2015, approximately 22 percent of GPs worked in a single-handed practice [40]. Many GPs also employ nurses and practice assistants.

The Dutch college of general practitioners (NHG) is a scientific association for GPs in the Netherlands. They provide evidence-based guidelines for primary care and also provides education for GPs based on the guidelines [41]. A guideline directive for the usage of POCT in primary care in the Netherlands [42] was developed by the Dutch Association for Clinical Chemistry and Laboratory Medicine (NVKC)

<figure>

General Practice

Value Transaction
Information Transaction
Financial Transaction

Patient

Diagnose

General Practitioner — Test Result → Assistant/Nurse

Diagnose

Test Result

POCT

Sample

Test Result

Secondary Care — Informed Referral

Dutch College of General Practitioners — Guidelines

NVKC — Guidelines

Health Insurer

Declaration
Compensation

Declaration   Compensation

Local Hospital Pathology Laboratory

POCT Delivery
POCT Services²
POCT Data³

POCT Delivery   POCT Investment

POCT Delivery*
POCT Services¹*
POCT Investment*

Manufacturer

</figure>

1 Some manufacturers provide initial set-up and training (if required).
2 Purchasing, training, interpretation of results, troubleshooting, quality control.
3 Data on usage of POC tests.
* Optional pathways: Practice can purchase directly from manufacturer, although it is preferred to work through a laboratory.

Figure 4. General practice point-of-care testing value network for the Netherlands

together with the NHG and other organizations. The guidelines are based on international standards and guidelines and provide GPs with recommendations on how to ensure that POCT is used safely and responsibly in practice.

The guidelines recommend that the practice should consult with a laboratory specialist to ensure that the POC test(s) under consideration is necessary to meet patient demands. Additionally, it is recommended that the practice works with a laboratory specialist throughout the entire implementation process. This includes maintenance of the devices, help with troubleshooting, setting up a quality assurance framework, and annual, or bi-annual verification from the laboratory of POCT performance in terms of diagnostic accuracy, utilization of the tests and whether treatment decisions based on test results are sensible [42]. Since the guidelines recommend close collaboration between the practice and a laboratory, it is also recommended that all of the POCT usage data (including test results) are recorded in a health information system. This is to enable laboratories to easily assess and compare the quality and utilization of POCT at different GPs [42].

The agreements between laboratories and GPs can vary between regions. For example, GPs can purchase POCTs from the manufacturer directly with guidance from laboratories. In most cases, laboratories purchase the POCTs and distribute them to GPs in their region. Reimbursements for the acquisition costs of a POC

test or the setup costs of an information system are not available. However, GPs can be reimbursed for the cost price of test kits and for certain (very limited) test devices [42]. In order for a POC test kit (and certain devices) to be eligible for reimbursement, evidence must show that the POC test is effective. This is a statutory requirement in the Health Insurance Act; specifically, that the test has clinical utility. The National Health Care institute has to issue a positive report on the clinical utility of a test and the Minister of Public Health, Welfare and Sport has to convert that report into a positive decision to reimburse the test and test kits [43]. For many POC tests the prerequisite of clinical utility has not yet been established in the Netherlands.

3.5 Comparison of Countries

The comparison of the four countries and how they support the successful implementation, sustainability and scale-up of POCT are provided in Table 1. A spider diagram comparing the extent to which each country's value network addresses aspects related to each of the seven factors is shown in Figure 5.

Table 1. Comparison of countries. The comparison is made in terms of the seven factors published by Nolte [25].

Factor	Australia	England	Norway	The Netherlands
Leadership & Management	Governance mechanisms to provide standards and guidelines for POCT to GPs have been set up. All formal contracts required by these standards are to be organised by the GP. No governance to ensure adherence to these standards. No dedicated leadership structure exists for POCT.	Governance mechanisms to provide standards and guidelines to GPs have been set up; however, there are a few contradictions between the different organizations and bodies. All arrangements required by these guidelines are to be done by the GP. No dedicated leadership structure exists for POCT; it falls under MHRA, NICE, NHS Trust.	A dedicated POCT organisation has been set up to handle all implementation aspects and provide support to GPs. Provides sustained support and guidance to all participating GPs. Involved with every aspect of the implementation and management process of POCTs.	Governance mechanisms to provide guidelines to GPs have been set up. Separate standards for specifically POCT have not been set up, but instead, standards for in-vitro diagnostics are applied.

Stakeholder Involvement	Not all stakeholders are involved in the development of standards and guidelines. Standards require a planning group (consisting of all stakeholders) to be set up by GP to make initial investment decisions. Day-to-day management and clinical governance fall under the responsibility of a single POCT supervisor.	Day-to-day management and clinical governance fall under the responsibility of a POCT committee that has to include several stakeholders. The committee has to set up an agreement with a local pathology laboratory for additional support.	Noklus has a Board consisting of representatives from the Government, the NMA (including representative from GP organisation) and the Norwegian Association for Clinical Chemistry. There is an agreement between Noklus and and all regional health authorities. Day-to-day management and clinical governance fall under the responsibility of the GP with continuous guidance from a laboratory advisor from Noklus.	Guidelines are determined by a reasonably wide range of stakeholders. Day-to-day management and clinical governance fall under the responsibility of the GP and laboratory.
Dedicated & Ongoing Resources	No dedicated resources for POCT. The only way to receive any support is to be registered as a pathology laboratory, which is very expensive and cumbersome.	No dedicated resources for POCT. GPs have to provide their own funding, staff, infrastructure and time.Most GPs would request additional funding from the CCG; however, the CCG has no dedicated funding, so would expect the cost to be covered by savings.	Noklus provides ongoing support. Noklus also offers valuable and low-cost courses for GPs,nurses and other practice assistants to ensure good quality in the use of POCT. Negotiates for reimbursements for tests with the government and the NMA.	Guidelines on implementation are available, but the practice (or local trust of GP practices) itself is responsible for setting up an agreement with a local laboratory to guide implementation. However, funding for the acquisition of a POC test is unavailable.
Effective Communication	No data is collected on how GPs follow or experience the guidelines and standards. No specific communication channels established. All communication regarding POCTs is done by or via the POCT supervisor, who is in charge of ensuring clinical governance.	No data is collected on how GPs follow or experience the guidelines and standards. In some cases, guidelines contradict each other. No concrete support is provided on the implementation or whom to report to. In some areas, GPs voluntarily share quality assurance information with hospitals through established channels.	Each county has 2-5 laboratory advisors from Noklus, situated in a local hospital or laboratory whose primary goal is to communicate with GPs in the region to provide support and feedback.	No specific communication channels established. Most laboratories have a POCT coordinator and quality assurance coordinator, who is responsible for quality checks in GP practices. No data is collected on how GPs follow or experience the guidelines and standards, although GPs can request a 'diagnostic test consultation' where they receive an analysis of how well the standards are being applied.

Adaption & Integration to Local Context	Standards and guidelines remain the same to everyone, and this is especially restricting in Australia for remote locations. The planning group is responsible for selecting appropriate tests for practice as well as manufacturers.	Local authorities exist that can aid the POCT committee with decisions. The primary responsibility still lies with the committee and the GP to select appropriate tests for practice as well as manufacturers.	Noklus analyzes GPs patients and history to determine which POCT repertoire will be best. The GP decides which POCTs to provide based on the advice from Noklus. Local laboratory advisors evaluate if the implementation can be improved for the area.	GPs are recommended to work with local laboratories to decide on which POCTs will be most useful for their patients.
Ongoing Monitoring & Feedback	GPs are required to monitor performance themselves. Data collection and management is the responsibility of the practice. If GP is registered at NPAAC, external quality assurance programs deliver peer review of the POCT systems and may monitor performance.	No data collection is done (or required). In some areas, GPs and hospitals voluntarily work together to apply monitoring and feedback processes.	Local laboratory advisors gather data from GPs in their area and send it to the Noklus main office for analysis. They provide ongoing monitoring, calibration, quality checks, and evaluates whether the tests are utilized. Everything is monitored on a web-based database accessible to both GPs and Laboratory advisors.	Guidelines recommend a Health Information System to be set up where usage data and results are collected to allow easier assessment. Costs for setting up such systems are not reimbursed. GPs can voluntarily request a 'diagnostic test consultation' put in place to support GPs using and interpreting POCT.
Evaluation and demonstration of the effectiveness	MSAC does evaluate POCTs, if a submission is made. GPs are not required to evaluate the effectiveness of POCT since the evidence is available from "other sources" such as suppliers and societies. GPs are responsible themselves to ensure implementation and usage is done according to the manufacturers' standards and guidelines.	No official evaluation (done by the government) is in place to evaluate the effectiveness of POCTs currently in place at GPs.	Provides quality assessment schemes (EQA) to monitor and improve the usage of devices. SKUP provides evaluations of, e.g. analytical quality and user-friendliness.	No official evaluation (done by the government) is in place to evaluate the effectiveness of POCTs currently in place at GPs.

CCG Clinical Commissioning Group, GP General practitioner, MHRA Medicine and Healthcare Products Regulatory Agency, MSAC Medical Services Advisory Committee, NHS National Health Service, NICE National Institute for Health and Care Excellence, NMA Norwegian Medical Association, NPAAC National Pathology Accreditation Advisory Council, POCT Point of care testing, SKUP Scandinavian evaluation of laboratory equipment for point of care testing

Norway addressed the most aspects of each factor, mainly due to the presence of a single national authority (Noklus) responsible for POCT. Of the four countries, only Norway has a dedicated leadership structure in place that actively supports the implementation and uptake of POCT. In the Netherlands, there are no POCT-specific standards, but instead, POCT falls under the in-vitro diagnostics standards. In Australia, standards and guidelines for pathology laboratories have to be followed, discouraging GPs to follow the typical route to implementation as laid out by the guidelines. Within England's healthcare system, there is a lack of clear understanding amongst stakeholders of who is responsible for the implementation of innovation [44]. This makes implementing a POC test in practice seem more complex than that of the Netherlands and Norway, and this complexity may limit the implementation of POC tests. Additional descriptions on the comparison of countries can be found in Appendix 2.
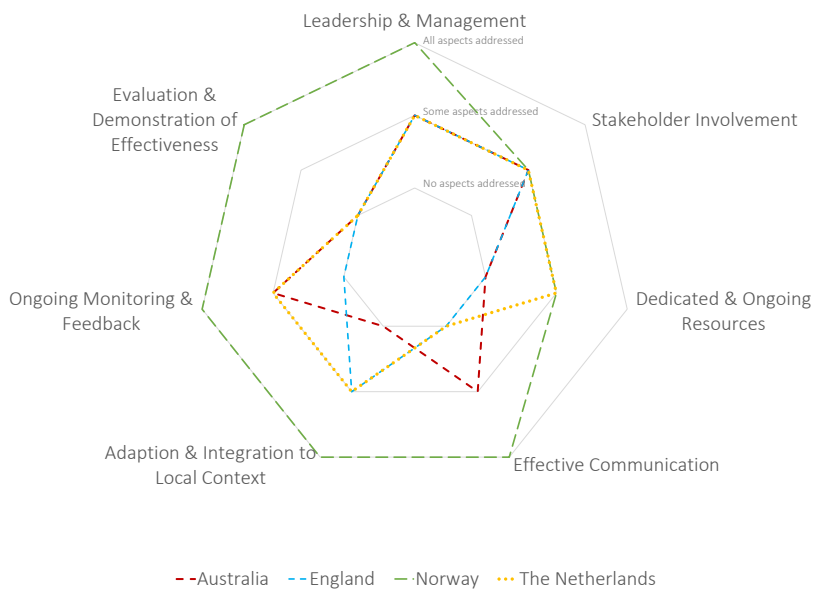
Figure 5. Comparison of the extent to which each country's value network addresses aspects related to seven factors.

DISCUSSION

The benefits of POCT can be substantial. However, although POC tests share characteristics they can differ in terms of, for example, the turnaround times, user-friendliness and associated workload. Similarly, the prevalence and incidence of different diseases in different countries will affect how beneficial a test will be in

a specific country. Therefore, the exact benefits will depend on the specific POC test and the context it is applied in. Generally, it can reduce unnecessary hospitalizations and referrals to secondary care, while patients benefit from shorter waiting times for results. It has also been shown to increase patient satisfaction [45]. Even though POCT has been proven to be a valuable tool in primary care, it does not necessarily incentivize GPs directly. Consequently, GPs might not be willing to take on an additional (high) workload or spend money to implement POCT in their practice. Therefore, support and guidance are necessary to encourage GPs to implement POCT in order to realize the benefits for patients and the health system. A dedicated leadership structure (such as Noklus) should be in place that actively supports the implementation and uptake of POCT. It seems likely that the organization and management of POCT would be more efficient if a separate team or organization, set up by the government, is responsible for all matters related to POCT. Each of the four countries, with their differences in health systems, has different principles when it comes to establishing a dedicated leadership structure or organization to facilitate implementation. As there are differences it is not possible to define one generalizable approach, and thus, the ministry of health should work together with the appropriate (existing) professional organizations, such as medical associations and professional societies for GPs and healthcare providers, to set up a system of quality improvement for laboratory services outside the laboratory and hospital. Clear, well-defined guidelines and standards should be in place that are specific to POCT. In the countries where POCT falls under the umbrella of other guidelines (such as in-vitro diagnostics or pathology guidelines), GPs can be discouraged from following the required route to implementation as it is too complex and cumbersome.

Such a POCT team should be involved throughout the implementation process, providing guidance to GPs on executing all aspects set out by the guidelines and standards. Furthermore, all stakeholders that would be affected by the implementation of POCT, including patients, manufacturers, and GPs, should be involved in setting up the standards and guidelines to improve commitment. One of the most significant barriers to POCT implementation for GPs is the high workload associated with setting up POCT in a practice. It is vital that GPs be part of setting up guidelines and standards to ensure enough support is provided and that the responsibilities expected of the GPs are reasonable.

Dedicated and ongoing resources is a factor that is especially important for the implementation of POCT. Financial resources can improve the uptake of POCT if it allows GPs to adopt POCT within their practice without additional cost. In the case of Norway, the Norwegian Medical Association in cooperation with Noklus negotiates reimbursements from the government for financial support, while in the Netherlands, GPs can make arrangements with laboratories. GPs could, potentially, also be offered a financial incentive to use POCT by returning the downstream cost savings realised in the healthcare system. Ongoing support for GPs is also a vital resource to reduce the workload and encourage implementation. Support during the initial implementation process is required to help GPs select a POCT repertoire that suits local needs. Ongoing monitoring and feedback are required to identify any opportunities for improvement within a practice. The guidelines and governing team should clearly provide GPs with instructions and support to set up a data collection system to collect and assess the performance of tests systematically. This will also simplify the process of quality assurance and evaluating the effectiveness of the POC tests in place at GPs.

Although the value network of one country cannot simply be transferred to another country, the results remain important in understanding the critical factors behind the successful implementation of POCT. These value networks help to comprehend what the value is of using a POC test, where this value is delivered, and which stakeholders are driving the value generation. These aspects, together with the strengths and weaknesses observed in the value networks, will be helpful when it comes to strategic thinking and can be used as a starting block to set up rigorous implementation plans and roll-out plans. One limitation of this paper is that the results are not applicable to low- and middle-income countries (LMICs). This is mainly due to the fact that the implementation of POC tests in these countries are mostly governed by both the healthcare system and by the World Health Organization and donors [46]. The value networks in these countries will, therefore, be very different than those in this paper, and will be hard to compare. Nonetheless, there are lessons that can be learned from the value networks presented in this paper and potentially from the value networks in LMICs. Future research should aim to identify the value networks in place in LMICs and investigate how comparable it is to those of high-income countries or what specific innovation and/or business models would apply.

It is expected that the global POC diagnostics market will reach $40.50 billion by 2022 [47]. However, efforts in developing POCTs and identifying cost-effective POCTs are wasted when their benefits are not realized. From the value networks identified in this paper, it is evident that differences exist in the organization of care between countries, which quite likely cause part of the observed differences in POCT adoption. The comparison of the value networks of different countries is useful in determining how countries can move forward in realizing the benefits of POCT, especially where adoption is low. It is observed that if a single national authority is responsible for POCT, the uptake of POCT may improve since they can govern the task of roll-out and management, and reduce the workload for GP's by assisting with set-up, quality control, training and support. However, this might be predicated on the governance of a country. For example, allocating a single national POCT authority, while feasible, could work differently in a federation (such as Australia) regarding establishing and delivering a value network for POCT. Although it is possible for day-to-day operations to fall under the responsibility of the GP, this is only feasible if support and guidance are readily available to ensure that the workload associated with POCT is limited and as low as possible. Bringing about the necessary changes and integration can be complex and time-consuming, but it is nonetheless feasible, given the example of Norway. Future quantitative analysis could indicate the magnitude of opportunity loss caused by a lack of POCT adoption as incentive for initiating these necessary changes.

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APPENDIX 1: DESCRIPTION OF FACTORS

Each of the value networks was summarized in terms of seven key factors that support the successful adoption, implementation, sustainability, spread, and scale-up of service innovations, as identified by Nolte [25]. A brief description of the seven factors is provided in Table S1. Details of these factors are published elsewhere [25].

Table 1.1. Description of the Seven Factors Outlined by Nolte [25].

Factor	Description
Leadership and management	Support from all tiers of leadership and management in the healthcare system, including clear goals and guidelines.
Stakeholder involvement	Widespread stakeholder involvement during the implementation process, including developing structures and guidelines.
Dedicated and ongoing resources	Funding and support throughout the implementation process to guide the design and implementation, as well as for staff and capacity building.
Communication	Effective communication across and between all organizations involved with the implementation and definite appointment of roles responsibilities.
Adaption and integration to local context	For sustainability, the implementation has to be adapted to the local needs and possibly integration with existing policies.
Ongoing monitoring and feedback	Assessing performance and identifying areas for improvement through data collection at each GP.
Evaluation and demonstration of effectiveness	Assessing effectiveness and utilization through quality checks and monitoring.

APPENDIX 2: ADDITIONAL DESCRIPTION AND COMPARISON OF EACH COUNTRY'S HEALTH SYSTEM

Description of Australia's Health System

In Australia, universal health care falls under the shared responsibility of three levels of government, namely, federal, state or territory, and local. The federal government plays a limited role in direct service delivery and is mostly responsible for the funding and (indirect) support to the states and their healthcare professionals. The federal government is the source of funding for primary care providers through the Medicare Benefits Scheme (MBS) and the Pharmaceutical Benefits Scheme (PBS) [1]. States or territories fund public hospitals, mental health, dental health and a limited range of primary care services, in particular the public community-based and allied health services, etc. The local governments provide certain co-republic health functions and some limited preventative health programs. This includes, for example, waste disposal, water supply, smoking cessation and weight loss programs [2].

Furthermore, the healthcare system has both a public and private system counterpart. Patients have access to healthcare through one of the systems or a mix of both. Both systems comprise of several components, such as hospitals, community services and other health organizations. The private system healthcare services are owned and operated privately [1,3]. These services are licensed and regulated by governments and funded by both government and private entities, including private health insurance (paid by patients), private organizations and private funding. The public system healthcare services are owned and operated solely by the state and territory governments [2]. Services in the public system are funded by local and state and federal governments, and healthcare access is covered by the MBS for free or at a lower cost to patients [2,3]. Patients that makes use of private insurance can also access all of the services, but the MBS only covers 75% - 85% of the cost, depending on the service. The remaining costs has to be paid by the private insurer or the patient themselves. MBS is funded, in part, from general taxes and free to all Australian citizens and residents with a permanent visa. It covers the costs to patients for public hospital services in full and some or all of the costs for other health services, such as services provided by a GP or specialist. The PBS provides subsidies to

patients for pharmaceuticals that are approved for cost-effectiveness by the Pharmaceutical Benefits Advisory Committee (PBAC) [2].

Description of England's Health System

The National Health Service (NHS) in the United Kingdom is paid from national insurance and free to all permanent residents at the point of use. England, Northern Ireland, Scotland and Wales each have their own, slightly different health care system in place that is funded and administered by separate 'devolved' governments, each with some individual policies and priorities. In terms of population, England is by far the largest and will be the focus of this study. The UK government is responsible for top-level priority setting and determines the budget for the NHS. Through the Department of Health, they oversee the healthcare system and set the overall policy, strategy, and funds. There is a range of organizations that the Department of Health provides funding to, but the most significant portion of the budget goes to NHS England. NHS England oversees the commissioning: the planning and buying of healthcare services. They pass the majority of their money (about 66% of the budget) to 135 clinical commissioning groups (CCGs), situated across England [4]. The CCGs (in partnership with Local Authorities) are responsible for identifying the healthcare needs of their area and for commissioning healthcare services for the residents of that area accordingly. They can commission services from any organization that provides care, such as GPs, community services, ambulances, etc. The CCGs have joint responsibility with NHS England; however, they can opt to take on full accountability for commissioning medical care services.

From 1 April 2019, NHS England is working together with NHS Improvement as a single organization. Since specialists (consultants) are all employed by the NHS (and GPs are not), the system does not facilitate referrals or seamless pathways. This is different from countries where consultants' incomes depend largely on accepting referrals and on a good relationship with GPs. At the inception of the NHS, it was considered too costly to bring GPs in. Some consultants do extra private work. NHS Improvement is responsible for administering NHS trusts and ensuring that trusts work efficiently and cost-effective. Hospital and specialist care are primarily delivered by NHS foundation trusts and NHS trusts, although they can sometimes be directly involved with some primary care services as well in areas of great need or when no local GPs are avaiable. Most consultants working

in primary care are working for private companies who have contracts commissioned by CCGs, as this is more cost effective than out patients in hospitals. Typically, an NHS trust provides care to a specific region or serves as a specialized function (e.g., an ambulance service). It is possible for one region to have several trusts working towards different aspects of healthcare. They work closely with CCGs in meeting the local needs. NHS England is currently developing a more integrated approach to services. There is an initial tranche of 14 integrated care services across England with the intention of complete coverage in 2020/21. The integrated care services are driving practices to merge together, thereby creating an environment more amenable to local testing such as POCT [5].

The Department of Health also provides funding to Public Health England and the Medicine and Healthcare Products Regulatory Agency (MHRA). Public Health England aims to serve the government, NHS, industry, and the public by providing evidence-based research, support, and expertise. They also run public health campaigns. The MHRA is in charge of regulating medicines, medical devices, and blood components for transfusion in the UK. Local authorities are responsible for public health, which includes a wide range of healthcare services, including education, transportation, waste disposal, environmental health, and many more. Since public health is their primary concern, they work in close collaboration with CCGs to ensure that the healthcare needs of the region are being met efficiently. GPs are independent contractors with an NHS contract to provide services to a population of patients. There are currently three main types of core contract: General Medical Services (GMS), Personal Medical Services (PMS) and Alternative Provider Medical Services (APMS). GMS is the contract agreed nationally and stipulates essential services to be provided through several types of GP contracts. PMS contracts are phased out. Private healthcare providers who manage walk-in clinics, have a five year APMS contract [6].

Description of Norway's Health System

Norway has a public healthcare system, financed by taxation and patient co-payments. Healthcare falls under the responsibility of three levels of government, namely the central State, regional health authorities (RHAs), and local municipalities [7,8]. Healthcare policies, legislation, and funding is managed centrally by the government and its ministries (Central state), while primary

healthcare provision is decentralized and falls under the responsibility of local municipalities. The ministry owns and funds most of the hospitals in the country and is responsible for specialist care, through its four RHAs [9]. There are a few private hospitals, some of which are funded through contracts with the public healthcare system [8]. All of Norway's inhabitants are covered by the National Insurance Scheme (NIS) that is managed by the Norwegian Health Economics Administration (Helfo). Private health insurance is also available from for-profit insurers, although only about 9% of the population has some kind of private insurance [7]. Pricing and reimbursement decisions are predominantly made on a national level, with separate systems for primary care and specialist care. The Norwegian Health Economics Administration (Helfo) is responsible for the actual reimbursement of all pharmaceuticals, devices and services covered by the NIS [9].

Description of the Netherlands' Health System

In the Netherlands, healthcare priorities, legislation and monitoring of access, quality and costs fall under the responsibility of the national government. In addition to general laws and acts set up by the government, the foundation of the healthcare system is formed by four acts, namely, the Health Insurance Act, the Long-Term Care Act, the Social Support Act, and the Youth Act. The Long-Term Care Act is there to aid the most vulnerable groups, specifically patients that require permanent care. It falls under the responsibility of the government, but there are several organizations involved with its implementation. Both the Social Support Act and the Youth Act falls under the responsibility of municipalities and local authorities. Under the Social Support Act, people who struggle to participate in society or cannot care for themselves, are provided for and supported by the municipality and local authorities. The Youth Act was introduced for the support and care of children and adolescents.

The Health Insurance Act is implemented by healthcare insurers and providers. Under the Health Insurance act, it is mandatory for everyone who lives or works in the Netherlands to have basic health insurance. Therefore, insurers are obliged to accept everyone that applies for the basic insurance and have to charge them the same premium. Insurers are allowed to try and attract customers by offering lower prices. However, they are not allowed to ask a higher premium for people with, for example, a certain disease. In addition to the nominal premium,

everybody pays an income-related contribution for the standard package that is remitted to the health insurance fund by the employer. Basic health insurance covers medical care, medicines and hospitalization. All insurers have to offer the same standard package, although it may have different premiums and may be extended with additional advantages. Additional insurance for eye care, dental care or physiotherapy can be added at an extra cost. In addition to the premiums set by the health insurer, every insured person has an annual own-contribution, which is the amount that is to be paid by each person themselves, before the insurer covers any medical costs. This does not apply to all medical care, for example, GP services or maternity care, but POCT and laboratory tests requested in primary care have to be paid by the patient from their annual own-contribution with a yearly determined maximum threshold.

Comparison of Country Performance

Stakeholder involvement is crucial to ensure that everyone who will be impacted by POCT is on board with the implementation process. For England and the Netherlands, the day-to-day management of POCT in a practice falls under the responsibility of the GP with support from a local laboratory (selected by the GP) with no concrete outside support. Only in Norway is there a dedicated advisor appointed by Noklus for each region to provide ongoing support and guidance to practices using POCT. In Australia, GPs who want to make use of POCT should register as a pathology laboratory, and consequently receives no support from an external laboratory.

Australia and England fall short in terms of dedicated and ongoing resources since no dedicated resources for POCT are available for GPs. In terms of financial resources, GPs in Australia could be eligible for some reimbursement, but only if the practice is registered as a pathology laboratory which is very expensive and cumbersome. In the Netherlands, funding is available for GPs to appoint a practice nurse or assistant, which is useful when using POCT. For Australia, England and the Netherlands, GPs have to take the initiative to adopt POCT in their practice and follow implementation procedures as laid out by the guidelines, without support. In Norway, there is ongoing support from Noklus and each region has a laboratory advisor. Noklus and the NMA also negotiate reimbursements from the government for financial support, based on the evaluations from SKUP.

As is clear from the value network of each country, there are several organizations involved with the implementation of POCT at a practice. In Norway, Noklus plays a critical part in ensuring effective communication, with a laboratory advisor acting as an intermediary for GPs and all other organizations. Noklus mainly works to ensure quality of the POCT, while it remains the responsibility of the general practice to ensure that the practice is properly run. The other countries do not have a dedicated communication channel established, and it is the practice's responsibility to ensure that guidelines and standards are being followed and that communication between the practice and a local laboratory (in the case of the Netherlands and England) takes place effectively.

England and the Netherlands both have some local adaption, with local authorities in England and local laboratories in the Netherlands helping POCT committees and GPs with decisions. In Australia, there is no support to adapt to a local context. This is especially problematic, seeing as the several remote areas that would benefit the most from POCT are held accountable under the same rules as GPs in urban areas. In Norway, Noklus is actively involved to help GPs implement a POCT repertoire that is specific to the practice's needs.

Setting up data collection systems to collect and assess performance systematically and to identify any opportunities for improvement. In Australia and England, no data collection is officially required, and any data collection and monitoring falls under the responsibility of the practice. If a practice is accredited in Australia, there is some performance monitoring. Guidelines in the Netherlands do recommend that an information system is set up between the practice and the laboratory to ensure the laboratory can monitor performance. In Norway, the local laboratory advisors gather data from the POCT of GPs to assess the quality of the tests, and also sends it to the Noklus main office for further analysis.

Evaluation and demonstration of the effectiveness of POCT implementation at the practice are only addressed in Norway, where Noklus provides quality assessment schemes. For the remaining three countries, there is no official evaluation in place to demonstrate the effectiveness of POCT. The countries do perform some health economic evaluations of devices, but they do not evaluate the effectiveness of the POC tests at each practice.

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Chapter 5:

The Societal Impact of Implementing an At-Home Blood Sampling Device for Chronic Care Patients: Patient Preferences and Cost Impact.

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ABSTRACT

BACKGROUND: Diabetes mellitus, cardiovascular diseases, chronic kidney disease, and thyroid diseases are chronic diseases that require regular monitoring through blood tests. This paper first investigates the experiences of chronic care patients with venipuncture and their expectations of an at-home blood-sampling device, and then assesses the impact on societal costs of implementing such a device in current practice.

METHODS: An online survey was distributed among chronic care patients to gain insight into their experience of blood sampling in current practice, and their expectations of an at-home blood-sampling device. The survey results were used as input parameters in a patient-level monte carlo analysis developed to represent a hypothetical cohort of Dutch chronically ill patients to investigate the impact on societal costs compared to usual care.

RESULTS: In total, 1311 patients participated in the survey, of which 31% experience the time spent on the phlebotomy appointment as a burden. Of all respondents, 71% prefer to use an at-home blood-sampling device to monitor their chronic disease. The cost analysis indicated that implementing an at-home blood-sampling device increases the cost of phlebotomy itself by €27.25 per patient per year, but it reduces the overall societal costs by €24.86 per patient per year, mainly due to limiting productivity loss.

CONCLUSIONS: Patients consider an at-home blood-sampling device to be more user-friendly than venous phlebotomy on location. Long waiting times and crowded locations can be avoided by using an at-home blood-sampling device. Implementing such a device is likely cost-saving as it is expected to reduce societal costs.

BACKGROUND

In 2018, approximately 58% (~9.9 million people) of the Dutch population were diagnosed with at least one chronic disease [1]. More specifically, ~1.2 million people suffer from diabetes mellitus (DM) [2], ~1.6 million from cardiovascular diseases (CVD) [3], ~1,7 million from chronic kidney disease (CKD) [4], and ~0,6 million from thyroid diseases (TD) [5-8]. The prevalence of all these diseases increases with age, with 95% of the people above the age of 75 years suffering from at least one chronic disease [1]. The number of people diagnosed with a chronic disease will further increase due to aging of the Dutch population resulting in a larger chronic disease burden [9]. In current practice, patients with DM, CVD, CKD or TD are monitored between one to four times a year through blood testing [10-13]. Venipuncture, the process of obtaining intravenous access to collect blood, is an invasive procedure that can cause pain, distress and anxiety to patients [14, 15]. Besides the fact that phlebotomy is experienced as inconvenient, it is also accompanied by high healthcare costs in the case of DM, CVD, CKD and TD patients due to the large number of patients that need to be monitored repeatedly [16, 17].

Self-management is becoming increasingly important in healthcare [18]. It can reduce unscheduled care by improving disease control and quality of life, potentially reducing costs, and improving healthcare outcomes as a result [19]. At-home blood-sampling empowers patients by allowing them to take more control of their own healthcare [20]. Patients have control over where and when they want to perform the blood sampling, which reduces the possible disruption of their daily routines. Importantly, blood does not have to be sampled via venipuncture but can be collected with a finger prick, which is less invasive [19]. It has been shown that patients prefer a finger prick over venipuncture [21, 22], mainly since it is experienced as being less painful, although contradictory results have also been reported [23]. In point-of-care (POC) testing, blood is drawn at home by the patients themselves (typically with a finger prick) and tested immediately. The main drawback of POC tests in self-management is that the devices are often expensive (especially for a patient to purchase themselves) and that the diagnostic accuracy can be lower than the reference laboratory tests [24, 25].

A novel blood collecting device is Hem-Col (designed by Labonovum, Limmen, The Netherlands). This is a microtube which enables patients to sample their own

blood via a finger prick, and send the blood sample through postage to the hospital or laboratory for analysis. The Hem-Col device allows reliable measurement after days of storage, resulting in a larger time frame for laboratories to analyze the sample [19]. Hem-Col tubes have the size of regular blood collection tubes, which makes analyzing by standard laboratory equipment possible [19]. Hem-Col is available to consumers outside hospital laboratories but is not yet implemented in current clinical practice. Implementing Hem-Col in clinical practice would allow physicians to order Hem-Col for patients when blood testing is needed.

An at-home blood sampling device as an alternative to venipuncture on location, has the potential to improve current practice for patients by saving time and introducing a more preferred sampling method. Given that only the sampling method and location are different, and that the analysis of the blood sample remains unaffected, the use of at-home blood sampling will, by definition, not affect patient health outcomes directly. However, it has the potential to improve convenience for patients, which has been shown to be an important aspect in overall healthcare delivery [26, 27]. Therefore, the aim of this paper is twofold. Firstly, to gain insight into how chronic care patients experience current practice (venipuncture on location) to monitor their disease and their expectations of and willingness to use an at-home device (specifically Hem-Col) for blood sampling as an alternative to current practice. Secondly, this paper also aims to perform a cost-minimisation analysis to investigate the impact on the societal costs if Hem-Col (as a realistic example of an at-home blood-sampling device) is implemented as compared to current practice. Although there are other aspects relevant to the actual implementation of an at-home blood sampling device, including potential organizational barriers, reiumbursement of the device or safety concerns, this paper will focus only on patient preferences and societal costs.

METHODS

A survey was used to investigate patients' recent experiences with venipuncture, their expectations of an at-home device, and their willingness to use such a device (specifically Hem-Col). A patient-level Monte Carlo analysis was performed to quantify the impact of implementing the Hem-Col device in clinical practice on the costs (from a societal perspective) using the survey results for some of the input parameters. As this is not an analytical study the accuracy and reliability of Hem-

Col (finger-prick) blood samples as compared with venous blood samples were not examined. Instead, it is assumed that the Hem-Col blood samples will render the same results as venous blood samples, which is also indicated by the manufacturer (Labonovum).

Survey

To design the survey, qualitative interviews with ten DM patients were held to gain insight into their perceptions of phlebotomy. The final survey consisted of 32 questions divided into four sections. Sections one and two comprised of questions to gather information on the patient's demographic factors (Section one), and the patient's current chronic disease(s), and details on their phlebotomy appointments (Section two). In Section three, patients were asked questions about their experience and preferences of phlebotomy appointments, while Section four introduced Hem-Col and asked about their expectations of the device. The full survey (translated to English) can be found in Appendix 1.

The survey was distributed among several Dutch patient associations and Facebook support groups for patients with DM, CVD, CKD, or TD. To participate in the survey, patients had to be 18 years or older, must be diagnosed with at least one of the chronic diseases, and must receive blood testing to monitor the disease at least once a year. All responses were anonymous and only surveys that were fully completed were included for analysis.

Several survey outcomes were used as input parameters for the cost-minimisation analysis, namely, the number of phlebotomy appointments per year, the appointments' location, the time spent per appointment (including travel time), the dependency on others, and the willingness to use Hem-Col.

Cost Minimisation Analysis

A patient-level Monte Carlo analysis was developed in Excel to represent the Dutch population that is suffering from DM, CVD, CKD, or TD. This analysis allows to estimate how the distribution of input parameters affects the distribution of the final results [28]. No actual simulation model was developed and used, since the aim was not to extrapolate beyond the current evidence base. Each hypothetical patient was assigned a gender and an age, based on data from the literature. Each patient was also assigned one (or multiple) of the four chronic diseases with a chance dependent on the age of the patient. Although it has been shown that

finger prick (i.e. capillary) sampling is more likely to lead to sampling errors than venous sampling [29, 30], the Hem-Col device is designed to avoid sampling errors by providing clear instructions on how to accurately sample blood via a finger prick and how to correctly package the sample when sending it via post. Nonetheless, a 5% sampling error rate was incorporated into the analysis, indicating that 5% of patients that uses Hem-Col will need to provide a new sample.

The primary outcome measure was the incremental societal costs when implementing Hem-Col (for at-home blood sampling) as compared with current practice (on-site blood sampling). The health effects are assumed to be negligible since the tests performed and therefore test results will remain the same whether Hem-Col is used or not, and Hem-Col will therefore not have any direct health effects in the long term. All costs were evaluated from a societal point of view, over a time horizon of one year. No discount rate was applied due to the time horizon.

Costs

The volume of the blood sample does vary and a fixed volume of buffer is added to the Hem-Col tube at the laboratory. Therefore, the tubes contain lithium as an internal standard that is measured to calculate the dilution factor. The costs of the dilution and examination were calculated by taking the average cost of three Dutch laboratories. The tariff for the order of the blood tests, which is the same for all phlebotomy locations and Hem-Col, and the costs of shipment by mail were also added to the Hem-Col costs. The selling price of the Hem-Col device was provided by the manufacturer.

In the Netherlands, phlebotomy can be performed at four potential locations, namely the hospital, a service phlebotomy center, the general practitioner (GP) or at home. The costs for a phlebotomy appointment at the hospital were calculated by taking the average reimbursement tariff of five hospitals, while the costs for the other locations were calculated by taking the average tariff per location as provided by ten large laboratories.

Additional potential costs that were taken into account include travel, parking, productivity losses, and time spent by an informal caregiver. An overview of these costs is provided in Table 1. Traveling costs, parking costs and costs of productivity

loss were derived from the Dutch Costing Manual [31]. With Hem-Col, traveling costs were seen as all costs associated with mailing the sample to the laboratory, including travel and postage. Full productivity loss costs were accounted for until the age of 65. Approximately 12.1% of the Dutch population remain in employment after the age of 65 and 1.8% after the age of 75 [32]. The productivity loss costs for these age groups were calculated by multiplying the full productivity loss costs with these percentages. Furthermore, patients may be dependent on others for the phlebotomy appointment resulting in additional productivity loss costs of an informal caregiver.

Table 1. Costs overview

Parameter	Category	Expected value	95% CI[1]
Phlebotomy Cost	Hospital	€ 9.04	€8.08 to €9.99
	Phlebotomy service center	€ 15.34	€14.09 to €16.60
	GP's office	€ 18.13	€17.92 to €18.34
	At home	€ 25.16	€19.36 to €30.96
	Hem-Col	€ 20.42[2]	€10.42 to €30.43
Traveling Cost	Hospital	€ 6.08	€3.10 to €9.07
	Phlebotomy service center	€ 1.02	€0.52 to €1.52
	GP's office	€ 0.45	€0.23 to €0.67
	Hem-Col	€ 1.02	€0.52 to €1.52
Productivity Lost Cost per Hour	Male age 18-64	€ 40.74	€20.78 to €60.70
	Male age 65-74	€ 4.91	€2.51 to €7.32
	Male age 75+	€ 0.73	€0.37 to €1.09
	Female age 18-64	€ 33.97	€17.32 to €50.61
	Female age 65-74	€ 4.10	€2.09 to €6.10
	Female age 75+	€ 0.61	€0.31 to €0.91
	Informal care giver	€ 15.05	€7.68 to €22.42
Waste Cost	Regular tube *(per 100 tubes)*	€ 1.22	€0.62 to €1.82
	Hem-Col tube *(per 100 tubes)*	€ 0.68	€0.35 to €1.01

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[1] based on normal distribution for the mean and corresponding standard error

[2] includes cost of the test and tube, postage and shipping to patient, dilution factor and order tariffs

After analysis the Hem-Col tube can be split into two parts, an upper and lower part. The upper part contains the blood sample, and the lower part contains no blood, meaning it can consequently be disposed of as residual waste, which is

less expensive to process than medical waste [33]. The medical waste costs were derived by taking the average of two waste process organizations: Renewi and Suez.

All costs are provided in Euros and were converted to 2020 prices using consumer price indices (CPI) provided by Statistics Netherlands [34].

Multiple diseases

No data could be found in the literature on the distribution of the patients with multiple of the chronic diseases included in this study (DM, CVD, CKD, TD) across the Dutch population, nor information on the age range or gender distribution of these patients. Therefore, the gender distribution, age distribution and the risk of a patient having multiple chronic diseases (per age group) were calculated as an average of the relevant data found for DM, CVD, CKD and TD.

Probabilistic analysis

Monte Carlo simulations were performed for a probabilistic analysis, using 10,000 iterations of 100,000 hypothetical chronic care patients with one of the four chronic diseases or multiple diseases. All input parameters were represented by a distribution to acquire probabilistic values and 95% confidence intervals. An overview of all parameters is provided in Appendix 3.

RESULTS

Survey responses

There were 1363 patients that completed the survey, of which 1311 patients were included in the analysis. Eleven patients were excluded since they did not want to participate and 41 patients were outside of the target group. The biggest patient groups are CVD (28%) and TD (26%), while patients with CKD, DM and multiple diseases make up 10%, 17% and 19% of the respondents.

A summary of the patient characteristics is provided in Table 2. Of the responding chronic care patients, 449 (34%) were male. The mean age of the respondents was 54.3 years (SD= 15.9), the mean number of phlebotomy appointments per year was 4.4 (SD=5.5), and the mean time spent per appointment including travel time was 1.1 hours (SD= 0.5). Most patients visit the hospital for their phlebotomy appointment (50%), followed by the phlebotomy service center (40%) and the GP's

office (7%). Three percent of patients already makes use of at-home sampling. This was incorporated in the estimation of usual care costs.

Table 2. Patient Characteristics of Survey Participants

	Total	DM	CVD	CKD	TD	Mult
Participants [n(%)]	1311 (100%)	222 (17%)	369 (28%)	127 (10%)	345 (26%)	248 (19%)
Male [n(%)]	449 (34.2%)	77 (35%)	229 (62%)	31 (24%)	19 (6%)	93 (38%)
Age in years [mean(sd)]	54.3 (15.9)	45.9 (18.8)	64.5 (10.0)	45.5 (14.8)	48 (12.3)	59.6 (14.4)
Phlebotomy appointments per year [mean(sd)]	4.4 (5.5)	3.6 (3.6)	3.9 (6.6)	6.2 (4.2)	4.6 (3.5)	4.7 (4.1)
Location						
Hospital [n(%)]	656 (50%)	127 (57%)	137 (37%)	105 (83%)	159 (46%)	128 (52%)
Phlebotomy service center [n(%)]	523 (40%)	81 (36%)	174 (47%)	18 (14%)	151 (44%)	99 (40%)
GP's office [n(%)]	96 (7%)	9 (4%)	34 (9%)	3 (2%)	35 (10%)	15 (6%)
At home [n(%)]	36 (3%)	5 (2%)	24 (7%)	1 (1%)	0 (0%)	6 (2%)
Time per appointment, incl. travel time (hours) [mean(sd)]	1.1 (0.5)	1.06 (0.5)	0.90 (0.5)	1.39 (0.60)[1]	0.97 (0.5)	1.11 (0.6)
Time spent seen as a burden [n(%)]	410 (31%)	84 (38%)	64 (17%)	50 (39%)	132 (38%)	80 (32%)
Feeling before phlebotomy appointment						
I don't care [n(%)]	959 (73%)	130 (59%)	295 (80%)	95 (75%)	250 (72%)	189 (76%)
I prefer not to go [n(%)]	189 (14%)	56 (25%)	39 (11%)	13 (10%)	48 (14%)	33 (13%)
Anxiety [n(%)]	163 (12%)	36 (16%)	35 (9%)	19 (15%)	47 (14%)	26 (10%)
Venous blood sampling is painful						
Yes [n(%)]	73 (6%)	17 (8%)	16 (4%)	6 (5%)	14 (4%)	20 (8%)
No [n(%)]	705 (54%)	105 (47%)	233 (63%)	59 (46%)	174 (50%)	134 (54%)
Sometimes [n(%)]	533 (41%)	100 (45%)	120 (33%)	62 (49%)	157 (46%)	94 (38%)

Feeling dependent on others [n(%)]	210 (16%)	36 (16%)	48 (13%)	21 (17%)	53 (15%)	52 (21%)
Affects their daily schedule [n(%)]	413 (32%)	75 (34%)	86 (23%)	49 (39%)	117 (34%)	86 (35%)

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[1] Four respondents were removed from the calculation of this parameter, since they included the time spent for dialysis in their survey response.

The mean age of CVD-patients is 64.5 years, which is 12-15 years higher than the mean age of DM-, CKD- and TD-patients. Patients with CKD have the most phlebotomy appointments (±6 times per year), visit the hospital most often for a phlebotomy appointment (83%) and spent the most time at the appointment including travel time (1.39 hours) compared with the other chronic diseases. Most CVD-patients go to the phlebotomy service center for an appointment (47%) and they spent the least time per appointment including travel time (0.9 hours). Compared with the other groups, fewer CVD-patients experience the time spent per appointment as a burden (17%) and fewer CVD-patients stated that the appointment affects their daily schedule (23%). More DM-patients prefer not to go to the appointment (25%) or experience anxiety (16%) compared with CVD-, CKD- and TD-patients. Most CVD-patients do not experience venous phlebotomy as painful (63%), while for the other groups, this is 54% or lower.

Survey results

A detailed summary of the survey results can be found in Appendix 2. Of all responding patients, 71% are willing to use Hem-Col; 81% of this group wants to use it for all tests that monitor their chronic disease. The biggest motivator for patients to use Hem-Col was the ability to do the blood sampling themselves and that the blood sampling would take less time. Diabetes patients were most willing to use Hem-Col (85% of DM patients) while CVD-patients were the least willing to use Hem-Col (70% of CVD patients).

Of all responding patients, 35.1% preferred a finger prick, 21.7% preferred venous sampling, 36.7% had no preference, and 6.5% did not know. The preference for a finger prick was the highest among DM patients (45%) and the preference for venous sampling was lowest (15%) compared with other groups.

Cost analysis

The average outcomes of the PA samples are presented in Figure 1. As seen in the Figure, the average cost savings are mainly due to a decreased time spent per phlebotomy appointment, resulting in a reduction of the productivity loss cost with €35.55 per patient per year. The results showed a negligible impact of the waste cost on the societal cost (€0.05), while the travel cost and informal care cost per patient per year decrease with €10.56 and €5.94, respectively. Although the cost of phlebotomy increases with €27.25 per patient per year when using Hem-Col, the overall societal cost (-€24.86 per patient per year) remains negative, indicating that the societal costs can be reduced when Hem-Col is implemented.
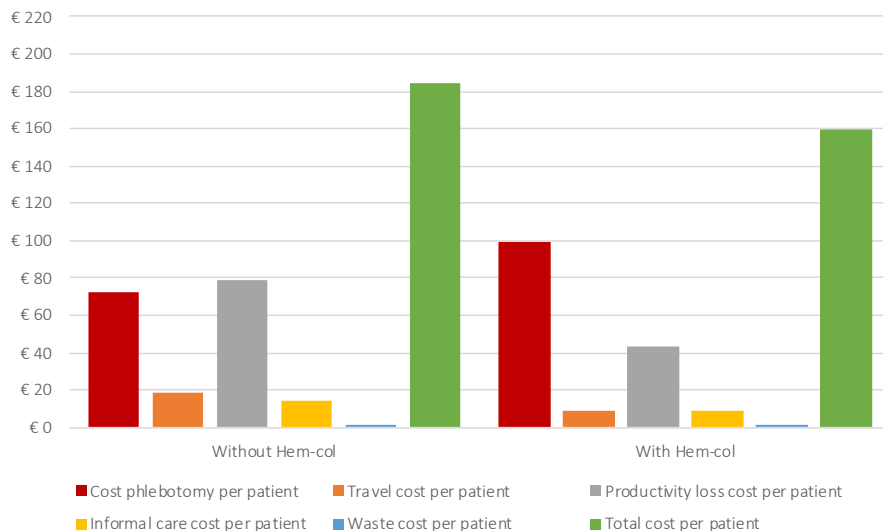
Figure 3. Analysis results of 100,000 hypothetical patients per year

As illustrated in Figure 2, the two largest patient groups were CVD (n = 26,608) and CKD patients (n = 30,556). Even though these two patient groups were both large, the total costs for CKD were much higher compared to CVD. This is mainly due to CKD patients having more phlebotomy appointments per year. The difference in costs when implementing Hem-Col versus without implementing Hem-Col is largest for TD and CKD patients, since these patients are, on average, younger and therefore have less productivity losses due to Hem-Col.
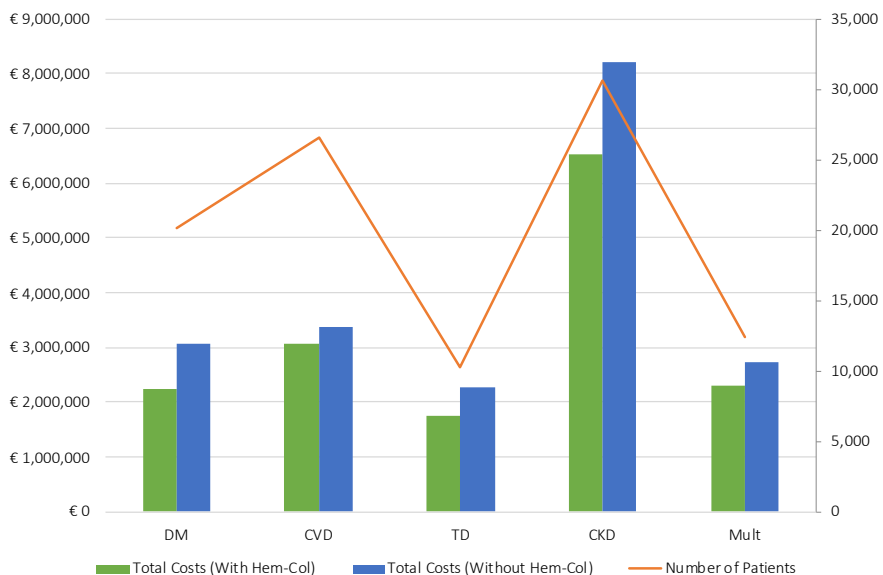
Figure 4. Summary of total costs per patient group

Probabilistic analysis

The result of the PA is shown in Figure 3, where the costs of current practice are plotted against the costs after implementing Hem-Col. The PA result indicates that phlebotomy with the possibility to use Hem-Col costs on average €159.44 (95% CI €119.10 to €208.35) per patient on a yearly basis, as compared with €184.30 (95% CI €159.08 to €212.53) for current practice, representing a cost savings of €24.86 (95% CI -€39.98 to -€4.18) per patient per year.

DISCUSSION

This study provided new insights into how patients experience venipuncture, their willingness to use an at-home blood sampling device such as Hem-Col, and the effect that such a device can have on societal costs. A significant number of chronic disease patients can be considered to adopt home-sampling devices that, from a societal perspective, are cost saving and moreover positively affects the self-management of their disease. One-third of the patients diagnosed with DM, CVD, CKD, TD or multiple diseases experience the phlebotomy appointment as a burden and indicated that it affects their daily schedule. Approximately 46% of the

Figure 5. PA result of 10,000 iterations of 100,000 patients
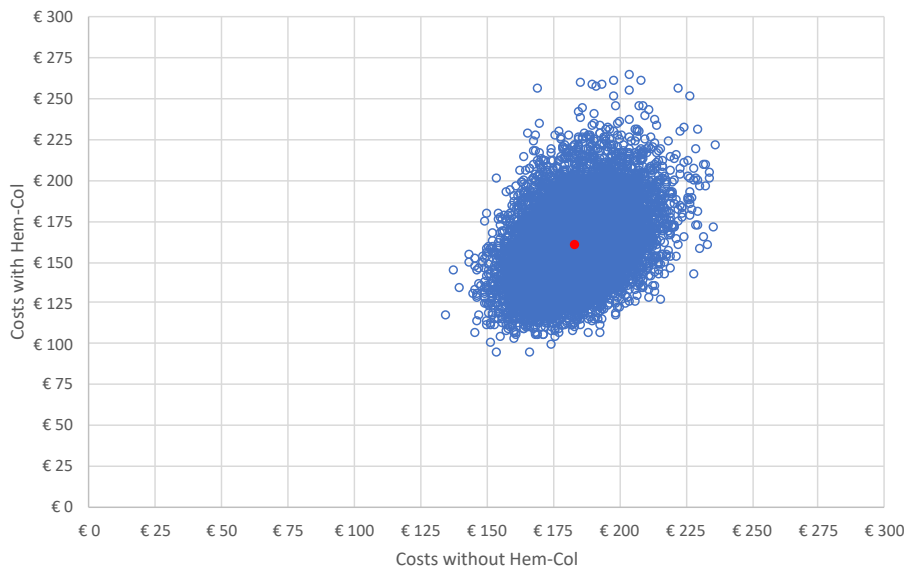
patients reported physical inconveniences after venous phlebotomy. Additionally, 16% feel dependent on others while 12% reported anxiety in anticipation of phlebotomy appointments. The most important factors of dissatisfaction towards phlebotomy were accredited to long waiting times and crowded phlebotomy locations. The recent outbreak of COVID-19 is likely to have provoked further dissatisfaction towards long waiting times and crowded phlebotomy locations. Chronic care patients are at higher risk for COVID-19 complications and this could have led to further adversity towards crowded phlebotomy locations.

Based on the responses from chronic care patients, blood sampling devices' success depends on its safety and trustworthiness, clarity of instructions, ease of use, and ease of sending it in for testing. Although a consistent preference for a finger prick is lacking, approximately two out of three patients are interested in Hem-Col, with about 71% of respondents preferring to use Hem-Col to monitor their chronic disease. The most prevalent reason for patients' indifference toward Hem-Col is attributable to the expectation of discomfort of self-administering the blood sampling. It has been shown that, in general, a finger prick is preferred over venous sampling, mainly due to patients experiencing a finger prick as less painful [21, 22, 35, 36]. In this study, the percentage of patients preferring a finger prick (35%) is higher than the percentage of patients preferring venous sampling (22%). The same proportion of patients who preferred a finger prick or venous sampling

found their preferred form of sampling less painful, indicating that patients' opinions vary within this topic. This could be since venipunctures are easier to perform on some patients compared to others.

The interest in using Hem-Col and patients' preference for finger prick instead of venous sampling varied between patient groups. Diabetes patients showed a higher interest in Hem-Col and had the highest preference for the finger prick sampling method compared with other patient groups. This can be explained by the reason they gave in the survey for preferring a finger prick: 'being used to it.' Diabetes patients are familiar with performing a finger prick to measure their blood glucose levels throughout the day. The preference for a finger prick was slightly lower among CKD patients compared to the other groups, which can be explained by the possibility of blood sampling during dialysis. When patients are on dialysis, the blood can be easily drawn without performing an extra venipuncture. CVD patients had the lowest interest in using Hem-Col, which could be due to their age. The mean age of respondents with CVD was approximately ten years higher compared with other groups. Older people are, in general, less eager to learn how to use a new system and prefer to use a system they are familiar with [37, 38]. Patients who are suffering from chronic diseases besides DM, CVD, CKD or TD had a lower willingness to use Hem-Col. This can be explained by the increased amount of hospital appointments of these patients, where phlebotomy is typically combined with another appointment. Consequently, for these patients, the impact of phlebotomy appointments on their daily schedule is less than that of other patients, and they may therefore value at-home blood sampling less.

Several limitations were perceived in this study. Firstly, splitting input parameters into multiple categories resulted in a few very small subgroups. Performing analysis on these small subgroups resulted in high parameter uncertainty and, therefore, large 95% CI intervals for the cost outcomes. Secondly, after analyzing the respondents' remarks at the end of the survey, some confusion among CVD-patients was observed. For some CVD-patients, it was not clear that Hem-Col cannot be used to examine their international normalized ratio (INR). Several CVD-patients indicated their INR is tested with a finger prick and therefore, they did not see the added value of Hem-Col. Lastly, the inevitable risk with an at home blood sampling device is the risk of a sampling error. Although this risk is minimized by detailed instructions provided along with the Hem-Col device, it is uncertain whether the assumed 5% sampling error rate adequately reflects clinical practice.

Simultaneously, the current analysis conservatively overestimates the success of venous blood sampling performed by a phlebotomist, by assuming that no sampling errors occur with this method. Therefore, it is unlikely that the uncertainty in sampling errors will have changed the main findings. However, it should be acknowledged that a higher sampling error rate of Hem-Col decreases satisfaction among patients which may eventually reduce the willingness to use Hem-Col.

On average, patients were willing to pay €2.15 per phlebotomy appointment to use the Hem-Col device. The financial contribution that DM-patients were willing to make was the lowest among all patient groups, even though they had the highest preference to use Hem-Col. This could be since type 2 diabetes occurs more frequently in people with a lower socio-economic status and less purchasing power [39].

CONCLUSIONS

Of the chronically ill patients, approximately 70% prefer to use Hem-Col for blood sampling to monitor their disease. Blood sampling with Hem-Col is considered more user-friendly compared with venous phlebotomy. Hem-Col may reduce the burden to patients, lower the impact of the phlebotomy appointment on their daily schedule, and reduce physical inconveniences. Long waiting times and crowded phlebotomy locations can be avoided when patients can self-manage using Hem-Col. Furthermore, implementing Hem-Col to monitor chronic diseases is likely cost-saving compared with current practice as it is expected to reduce societal cost. The total cost saving per patient might seem small or limited, but when considering how large each of the patient groups is, the implementation of Hem-Col could have a substantial impact nationwide. Seeing as the willingness to use Hem-Col is different between subgroups, it would be useful to start with a small-scale implementation in one of the more willing groups (such as DM patients) before implementing across different disease areas. Although Hem-Col will reduce costs from a societal perspective, the same can not be said for the healthcare system perspective. The most significant impact on costs was the reduced productivity loss costs, meaning foremost patients and their employers will benefit from implementing an at-home sampling device. This comes at the expense of the healthcare system (that is, at the expense of all Dutch citizens together funding the reimbursements through this system) due to the increased

phlebotomy costs. That said, the current cost of the Hem-col device is a starting price and is likely to be reduced when Hem-Col is used on a larger scale. This will result in lower phlebotomy costs for Hem-Col and therefore larger cost-savings when Hem-Col is implemented in clinical practice.

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APPENDIX 1: SURVEY

Welcome,

This research focuses on at-home phlebotomy possibilities for chronically ill patients. The purpose of this survey is to gain insight into your perspective. You are requested to answer a few questions about your experiences with phlebotomy appointments in the hospital or at a service phlebotomy center. Afterwards, we will ask you about your opinion of a new system that enables blood sampling at home.

It will take approximately 10 minutes to complete the survey. The answers you provide will be processed anonymously and cannot be traced back to you. Your participation in this survey is voluntary. You have the right to quit the survey at all times without giving a reason and this will not lead to negative consequences for you. The results are owned by the University of Twente and will only be used for scientific purposes. In case you have any questions, feel free to contact the researcher via e-mail (...).

By clicking the button below, you agree to participate on voluntary basis to this research, you are at least 18 years old and you are aware of the possibility to withdraw from the survey at any time without giving a reason.

Thank you in advance for your time and effort.

○ I agree, start the survey

○ I do not agree, I wish not to participate

In case "I do not agree, I wish not to participate" was chosen, the survey ends.

---

1. What is your age? _____

2. What is your gender?

○ Male

○ Female

○ Different

3. In what province do you live? Please, indicate in the figure.

4. With which chronic disease are you diagnosed that your blood needs to be tested on a regular basis? (Multiple answers are possible)

○ Diabetes mellitus type 1

○ Diabetes mellitus type 2

○ Cardiovascular disease

○ Chronic kidney disease

○ Thyroid disease

○ Different, namely: _____

5. How many phlebotomy appointments do you have per year to monitor this chronic disease?

○ 1 appointment

○ 2 appointments

○ 3 appointments

○ 4 appointments

○ 5 appointments

○ 6 appointments

○ More than 6 appointments

In case "More than 6 appointments" was chosen, the survey continues with question 6, otherwise question 6 was skipped.

6. You indicated to have more than 6 phlebotomy appointments per year, how many appointments do you have? _____

7. Which location do you visit the most for phlebotomy?

○ The hospital

○ The service phlebotomy center

○ The general practitioners office

○ Phlebotomy appointments often take place at home

8. How much time do you spent per phlebotomy appointment, including travel time from and to the location?

○ Less than half an hour

○ Half an hour till an hour

○ An hour till one and a half hour

○ One and a half hour till two hours

○ More than two hours, namely: _____

9. Is the time spent per phlebotomy appointment a burden to you?

○ Yes

○ No

---

10. How do you feel when you think about the fact that your blood must be drawn venously?

○ I don't care

○ I don't feel anxiety, but I prefer not to go

○ I feel anxiety

In case "I feel anxiety" was chosen, the survey continues with question 11, otherwise question 11 and 12 were skipped.

11. How much anxiety do you experience before a phlebotomy appointment? 0 indicates that you feel no anxiety at all and 10 indicates that you feel an extreme amount of anxiety.

12. Do you fear needles?

○ Yes

○ No

13. Would you describe venous phlebotomy as painful?

○ Yes

○ No

○ Sometimes

14. Do you feel dependent on others to go to the hospital, the service phlebotomy center or the GP's office for the phlebotomy?

○ Yes

○ No

In case "Phlebotomy appointments often take place at home" was chosen in question 7, question 15 was skipped

15. How do you experience the phlebotomy at your chosen location (hospital, service phlebotomy center or the GP's office)?

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
I experience the waiting room as unpleasant	O	O	O	O	O
It is hard to find a parking spot	O	O	O	O	O
It is always busy	O	O	O	O	O
I have to wait for a long time	O	O	O	O	O
The blood sampling itself takes a long time	O	O	O	O	O
The phlebotomist is unfriendly	O	O	O	O	O
The phlebotomist is not good at her job	O	O	O	O	O

16. After blood is drawn from a vein ... (multiple answers possible)

O   I often get bruises

O   I bleed frequently

O   I have muscle pain

O   I feel lightheaded

O   I pass out sometimes

O   None of the above

17. Does the phlebotomy appointment affects your daily schedule, besides the phlebotomy itself and the travel time?

O   Yes

O   No

In case "Yes" was chosen, the survey continues with question 18, otherwise question 18 was skipped.

18. How does the phlebotomy appointment affects your daily schedule?

_____

_____

19. What is your preference, based only on the blood-sampling method itself; a finger prick or venous sampling? We request you to base your preference only on the method itself, and not on the location where the blood-sampling can take place (e.g. at home/hospital).

○ A finger prick

○ Venous sampling

○ I don't have a preference

○ I don't know

In case "A finger prick" was chosen, the survey continues with question 20. In case "Venous sampling" was chosen, the survey continues with question 21. In case "I don't know" was chosen, the survey continues with question 22. In case "I don't have a preference" was chosen, the survey continues with question 23.

20. Why do you have a preference for the finger prick? (Multiple answers possible)

○ It is less painful

○ I am used to a finger prick

○ It is quicker

○ It is easier

○ My veins are hard to find

○ I have a fear of needles

○ The bleeding stops sooner

○ No bruises

○ No muscle pain

○ Different, namely: _____

The survey continues with question 23.

21. Why do you have a preference for venous sampling? (Multiple answers possible)

○ It is less painful

○ I am used to venous sampling

○ I don't have to do it myself

○ It seems uncomfortable to get enough blood in a tube after a finger prick

○ Different, namely: _____

The survey continues with question 23.

22. Did you ever use a finger prick, or someone else on you?

○ Yes

○ No

23. A new blood-sampling system has been developed which makes it possible for patients to do the blood-sampling themselves at home. The package will be send via mail and contains the following items (see the figure):

- A sterile cloth
- A lancet to prick the finger
- Tube to collect the blood
- A band aid
- Shipping material

The patient does the finger prick him-/herself, or someone nearby who is willing to help. After the prick, the blood can be collected in the tube. Approximately 5 blood drops are needed to fill the tube. Finally, the package can be send via mail.

What do you think when you are able to do the blood-sampling at home with a finger prick?

○ Great

○ GoodAverage

○ Not good

○ Terrible

In case "Great" or "Good" was chosen, the survey continues with question 24. In case "Not good" or "Terrible" was chosen, the survey continues with question 25. In case "Average" was chosen, the survey continues with question 26.

24. For what reasons are you interested in blood-sampling at home with a finger prick? (Multiple answers possible)

○ I can do it myself

○ It is easier to schedule

○ It takes less time

○ I don't have to travel back and forth

○ Different, namely: _____

Survey continues with question 26.

25. For what reasons are you not interested in blood-sampling at home with a finger prick? (Multiple answers possible)

○ I think it is a hassle to do it myself

○ I am afraid to prick myself

○ I see it as a trip to go to the hospital, the service phlebotomy center or the GP's office for phlebotomy

○ Different, namely: _____

26. What do you think is important for a blood-sampling system usable at home? 5 Stars indicate that you think it's extremely important, 1 star indicates that you think it's not important.

It must be easy to use	☆☆☆☆☆
It must be quick	☆☆☆☆☆
It must be less painful than venous sampling	☆☆☆☆☆
The system must be safe and trustworthy	☆☆☆☆☆
The system must be usable anywhere	☆☆☆☆☆
It must contain clear instructions	☆☆☆☆☆
It must be easy to send to the laboratory	☆☆☆☆☆
The lancet must be adjustable in height	☆☆☆☆☆
Only a small amount of blood is required	☆☆☆☆☆

27. A blood collection tube needs approximately 5 blood drops, do you think that is a lot?

○ No, that's fine

○ Yes, I think that is a lot but it's still doable

○ Yes, that seems hard to me

28. How much are you willing to spend on an additional contribution to be able to do the blood-sampling at home? The costs mentioned are per phlebotomy appointment.

○ Nothing

○ €5,00

○ €10,00

○ €20,00

○ €30,00

○ I am willing to pay more than €30,00

In case "I am willing to pay more than €30,00" was chosen, the survey continues with question 29, otherwise question 29 was skipped.

29. You indicated that you are willing to pay more than €30,00 on an additional contribution to be able to do the blood-sampling at home. How much are you willing to pay?

_____

30. Are you willing to use this system, assuming that the costs are not higher than the additional contribution you are willing to pay? For example: If you have answered with €5,00 ; the costs of the system will not be higher than €5,00.

  ○ Yes

  ○ No

In case "No" was chosen, the survey continues with question 32.

31. How often do you want to use this system?

  ○ For all blood tests I do on a yearly basis to monitor my chronic disease

  ○ For a part of the blood tests I do on a yearly basis to monitor my chronic disease, amount: _____

32. Do you have any remarks?

_____
_____

Thank you for your participation, your answers have been recorded.

APPENDIX 2: SURVEY RESULTS

Table B1. Reasons for having a preference for a particular sampling method.

	Total	DM	CVD	CKD	TD	Mult
Preference for blood-sampling						
Finger Prick	460 (35%)	100 (45%)	120 (33%)	33 (26%)	106 (31%)	101 (41%)
I don't know	85 (6%)	6 (3%)	27 (7%)	15 (12%)	25 (7%)	12 (5%)
No preference	481 (37%)	82 (37%)	147 (40%)	49 (39%)	123 (36%)	80 (32%)
Venous	285 (22%)	34 (15%)	75 (20%)	30 (24%)	91 (26%)	55 (22%)
Reasons for preferring a finger prick						
Quicker [n(%)]	316 (69%)	77 (77%)	66 (55%)	23 (70%)	78 (74%)	72 (71%)
More comfortable [n(%)]	301 (65%)	72 (72%)	67 (56%)	24 (73%)	78 (74%)	60 (59%)
Less painful [n(%)]	194 (42%)	54 (54%)	33 (28%)	15 (45%)	46 (43%)	46 (46%)
No bruises [n(%)]	172 (37%)	35 (35%)	48 (40%)	14 (42%)	39 (37%)	36 (36%)
I am used to it [n(%)]	154 (33%)	68 (68%)	35 (29%)	5 (15%)	4 (4%)	42 (42%)
Hard to find my vein [n(%)]	133 (29%)	23 (23%)	30 (25%)	16 (48%)	34 (32%)	30 (30%)
No bleeding afterwards [n(%)]	83 (18%)	11 (11%)	26 (22%)	6 (18%)	17 (16%)	23 (23%)
No muscle pain [n(%)]	55 (12%)	13 (13%)	15 (13%)	5 (15%)	15 (14%)	7 (7%)
Afraid of needles [n(%)]	44 (10%)	13 (13%)	6 (5%)	5 (15%)	10 (9%)	10 (10%)
Different reason [n(%)]	12 (3%)	2 (2%)	5 (4%)	1 (3%)	1 (1%)	3 (3%)
Reasons for preferring venous sampling						
I am used to it [n(%)]	163 (57%)	18 (53%)	41 (55%)	14 (47%)	53 (58%)	37 (67%)
Less painful [n(%)]	114 (40%)	13 (38%)	24 (32%)	12 (40%)	42 (46%)	23 (42%)
Uncomfortable to use a finger prick [n(%)]	107 (38%)	18 (53%)	30 (40%)	11 (37%)	27 (30%)	21 (38%)
I don't want to do it myself [n(%)]	35 (12%)	8 (24%)	10 (13%)	1 (3%)	10 (11%)	6 (11%)
Different reason [n(%)]	7 (2%)	0 (0%)	2 (3%)	3 (10%)	2 (2%)	0 (0%)

CKD = chronic kidney disease, CVD = cardiovascular diseases, DM = diabetes mellitus, GP = general practitioner, TD = thyroid diseases.

Table B2. Reasons for being interested in Hem-Col versus not being interested in Hem-Col.

	Total	DM	CVD	CKD	TD	Mult
Interested [n(%)]	859 (66%)	172 (77%)	212 (57%)	84 (66%)	228 (66%)	163 (66%)
Reasons						
I can do it myself [n(%)]	643 (75%)	128 (74%)	152 (72%)	57 (68%)	176 (77%)	130 (80%)
Easier to plan into my schedule [n(%)]	463 (54%)	117 (68%)	82 (39%)	46 (55%)	129 (57%)	90 (55%)
Takes less time [n(%)]	510 (60%)	120 (70%)	85 (40%)	63 (75%)	139 (61%)	104 (64%)
No travelling needed [n(%)]	467 (54%)	102 (59%)	90 (42%)	56 (67%)	121 (53%)	98 (60%)
Different reason [n(%)]	55 (6%)	9 (5%)	16 (8%)	3 (4%)	14 (6%)	13 (8%)
Not interested [n(%)]	196 (15%)	19 (9%)	64 (17%)	17 (13%)	58 (17%)	38 (15%)
Reasons						
Uncomfortable to do it myself [n(%)]	103 (52%)	10 (53%)	37 (58%)	7 (41%)	33 (57%)	16 (42%)
Fear to do it myself [n(%)]	59 (30%)	6 (32%)	17 (27%)	4 (24%)	25 (43%)	7 (18%)
I see it as a trip [n(%)]	15 (8%)	3 (16%)	7 (11%)	0 (0%)	0 (0%)	6 (16%)
Different reason [n(%)]	67 (34%)	6 (32%)	24 (38%)	7 (41%)	12 (21%)	18 (47%)
Indifferent [n(%)]	256 (20%)	31 (14%)	93 (25%)	26 (20%)	59 (17%)	47 (19%)

CKD = chronic kidney disease, CVD = cardiovascular diseases, DM = diabetes mellitus, GP = general practitioner, TD = thyroid diseases.

Table B3. Willingness to use Hem-Col among participants.

	Total	DM	CVD	CKD	TD	Mult
Willingness to use hem-col [n(%)]	933 (71%)	181 (82%)	230 (62%)	96 (76%)	257 (74%)	169 (68%)
For all blood tests [n(%)]	751 (81%)	151 (68%)	196 (53%)	65 (51%)	209 (61%)	130 (52%)
Contribution willing to pay [mean(sd)]	€2.12 (4.44)	€1.91 (3.72)	€2.18 (4.21)	€2.32 (5.90)	€2.75 (5.31)	€1.41 (2.78)

CKD = chronic kidney disease, CVD = cardiovascular diseases, DM = diabetes mellitus, GP = general practitioner, TD = thyroid diseases.

APPENDIX 3: SUMMARY OF INPUT PARAMETERS

Table 3.1. Input probability parameters used in the patient-level monte carlo simulation.

Parameters	Category	Probability	95% CI	Distribution	Source
Probability of chronic disease	DM	20.12%	20.09% to 20.15%	Dirichlet	[1, 2]
	CVD	26.65%	26.62% to 26.69%	Dirichlet	[3, 4]
	CKD	30.46%	30.42% to 30.49%	Dirichlet	[5-7]
	TD	10.11%	10.08% to 10.13%	Dirichlet	[8-11]
	Mult	12.66%	12.64% to 12.69%	Dirichlet	Derived
Male gender	DM	52.64%	52.55% to 52.73%	Beta	[12]
	CVD	52.09%	52.01% to 52.17%	Beta	[3]
	CKD	29.22%	29.14% to 29.29%	Beta	[13]
	TD	15.50%	15.33% to 15.67%	Beta	[14]
	Mult	42.95%	42.86% to 43.04%	Beta	Derived
Population age distribution (male with DM)	18-24	1.01%	0.98% to 1.03%	Dirichlet	[12, 15]
	25-34	1.62%	1.58% to 1.65%	Dirichlet	[12, 15]
	35-44	3.91%	3.87% to 3.96%	Dirichlet	[12, 15]
	45-54	12.81%	12.73% to 12.90%	Dirichlet	[12, 15]
	55-64	23.62%	23.52% to 23.73%	Dirichlet	[12, 15]
	65-74	31.92%	31.81% to 32.04%	Dirichlet	[12, 15]
	75+	25.10%	25.00% to 25.21%	Dirichlet	[12, 15]
Population age distribution (female with DM)	18-24	1.24%	1.21% to 1.27%	Dirichlet	[12, 15]
	25-34	1.74%	1.71% to 1.78%	Dirichlet	[12, 15]
	35-44	3.48%	3.43% to 3.53%	Dirichlet	[12, 15]
	45-54	10.83%	10.75% to 10.91%	Dirichlet	[12, 15]
	55-64	19.95%	19.85% to 20.06%	Dirichlet	[12, 15]
	65-74	27.70%	27.58% to 27.82%	Dirichlet	[12, 15]
	75+	35.06%	34.94% to 35.19%	Dirichlet	[12, 15]
Population age distribution (male with CVD)	18-24	1.28%	1.26% to 1.31%	Dirichlet	[3]
	25-34	2.14%	2.11% to 2.17%	Dirichlet	[3]
	35-44	2.14%	2.11% to 2.17%	Dirichlet	[3]
	45-54	2.47%	2.44% to 2.50%	Dirichlet	[3]
	55-64	8.64%	8.58% to 8.70%	Dirichlet	[3]
	65-74	19.14%	19.05% to 19.22%	Dirichlet	[3]
		64.20%	64.09% to 64.30%	Dirichlet	[3]
	75+				

Population age distribution (female with CVD)	18-24	1.70%	1.67% to 1.73%	Dirichlet	[3]
	25-34	2.84%	2.80% to 2.88%	Dirichlet	[3]
	35-44	2.84%	2.80% to 2.88%	Dirichlet	[3]
	45-54	3.36%	3.31% to 3.40%	Dirichlet	[3]
	55-64	8.72%	8.66% to 8.79%	Dirichlet	[3]
	65-74	15.44%	15.35% to 15.52%	Dirichlet	[3]
	75+	65.10%	64.99% to 65.21%	Dirichlet	[3]
Population age distribution (male with CKD)	18-24	0.00%	0.00% to 0.00%	Dirichlet	[13, 15]
	25-34	0.00%	0.00% to 0.00%	Dirichlet	[13, 15]
	35-44	3.52%	3.47% to 3.57%	Dirichlet	[13, 15]
	45-54	13.06%	12.96% to 13.16%	Dirichlet	[13, 15]
	55-64	19.86%	19.74% to 19.98%	Dirichlet	[13, 15]
	65-74	25.08%	24.96% to 25.21%	Dirichlet	[13, 15]
	75+	38.47%	38.33% to 38.62%	Dirichlet	[13, 15]
Population age distribution (female with CKD)	18-24	0.97%	0.95% to 0.99%	Dirichlet	[13, 15]
	25-34	3.52%	3.48% to 3.55%	Dirichlet	[13, 15]
	35-44	3.89%	3.85% to 3.93%	Dirichlet	[13, 15]
	45-54	12.49%	12.43% to 12.55%	Dirichlet	[13, 15]
	55-64	19.67%	19.60% to 19.75%	Dirichlet	[13, 15]
	65-74	26.54%	26.46% to 26.63%	Dirichlet	[13, 15]
	75+	32.91%	32.83% to 33.00%	Dirichlet	[13, 15]
Population age distribution (male with TD)	18-24	2.37%	2.19% to 2.55%	Dirichlet	[14, 15]
	25-34	5.44%	5.17% to 5.71%	Dirichlet	[14, 15]
	35-44	5.44%	5.17% to 5.71%	Dirichlet	[14, 15]
	45-54	18.64%	18.18% to 19.11%	Dirichlet	[14, 15]
	55-64	18.64%	18.18% to 19.11%	Dirichlet	[14, 15]
	65-74	27.35%	26.82% to 27.88%	Dirichlet	[14, 15]
	75+	22.11%	21.62% to 22.60%	Dirichlet	[14, 15]
Population age distribution (female with TD)	18-24	2.23%	2.16% to 2.31%	Dirichlet	[14, 15]
	25-34	8.20%	8.06% to 8.34%	Dirichlet	[14, 15]
	35-44	8.20%	8.06% to 8.34%	Dirichlet	[14, 15]
	45-54	20.07%	19.86% to 20.27%	Dirichlet	[14, 15]
	55-64	20.07%	19.86% to 20.27%	Dirichlet	[14, 15]
	65-74	22.59%	22.38% to 22.80%	Dirichlet	[14, 15]
		18.64%	18.45% to 18.84%	Dirichlet	[14, 15]
	75+				

Population age distribution (male with mult)	18-24	0.91%	0.88% to 0.94%	Dirichlet	Derived
	25-34	1.52%	1.48% to 1.55%	Dirichlet	Derived
	35-44	3.08%	3.04% to 3.13%	Dirichlet	Derived
	45-54	8.53%	8.45% to 8.61%	Dirichlet	Derived
	55-64	16.27%	16.16% to 16.37%	Dirichlet	Derived
	65-74	24.80%	24.67% to 24.92%	Dirichlet	Derived
	75+	44.89%	44.75% to 45.03%	Dirichlet	Derived
Population age distribution (female with Mult)	18-24	1.32%	1.29% to 1.35%	Dirichlet	Derived
	25-34	3.20%	3.16% to 3.25%	Dirichlet	Derived
	35-44	3.74%	3.70% to 3.79%	Dirichlet	Derived
	45-54	9.87%	9.79% to 9.94%	Dirichlet	Derived
	55-64	16.51%	16.42% to 16.61%	Dirichlet	Derived
	65-74	23.28%	23.17% to 23.38%	Dirichlet	Derived
	75+	42.08%	41.95% to 42.20%	Dirichlet	Derived
Location for DM 18-24	Hospital	70.73%	56.80% to 84.66%	Dirichlet	Survey
	SPC	29.27%	15.34% to 43.20%	Dirichlet	Survey
	GP's office	0.00%	0.00% to 0.00%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for DM 25-34	Hospital	72.97%	58.66% to 87.28%	Dirichlet	Survey
	SPC	24.32%	10.50% to 38.15%	Dirichlet	Survey
	GP's office	2.70%	0.00% to 7.93%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for DM 35-44	Hospital	64.00%	45.18% to 82.82%	Dirichlet	Survey
	SPC	36.00%	17.18% to 54.82%	Dirichlet	Survey
	GP's office	0.00%	0.00% to 0.00%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for DM 45-54	Hospital	67.50%	52.98% to 82.02%	Dirichlet	Survey
	SPC	25.00%	11.58% to 38.42%	Dirichlet	Survey
	GP's office	2.50%	0.00% to 7.34%	Dirichlet	Survey
	At home	5.00%	0.00% to 11.75%	Dirichlet	Survey
Location for DM 55-64	Hospital	43.75%	26.56% to 60.94%	Dirichlet	Survey
	SPC	40.63%	23.61% to 57.64%	Dirichlet	Survey
	GP's office	12.50%	1.04% to 23.96%	Dirichlet	Survey
	At home	3.13%	0.00% to 9.15%	Dirichlet	Survey

Location for DM 65-75+	Hospital	29.79%	16.71% to 42.86%	Dirichlet	Survey
	SPC	59.57%	45.54% to 73.60%	Dirichlet	Survey
	GP's office	6.38%	0.00% to 13.37%	Dirichlet	Survey
	At home	4.26%	0.00% to 10.03%	Dirichlet	Survey
Location for CVD 18-54	Hospital	36.76%	25.30% to 48.23%	Dirichlet	Survey
	SPC	51.47%	39.59% to 63.35%	Dirichlet	Survey
	GP's office	8.82%	2.08% to 15.57%	Dirichlet	Survey
	At home	2.94%	0.00% to 6.96%	Dirichlet	Survey
Location for CVD 55-64	Hospital	39.58%	29.80% to 49.37%	Dirichlet	Survey
	SPC	42.71%	32.81% to 52.60%	Dirichlet	Survey
	GP's office	11.46%	5.09% to 17.83%	Dirichlet	Survey
	At home	6.25%	1.41% to 11.09%	Dirichlet	Survey
Location for CVD 65-74	Hospital	38.36%	30.47% to 46.24%	Dirichlet	Survey
	SPC	50.00%	41.89% to 58.11%	Dirichlet	Survey
	GP's office	8.22%	3.76% to 12.67%	Dirichlet	Survey
	At home	3.42%	0.47% to 6.37%	Dirichlet	Survey
Location for CVD 75+	Hospital	30.51%	18.76% to 42.26%	Dirichlet	Survey
	SPC	42.37%	29.76% to 54.98%	Dirichlet	Survey
	GP's office	8.47%	1.37% to 15.58%	Dirichlet	Survey
	At home	18.64%	8.71% to 28.58%	Dirichlet	Survey
Location for CKD 18-34	Hospital	94.59%	87.31% to 88.88%	Dirichlet	Survey
	SPC	2.70%	0.00% to 7.93%	Dirichlet	Survey
	GP's office	2.70%	0.00% to 7.93%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for CKD 35-44	Hospital	83.33%	68.42% to 98.24%	Dirichlet	Survey
	SPC	16.67%	1.76% to 31.58%	Dirichlet	Survey
	GP's office	0.00%	0.00% to 0.00%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for CKD 45-54	Hospital	77.78%	62.10% to 93.46%	Dirichlet	Survey
	SPC	18.52%	3.87% to 33.17%	Dirichlet	Survey
	GP's office	3.70%	0.00% to 10.83%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for CKD 55-75+	Hospital	74.36%	60.65% to 88.06%	Dirichlet	Survey
	SPC	20.51%	7.84% to 33.19%	Dirichlet	Survey
	GP's office	2.56%	0.00% to 7.52%	Dirichlet	Survey

	At home	2.56%	0.00% to 7.52%	Dirichlet	Survey
Location for TD 18-34	Hospital	57.63%	45.02% to 70.24%	Dirichlet	Survey
	SPC	33.90%	21.82% to 45.98%	Dirichlet	Survey
	GP's office	8.47%	1.37% to 15.58%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for TD 35-44	Hospital	43.55%	31.21% to 55.89%	Dirichlet	Survey
	SPC	48.39%	35.95% to 60.83%	Dirichlet	Survey
	GP's office	8.06%	1.29% to 14.84%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for TD 45-54	Hospital	46.22%	37.26% to 55.18%	Dirichlet	Survey
	SPC	47.06%	38.09% to 56.03%	Dirichlet	Survey
	GP's office	6.72%	2.22% to 11.22%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for TD 55-64	Hospital	42.50%	31.67% to 53.33%	Dirichlet	Survey
	SPC	41.25%	30.46% to 52.04%	Dirichlet	Survey
	GP's office	16.25%	8.17% to 24.33%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for TD 65-75+	Hospital	36.00%	17.18% to 54.82%	Dirichlet	Survey
	SPC	48.00%	28.42% to 67.58%	Dirichlet	Survey
	GP's office	16.00%	1.63% to 30.37%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for Mult 18-44	Hospital	68.57%	53.19% to 83.95%	Dirichlet	Survey
	SPC	28.57%	13.60% to 43.54%	Dirichlet	Survey
	GP's office	2.86%	0.00% to 8.38%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for Mult 45-54	Hospital	56.82%	42.18% to 71.45%	Dirichlet	Survey
	SPC	38.64%	24.25% to 53.02%	Dirichlet	Survey
	GP's office	4.55%	0.00% to 10.70%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for Mult 55-64	Hospital	66.67%	54.74% to 78.59%	Dirichlet	Survey
	SPC	26.67%	15.48% to 37.86%	Dirichlet	Survey
	GP's office	6.67%	0.35% to 12.98%	Dirichlet	Survey
	At home	0.00%	0.00% to 0.00%	Dirichlet	Survey
Location for Mult 65-74	Hospital	37.33%	26.39% to 48.28%	Dirichlet	Survey
	SPC	53.33%	42.04% to 64.62%	Dirichlet	Survey

	GP's office	6.67%	1.02% to 12.31%	Dirichlet	Survey
	At home	2.67%	0.00% to 6.31%	Dirichlet	Survey
Location for Mult 75+	Hospital	32.35%	16.63% to 48.08%	Dirichlet	Survey
	SPC	47.06%	30.28% to 63.84%	Dirichlet	Survey
	GP's office	8.82%	0.00% to 18.36%	Dirichlet	Survey
	At home	11.76%	0.93% to 22.59%	Dirichlet	Survey
Dependency on others for DM	18-24	17.07%	5.56% to 28.59%	Beta	Survey
	25-34	13.51%	2.50% to 24.53%	Beta	Survey
	35-44	28.00%	10.40% to 45.60%	Beta	Survey
	45-54	10.00%	0.70% to 19.30%	Beta	Survey
	55-64	18.75%	5.23% to 32.27%	Beta	Survey
	65-75+	17.50%	6.64% to 28.36%	Beta	Survey
Dependency on others for CVD	18-54	22.06%	12.20% to 31.91%	Beta	Survey
	55-64	14.58%	7.52% to 21.64%	Beta	Survey
	65-74	7.53%	3.25% to 11.82%	Beta	Survey
	75+	13.56%	4.82% to 22.30%	Beta	Survey
Dependency on others for CKD	18-34	15.63%	3.93% to 27.32%	Beta	Survey
	35-44	20.83%	4.59% to 37.08%	Beta	Survey
	45-54	14.81%	1.41% to 28.21%	Beta	Survey
	55-75+	21.88%	8.90% to 34.85%	Beta	Survey
Dependency on others for TD	18-34	18.00%	8.20% to 27.80%	Beta	Survey
	35-44	12.90%	4.56% to 21.25%	Beta	Survey
	45-54	12.61%	6.64% to 18.57%	Beta	Survey
	55-64	21.25%	12.29% to 30.21%	Beta	Survey
	64-75+	19.05%	3.65% to 34.44%	Beta	Survey
Dependency on others for Mult	18-44	40.00%	23.77% to 56.23%	Beta	Survey
	45-54	20.45%	8.54% to 32.37%	Beta	Survey
	55-64	20.00%	9.88% to 30.12%	Beta	Survey
	65-74	18.67%	9.85% to 27.49%	Beta	Survey
	75+	20.59%	7.00% to 34.18%	Beta	Survey
Willing to use hem-col DM	18-24	89.02%	79.46% to 98.59%	Beta	Survey
	25-34	81.08%	68.46% to 93.70%	Beta	Survey
	35-44	88.00%	75.26% to 99.74%	Beta	Survey
	45-54	87.50%	77.25% to 97.75%	Beta	Survey
	55-64	90.63%	80.53% to 99.72%	Beta	Survey
	65-75+	74.47%	62.00% to 86.93%	Beta	Survey

Willing to use hem-col CVD	18-54	77.21%	67.31% to 87.10%	Beta	Survey
	55-64	68.75%	59.48% to 78.02%	Beta	Survey
	65-74	67.47%	59.87% to 75.07%	Beta	Survey
	75+	70.34%	58.68% to 81.99%	Beta	Survey
Willing to use hem-col CKD	18-34	78.38%	65.11% to 91.64%	Beta	Survey
	35-44	85.42%	71.58% to 99.25%	Beta	Survey
	45-54	74.07%	57.54% to 90.60%	Beta	Survey
	55-75+	70.51%	56.38% to 84.64%	Beta	Survey
Willing to use hem-col TD	18-34	72.03%	60.68% to 83.39%	Beta	Survey
	35-44	79.84%	69.85% to 89.83%	Beta	Survey
	45-54	73.11%	65.14% to 81.08%	Beta	Survey
	55-64	76.25%	66.92% to 85.58%	Beta	Survey
	64-75+	70.00%	52.39% to 87.61%	Beta	Survey
Willing to use hem-col Mult	18-44	85.71%	74.12% to 97.31%	Beta	Survey
	45-54	78.41%	66.25% to 90.57%	Beta	Survey
	55-64	81.67%	71.88% to 91.46%	Beta	Survey
	65-74	70.00%	59.63% to 80.37%	Beta	Survey
	75+	60.29%	43.85% to 76.74%	Beta	Survey

CI = confidence interval, CKD = chronic kidney disease, CVD = cardiovascular diseases, DM = diabetes mellitus, GP = general practitioner, SPC = Service phlebotomy center, TD = thyroid diseases.

Table 3.2. Input parameters used in the patient-level monte carlo simulation.

Parameters	Category	Value	95% CI	Distribution	Source
Amount of phlebotomy appointments per year for DM	18-24	3.00	2.54 to 3.46	Gamma	Survey
	25-34	3.59	3.05 to 4.14	Gamma	Survey
	35-44	3.28	2.88 to 3.68	Gamma	Survey
	45-54	3.83	3.37 to 4.28	Gamma	Survey
	55-64	3.22	2.71 to 3.73	Gamma	Survey
	65-75+	3.91	1.8 to 6.01	Gamma	Survey
Amount of phlebotomy appointments per year for CKD	18-34	7.23	4.91 to 9.56	Gamma	Survey
	35-44	5.63	4.34 to 6.91	Gamma	Survey
	45-54	4.41	3.7 to 5.12	Gamma	Survey
	55-75+	5.78	4.45 to 7.12	Gamma	Survey
Amount of phlebotomy appointments per year for TD	18-34	5.05	3.67 to 6.43	Gamma	Survey
	35-44	5.02	4.17 to 5.86	Gamma	Survey
	45-54	4.43	3.87 to 4.99	Gamma	Survey
	55-64	3.88	3.22 to 4.53	Gamma	Survey
	64-75+	2.60	1.34 to 3.86	Gamma	Survey

Amount of phlebotomy appointments per year for Mult	18-44	4.28	3.37 to 5.18	Gamma	Survey
	45-54	5.00	3.81 to 6.19	Gamma	Survey
	55-64	4.98	3.88 to 6.08	Gamma	Survey
	65-74	4.41	3.32 to 5.5	Gamma	Survey
	75+	7.91	1.14 to 14.69	Gamma	Survey
Amount of phlebotomy appointments per year for CVD	18-54	4.52	3.18 to 5.85	Gamma	Survey
	55-64	3.66	2.31 to 5.01	Gamma	Survey
	65-74	3.51	2.54 to 4.48	Gamma	Survey
	75+	6.24	3.89 to 8.59	Gamma	Survey
Time spent at the hospital in hours	DM	1.22	1.14 to 1.31	Gamma	Survey
	CVD	1.15	1.06 to 1.23	Gamma	Survey
	CKD	1.39	1.28 to 1.5	Gamma	Survey
	TD	1.11	1.03 to 1.19	Gamma	Survey
	Mult	1.34	1.22 to 1.45	Gamma	Survey
Time spent at the service phlebotomy center in hours	DM	0.85	0.77 to 0.93	Gamma	Survey
	CVD	0.82	0.77 to 0.87	Gamma	Survey
	CKD	0.75	0.62 to 0.88	Gamma	Survey
	TD	0.86	0.8 to 0.93	Gamma	Survey
	Mult	0.89	0.81 to 0.97	Gamma	Survey
Time spent at the GP's office in hours	DM	0.83	0.67 to 1	Gamma	Survey
	CVD	0.65	0.57 to 0.72	Gamma	Survey
	CKD	0.83	0.51 to 1.16	Gamma	Survey
	TD	0.80	0.68 to 0.92	Gamma	Survey
	Mult	0.83	0.65 to 1.02	Gamma	Survey
Time spent at home in hours	DM	0.80	0.21 to 1.39	Gamma	Survey
	CVD	0.46	0.34 to 0.58	Gamma	Survey
	CKD	1.00	0	Gamma	Survey
	TD	1.00	0	Gamma	Survey
	Mult	0.42	0.25 to 0.58	Gamma	Survey
Time spent with hem-col in hours		0.54	0.28 to 0.81	Gamma	[16]

CI = confidence interval, CKD = chronic kidney disease, CVD = cardiovascular diseases, DM = diabetes mellitus, GP = general practitioner, TD = thyroid diseases.

Table 3.3. Input cost parameters used in the patient-level monte carlo simulation.

Parameters	Category	Cost	95% CI*	Distribution	Source
Costs venous	Hospital	€ 9.04	€8.08 to €9.99	Gamma	[17-21]
	SPC	€ 15.34	€14.09 to €16.60	Gamma	[22-31]
	GP's office	€ 18.13	€17.92 to €18.34	Gamma	[22-31]
	At home	€ 25.16	€19.36 to €30.96	Gamma	[22-31]
Costs Hem-col	Hem-col	€ 20.42	€10.42 to €30.43	Gamma	[16, 32, 33]
	Extra tube	€ 1.95	€0.99 to €2.91	Gamma	[16]
Waste processing per tube	Venous	€ 0.01223	€0.006 to €0.0182	Gamma	[34-38]
	Hem-col	€ 0.00679	€0.004 to €0.0101	Gamma	[34-39]
Travel costs[1]	Hospital	€ 6.08	€3.10 to €9.07	Gamma	[40]
	SPC	€ 1.02	€0.52 to €1.52	Gamma	[40]
	GP's office	€ 0.45	€0.23 to €0.67	Gamma	[40]
	Hem-col	€ 1.02	€0.52 to €1.52	Gamma	[40-42]
Productivity loss costs per hour per male patient	18-24	€ 40.74	€20.78 to €60.70	Gamma	[40]
	25-34	€ 40.74	€20.78 to €60.70	Gamma	[40]
	35-44	€ 40.74	€20.78 to €60.70	Gamma	[40]
	45-54	€ 40.74	€20.78 to €60.70	Gamma	[40]
	55-64	€ 40.74	€20.78 to €60.70	Gamma	[40]
	65-74	€ 4.91	€2.51 to €7.32	Gamma	[40, 43]
	75+	€ 0.73	€0.37 to €1.09	Gamma	[40, 43]
Productivity loss costs per hour per female patient	18-24	€ 33.97	€17.32 to €50.61	Gamma	[40]
	25-34	€ 33.97	€17.32 to €50.61	Gamma	[40]
	35-44	€ 33.97	€17.32 to €50.61	Gamma	[40]
	45-54	€ 33.97	€17.32 to €50.61	Gamma	[40]
	55-64	€ 33.97	€17.32 to €50.61	Gamma	[40]
	65-74	€ 4.10	€2.09 to €6.10	Gamma	[40, 43]
	75+	€ 0.61	€0.31 to €0.91	Gamma	[40, 43]
Costs informal care giver per hour		€ 15.05	€7.68 to €22.42	Gamma	[40]

GP = general practitioner; SPC = Service Phlebotomy Center

* 95% CI is based on an assumed standard error of 25%, except for the costs of venous sampling.

[1] Parking costs were added to the traveling costs when traveling to the hospital since almost all hospitals in the Netherlands have a paid parking lot . With Hem-Col, traveling costs were seen as the costs associated with mailing the sample to the laboratory. This was calculated by looking at the maximum distance to a mailbox (derived from PostNL, the Dutch postal network [29]) and the average cost per kilometer when traveling by car or public transport.

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Chapter 6:

General Discussion

DISCUSSION

The number of available point-of-care (POC) tests continues to increase along with the research and development of new tests. At the same time, the growing demand for patient-centred healthcare continue to challenge the efficiency of healthcare systems, and POC testing may be part of a solution to increase this efficiency. Nonetheless, the adoption of POC testing is relatively slow, and many POC tests are not utilised in clinical practice, especially on a wider scale. Nations around the world are realising that healthcare budgets cannot continue to increase at the current rate [1], and plans are being made in an attempt to stabilise or even decrease the healthcare budgets. Consequently, health economics and the efficient distribution of healthcare resources are more critical than ever. This thesis confirmed that there indeed is a broad spectrum of available POC tests for a wide range of health problems and applications. POC testing can be used by general practitioners (GPs) to prevent unnecessary prescriptions and referrals to specialised and secondary care. In the emergency room and secondary care, POC testing can aid in discharging patients more rapidly, thereby reducing the patients' length of stay and freeing up bed space (which has become even more valuable during the recent COVID-19 pandemic). Further value is added through patient convenience and overall improvement of care provision [2,3]. In contrast, it is also clear that there may be negative aspects related to POC testing, such as increased labour requirements and required alterations to existing processes and workflow [4,5]. This could discourage GPs and other healthcare providers from implementing POC testing [6].

It is important to note that although POC tests share some aspects and characteristics, the exact benefits will depend on the specific POC test, the setting it is applied in, the type of disease (acute vs chronic) and the reason for its use (for example, diagnosis vs monitoring or ruling out a disease vs monitoring a disease). When considering the wide-scale implementation of POC testing, there are some POC tests that have a higher chance of successful implementation in primary care than others. For example, c-reactive protein POC tests have been proven to be useful in primary care to support the early detection of serious infections and diseases [7,8]. POC tests that measure glycated haemoglobin have been shown to be particularly useful in the primary care pathways for both diagnosing and monitoring patients with diabetes [9,10]. In contrast, the implementation of a

troponin POC test (as an indicator for myocardial damage) might be limited in primary care since the diagnosis of exclusion of acute coronary syndrome needs sequential testing of troponin together with an electrocardiogram [11]. Therefore, as a POC test, it will probably have a much higher potential in an ambulance or hospital setting [12].

Several studies have demonstrated the cost-effectiveness of specific POC tests and have shown that they can maintain, or even improve on, the current quality of care; however, the implementation of these tests is limited [13]. As discussed in Chapter 4, the introduction of POCTs in general practice is not a single step but requires a series of interlinked processes involving several stakeholders with different responsibilities. In fact, the successful implementation of POC tests requires a transformation of the care pathway and demands the integration of services across the healthcare system. However, understanding the potential impact (on patients, healthcare providers and the healthcare system) of implementing POC tests on a wide scale is necessary to plan exactly how the care pathways and services should be transformed and integrated.

HEALTH ECONOMIC EVIDENCE OF POC TESTING

POC testing is accompanied by both potential benefits and drawbacks. Therefore, health economic evidence is required to establish whether the implementation of POC testing has a favourable cost-effectiveness ratio and whether there are economic factors preventing their use. In Chapter 3, it was shown that most health economic evaluations of POC tests recommend the implementation of POC testing. However, the system-level health economic evidence provided in the evaluations is not necessarily relevant to the stakeholders (in the healthcare system) that have influence over the implementation of POC testing. This could explain why a lack of evidence is still seen as a barrier to the implementation of POC testing, even though health economic evidence of POC testing exists. As identified in Chapter 3, a common limitation in available health economic evidence of POC tests is that it is somewhat restricted or non-transferrable. Evaluations are typically cohort-and context-specific and not enough effort is made to ensure the transferability of their results to other contexts. For example, most evaluations would investigate the impact of POC testing in a single region when applied to a specific cohort. However, health economic evidence generated from such an evaluation would not necessarily apply to other general practices

in other regions, due to differences in the incidence of the disease, the availability of health care resources or clinical practice patterns [14]. Consequently, the evidence generated from these evaluations, is not as comprehensive and is more difficult to generalise to other cohorts or (similar) settings. The value of health economic evidence would be greatly increased if the results are generalisable beyond the cohort and context in which the evaluation is undertaken, eliminating the need to repeat studies (with additional costs, efforts and time) in different contexts.

Furthermore, in Chapter 3 it was observed that, in most evaluations, POC testing is compared to traditional laboratory testing (or no testing) and costs and (typically) a single outcome are reported. However, an evaluation should not base the effectiveness of a POC test on a single outcome, but also investigate and report on all of the potential (long term) benefits of the test [15]. For example, if an evaluation found that a POC test reduced unnecessary referrals to specialists, the impact that this will have on secondary care (since POC testing may prevent referrals and thereby will free up time for specialists) should also be investigated. This is echoed by the evaluations (in Chapter 3) that incorporated a longer time horizon and found that the cost savings continue to increase over time when the POC test is implemented. Similarly, negative aspects should also be included in the evaluation, such as the additional time that staff had to spend on training and performing the tests. This will ensure that the full impact of a POC test becomes more evident in evaluations. In this context, evidence on aspects around the organisation of care, support of healthcare providers and quality management may be crucial in the recognition of the benefits accompanying POC testing and consequently the widespread implementation. Although dimensions of value for POC testing have been defined in the literature [15,16], it remains a challenge to include all of the relevant impact elements in an evaluation [17]. A typical health economic analysis does not necessarily require the inclusion of these aspects or dimensions of value to estimate cost-effectiveness. If, however, health economic analyses are also intended to support the adoption of POC testing, then these elements need to be included in addition to traditional health economic measurements (costs and/or effectiveness).

Even though there has been an increase in evaluations of POC tests over the last decade; it seems that the evidence provided in these evaluations is not always as comprehensive as it could be, and studies evaluating POC tests often fail to report

on some of the key factors that are considered important to the implementation of innovative diagnostics in primary care. In Chapter 2, it was found that there is a clear inconsistency between what is reported in evaluations and what GPs consider to be important. Even though GPs perceive clinical utility to be the most important aspect of POC testing, it was rarely included in test evaluations. Similarly, two of the concerns that GPs have with the implementation of POC testing, are legislation and the funding and reimbursement structures. Nevertheless, evaluations seldom report on any aspects related to the (potential) reimbursement and legislation of the test. To ensure that an evaluation of a POC test is useful to GPs, future evaluations should not only focus on costs, potential health benefits, and the technical and clinical performance aspects of a test, but also report on the aspects important to GPs and healthcare providers in general.

IMPLICATIONS FOR PATIENTS AND HEALTHCARE PROVIDERS

In Chapter 3 it was confirmed that patients could benefit from POC testing through early, faster diagnosis, a decrease in the number of unnecessary hospital admissions and referrals to specialised care, reduced risks of infection and antibiotic prescription, and a decrease in additional burden and costs associated with referrals and additional testing. This aligns with previous studies that have proven similar benefits [18,19]. As seen in Chapter 3, the majority of the health economic evaluations of POC tests included in the review reported an increase in effectiveness when POC testing is implemented. The effectiveness measures used the most by evaluations in Chapter 3, were associated with patient outcomes or benefits, such as time to diagnosis, antibiotic prescriptions avoided, and survival. Additionally, it was found that the implementation of POC testing in primary care will also lead to downstream implications. For example, it would free up resources in secondary care since fewer patients are being referred from primary care to secondary care. Therefore, POC testing can be seen as beneficial to the GPs' job as gatekeepers.

As described in Chapter 4, the implementation of POC testing in practice would require additional work in terms of initial set-up but also to manage POC testing usage. In most countries, this additional workload would fall under the responsibility of the GPs themselves. There likely are support structures in place in the form of guidelines and quality frameworks, but the GPs would still need to

spend additional time (and money) to ensure that these guidelines and frameworks are being followed and adhered to. Most countries also recommend that GPs work in close collaboration with hospitals and laboratories for support, especially regarding the purchase of devices, quality control and assessment, training, and safety provisions. Nonetheless, it remains the responsibility of the general practice to decide whether or not to implement POC testing; and to take responsibility for setting up the necessary structures and collaborations that have to be in place if they decide to implement it. Healthcare providers are not necessarily incentivised to apply POC testing directly. As a result, this could discourage them from undertaking the additional (high) workload or spending funds on the implementation of POC testing in their practice. Therefore, active additional support will be required to encourage healthcare providers to implement POC testing in primary care.

Similarly, other novel diagnostic devices can also benefit patients, and healthcare providers to some extent. As described in Chapter 5, the use of an at-home blood-sampling device will benefit patients not only by providing them with a preferred sampling method, but also through convenience from not having to travel for on-site sampling. An at-home sampling device will also free up time for some healthcare providers who would have been responsible for sampling blood on-site, such as GPs, phlebotomy centres and hospitals. The laboratory personnel responsible for analysing the blood would not be impacted by the implementation, since they remain responsible for this task.

IMPLICATIONS FOR THE HEALTHCARE SYSTEM

The broader implementation of POC testing in primary care will change the current care pathways by eliminating the need to wait for samples to be sent to a central laboratory before getting results [18]. Although this is beneficial, in the sense that clinical decisions can be made much faster, this also means that sites where POC testing is implemented are often seen as independent laboratories by the health care system (as discussed in Chapter 4) and are then required to fulfil the corresponding country-specific requirements and comply with local/nationwide regulations [20]. Consequently, in the case of wide-scale implementation, there will be thousands of POC testing sites, operators and POC devices that need to be monitored to ensure regulatory compliance [20]. Functions that are important in maintaining the required performance of diagnostic

tests, such as quality control, quality assurance, calibration, etc., would typically be built into the laboratory (a single laboratory where several tests are conducted). With POC testing, these and similar functions will now have to be conducted separately at each POC testing site [1,20].

As described in Chapter 4, one of the biggest implementation barriers in Australia, is that the GP has to register as a pathology laboratory to be able to implement POC testing. The practice, as a legal entity, is then responsible for meeting all related conditions with only limited support and guidance. This means that these functions are often left unchecked and not conducted up to standard. Shaw (2016) [21] has stated that errors in POC testing can be due to limited resources and support, and a lack of knowledge of POC testing among the users of the tests, who can be less experienced in quality control and assurance than laboratory personnel. For example, in blood gas analysis, it has been shown that the most common error in POC testing was due to healthcare providers being unable or unwilling to perform minor maintenance [22]. As indicated in Chapter 4, GPs in the Netherlands have the option to overcome this issue by working in close collaboration with hospitals or laboratories who are actively involved in managing some of these functions, thereby alleviating the practitioners from some of the workload. In Norway, a national authority, Noklus, takes complete ownership of these responsibilities and works in close collaboration with healthcare providers to ensure these functions are performed correctly.

Furthermore, the costs associated with the functions that are important in maintaining the required performance of diagnostic tests, are typically included in the laboratory's overhead costs and reimbursement regulations. In contrast, when POC testing is implemented in general practice, for example, some of these costs typically are not reimbursed. This could discourage GPs from implementing POC tests in their practice due to the high perceived associated costs. Additionally, where central laboratories benefit from economy of scale (ordering reagents and test consumables in bulk), POC testing can be perceived as being more expensive since the practice has to order reagents and strips in smaller batches. Even though the practice has to fund a portion (or all) of the implementation costs, it is the healthcare system that will potentially benefit from the implementation through, for example, the rapid delivery of results and the reduction of unnecessary referrals to secondary care [1]. In contrast, it was observed in Chapter 5, that the implementation of an at-home blood-sampling device, will reduce costs

from a societal perspective, but not from a healthcare system perspective. This is mainly since the most substantial impact on costs was reduced productivity loss costs, meaning patients (and their employers) will benefit the most from implementing such a blood-sampling device. This comes at the expense of the healthcare system due to the increased phlebotomy costs. That being said, it should also be noted that at-home devices and tests can help reduce the burden on healthcare systems, especially those that are already overwhelmed, as was evident during the recent COVID-19 outbreak [23]. Financial structures and reimbursement policies should be redefined to ensure that those stakeholders responsible for POC test implementation (such as GPs) are incentivised to implement, by allowing them to experience the benefits from the implementation without additional costs.

SUCCESSFUL IMPLEMENTATION OF POC TESTING

All of the stakeholders that influence, or are influenced by the implementation of POC testing in primary care, have to be considered when evaluating the implementation process. Wide-scale implementation of POC testing in primary care is a policy concern, and if it is to be realised, it should not be left to healthcare providers own initiatives, but instead receive active involvement from the government and the right incentives. In Chapter 4, it was observed that if a single national authority (a separate organisation or body) takes responsibility for the implementation process of POC testing, the overall uptake may improve. For such an organisation to be realised, the appropriate (existing) professional organisations, such as medical associations and professional societies for GPs and healthcare providers, should work together with the ministry of health to set up a system of quality improvement for laboratory services outside the laboratory and hospital. The main goal of this organisation should be to take responsibility for POC testing by ensuring that these laboratory analyses are set up, managed, carried out and utilised in accordance with patient's needs. With such an organisation in place, healthcare providers would be relieved of the full responsibilities associated with the set-up and management of POC testing, allowing them to continue to focus on patient care and not on the management of a POC testing system. Healthcare providers might be more willing to change their workflow and implement POC tests in their primary care practice, if the appropriate guidance (throughout the entire implementation process) and active

support after implementation is made available and if they do not have to pay for this process. It has also been shown, that when such an organisation (with the appropriate quality assurance shemes in place) takes responsibility for the management of POC testing in primary care, the preanalytical error rates can be greatly reduced, thereby increasing the performance of the POC tests in practice [24,25].

As mentioned earlier, a possible obstacle for such an organisation would be the effective management of thousands of testing sites, devices and operators. However, several structures already exist to simplify the process, such as streamlined online information systems to easily manage test results. In the past, POC testing devices that were developed by different manufacturers had their own manufacturing elements, such as data communication protocols and physical connector cables. This is problematic when devices developed by different manufacturers are implemented at a POC testing site, since it requires additional funding and time to purchase and learn to navigate different computer software to allow data transfers [20]. To combat this, the Clinical and Laboratory Standards Institute (CLSI) developed the POCT1 standard [26] that defines the physical connections and communication protocols that are required by POC testing manufacturers, with some aspects being mandatory. This allows easier sharing of data between the device and information systems.

Dedicated and ongoing financial resources can also greatly improve the implementation of POC testing in primary care, especially if the healthcare provider will be able to adopt POC tests in their practice without incurring any additional costs to the practice itself. This includes costs related to the device itself, but also costs associated with training, quality control and maintenance. As mentioned in Chapter 4, there are many ways to ensure financial support; for example, the Norwegian Medical Association, in cooperation with Noklus, negotiates reimbursements from the government for financial support, while in the Netherlands, primary healthcare providers can make arrangements with laboratories to receive POC devices at no additional cost. In addition to financial support, healthcare providers would also benefit from ongoing monitoring and feedback from the national POC testing authority to identify any opportunities for improvement within a practice. The guidelines and governing team should clearly provide healthcare providers with instructions and support to set up a data collection system to collect and assess the performance of tests systematically.

This will also simplify the process of quality assurance and evaluating the effectiveness of the POC tests in place in primary care.

Another aspect of successful wide-scale implementation is the selection of the tests itself. As mentioned at the start of this chapter, there is a wide range of available POC tests for different disease areas. If POC tests are to be implemented across primary care locations, with different operators and pathways, increasing the number of different POC devices will complicate the capability to monitor and manage the usage of these tests effectively. Each device might have different calibration, validation and usage procedures. Simplicity and standardisation will, therefore, play an important part in wide-scale implementation. Another option is the use of POC devices with the ability to perform multiple tests. As mentioned in Chapter 2, GPs have previously stated during interviews that they would be more willing to purchase devices that can perform multiple tests, compared to single-test devices [27]. The number of POC test operators should be kept at a minimum in order to simplify the management of POC testing and to guarantee quality by ensuring sufficient experience of the operator. As discussed in Chapter 4, a national POC testing authority should work closely with primary care locations to ensure only the POC tests that would benefit the site the most are chosen and implemented. In the Netherlands, for example, local hospitals or laboratories often guide and provide insight to GPs on the repertoire of POC tests that would be beneficial to the practices' specific needs (according to the patient profiles at the practice). Using online information systems, the usage of the implemented devices should be constantly monitored to ensure that only devices being utilised frequently remain implemented.

ALIGNING HEALTH ECONOMIC MODELS AND IMPLEMENTATION

With pharmaceuticals, health economic analyses often play an important part in the implementation as they guide access and reimbursements decisions. This is not always the case with diagnostics. There are several factors, dependent on the diagnostics under evaluation, that complicate the health economic analysis and limit the value of the results. Diagnostics differ from pharmaceuticals, not only in terms of physical properties but also regarding manufacturing environment and regulation. The impact of pharmaceuticals is easier to measure (the patient recovers or not) compared to diagnostics, where the impact is more indirect

(results are used to guide decisions) and has an indirect effect on patient outcomes. However, many official health technology assessment (HTA) guidelines only address pharmaceuticals, and only a small number of HTA institutions provide specific guidelines for devices, which can include diagnostics [28].

There are several issues that might limit the commercial value of a diagnostic, such as risks (overutilization or incorrect use), logistical issues, or the budget impact. These issues are, however, rarely quantified in a typical health economic evaluation or model. In many health economic evaluations, a device might be regarded as cost-effective, but these evaluations fail to include how actual implementation and use in practice may influence real-world cost-effectiveness. A novel diagnostic will typically lead to care being reallocated from one point in the care pathway to another. This is also the case with POC testing, for example, where a POC device implemented in the general practice might move care away from secondary care to primary care. However, the consultation received in secondary care would have been reimbursed (either completely or partially), whereas the test received with the POC device might not always be. Consequently, the use of the POC test would cost the healthcare provider money while leading to societal benefits and freeing up time and resources in secondary care. This makes it unattractive for healthcare providers to implement the device in general practice since it would not directly benefit the practice and underlines the need to incorporate the context of the healthcare setting in health economic evaluations, in particular, the financial structures and reimbursement policies. This is already done when evaluating screening programs, where a diagnostic device is to be used to screen a large population for a certain disease. Here, the link between health economic modelling and implementation (and organisation of care) is much stronger. A health economic analysis is typically applied to guide the implementation process by looking at implementation aspects around the organisation of care, such as the capacity of the system, follow-up tests, etc. Screening programs are nationwide programs that are only initiated when all care stakeholders are convinced of the benefit and when there is some (minimal) benefit for all stakeholders involved. This nationwide driver, aligning and redistributing benefits, is not present when implementing POC tests.

A systematic review on the causes of the evidence to practice gap, found that "the lack of cost-effectiveness evidence relevant to the setting or poor cost-

effectiveness could impede implementation" [29]. This emphasises what was stated earlier, that the evidence generated in context-specific health economic evaluations would not be enough to encourage adoption. In addition to more generalisable health economic analyses, more focus should also be placed on implementation studies. These studies should focus, among other factors, on whether the implementation of POC testing would require changes to national and local policies, how financial and non-financial incentives can be used to facilitate adoption, and whether the infrastructure in place (for example, connectivity, access to information and training) is sufficient for implementation. Furthermore, tailored evidence is required to support adoption in primary care. This may include, for example, how a POC test is best used in practice. GPs might be limited to a 10-15min consultation which does not allow enough time to administer a test during the consultation, but instead, a healthcare assistant could administer the test prior to the consultation to allow sufficient time with the GP for discussion. The implementation of POC testing is considered to be of high complexity since the scale of implementation can be quite high, with several sites and processes [30]. This further emphasises the need for implementation studies to identify an incremental implementation approach that would allow for a transition period [31].

RECOMMENDATIONS FOR FUTURE RESEARCH

Most health economic evaluations consider only one (or in rare cases, two) measure(s) of effectiveness. Consequently, the evidence generated from these evaluations is not as comprehensive as it could have been. The true potential value of POC testing lies in several aspects, including aspects related to how the patient benefits from POC testing (e.g., increased satisfaction) as well as how the healthcare system and society as a whole benefit from the implementation. Future research efforts should look into methods of evaluating diagnostics in such a way that the full impact of the diagnostic across the entire clinical pathway is measured or quantified. The outcomes associated with POC testing are quite diffused and are not limited to only health outcomes. Future research would require thinking beyond traditional health economic evaluations to include all outcomes (in addition to just health outcomes) and map the flow of patients and outcomes across the entire pathway. This could be done by applying, for example, advanced Markov models, discrete event simulation or system dynamics models

that investigate the cause-and-effect relationships in the healthcare system when POC testing is implemented in primary care.

One of the barriers identified in Chapter 4 was the lack of financial support for the implementation of POC testing. Financial resources can improve the uptake of POC testing if it allows healthcare providers to adopt POC testing within their practice without any additional cost or investment. Future research should investigate the reimbursement systems and financial flows within healthcare systems to gain insight into their strengths and weaknesses. Incentives for healthcare providers to use POC testing would facilitate its adoption. This research should aim to formulate policy recommendations or a business case(s) that would incentivise health care providers to implement POC testing. Further research should also be performed to formulate and support policy changes/recommendations that would allow the necessary changes as recommended in Chapter 4. Additionally, future quantitative analysis should be performed that would indicate the magnitude of opportunity loss caused by a lack of POCT adoption as an incentive for initiating these necessary changes.

GENERAL CONCLUSION / KEY MESSAGES

The successful implementation and utilisation of POC tests is not an easy feat, but it is also not an impossible one. There is certainly no shortage of effective and reliable POC tests, but what is lacking is innovation in the organisation of care, reimbursement policies, and support structures for POC testing, preferably driven by nationwide initiatives balancing all stakeholders' interests. Patients are provided with healthcare services that are often inconvenient and inconsiderate of their needs. POC testing can potentially improve patient convenience but also save much-needed healthcare resources that will benefit the entire health system. Most healthcare providers remain hesitant to the idea of wide-scale implementation, and rightfully so since primary care practices are inherently overloaded with patients and have high workloads. The successful implementation of a new intervention in such a setting will be dependent on whether the healthcare providers adopt the intervention and thereby changing previous workflow and processes. The healthcare system needs to be reorganised with improved support structures to ensure that the workload associated with POC testing is limited and as low as possible. Additionally, changes in the financial structures and reimbursement policies are required.

Health economic evidence is often used to inform such decisions, but the available evidence is mainly considered inadequate due to the limited scope. Developers need to ensure that POC tests are evaluated in such a way that the full impact of the test is measured and that all necessary aspects (relevant to all stakeholders) are reported.

Finally, the implementation of POC tests alone is not enough to guarantee improved patient outcomes. It is necessary to continuously monitor the implementation and performance of POC testing for quality management and to ensure that resources are consistently allocated to the proper tests, settings and cohorts.

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Summary

SUMMARY

The ageing population and growing demand for patient-centred healthcare continues to challenge the efficiency of healthcare systems. Diagnostics are valuable tools in disease management and are becoming increasingly important to improve patient outcomes through informed patient management decisions. A format of diagnostic tests that can potentially increase the efficiency of the healthcare system is point-of-care testing (POCT), which is performed nearby the patient, usually needs only a small volume of blood, and provides test results at the time of the clinical decision making. When properly utilized, accurate POC tests can improve patient outcomes and increase the efficiency of health care by providing test results rapidly, resulting in earlier treatment decisions without having to wait for results from a central laboratory. Although the number of commercially available POC tests continues to increase, only a few POC tests have been widely adopted. Some of the main barriers to adoption have been identified as a lack of reliable health economic evidence, concerns around quality control and quality assurance, costs and reimbursements, and the high workload and complicated processes associated with the implementation.

The wide-scale implementation of POCT would (partly) cause a shift of diagnostic testing from the centralized laboratory to primary care. This will result in a higher workload (and in some countries, higher costs) for healthcare providers in primary care related to the set-up, training and general organization and management. The aim of this thesis was, therefore, to study health economic evidence and organizational factors explaining the slow adoption of POC testing in primary care and to generate insight into factors that improve the potential use and impact of POC testing.

Chapters 2 and 3 provide an overview of the available health and economic evidence of POC testing to investigate whether sufficient evidence supporting the implementation of POC testing is available. The systematic review presented in Chapter 2 shows that most studies evaluating POC tests fail to report on known aspects that GPs find important in the decision to implement a POC test in their practice. In the evaluations of 83 identified POC tests, there was a clear inconsistency between what is reported in the studies and what GPs consider important. For example, GPs perceive clinical utility as the most important aspect when considering whether to make use of a specific POC test; however, only 8%

of evaluations included in this review incorporated this aspect in their analysis or discussion. Results from this review highlighted the importance of including not only the technical performance aspects of a test but also the aspects relating to their clinical utility and risks.

Chapter 3 illustrates that the lack of evidence on POCT is not the primary barrier to its implementation. In this systematic review, more than 75% of the included health economic evaluations of POC tests recommend its implementation. Even though the full and long-term benefits of POCT were not always covered in the health economic evaluations, it was clear that high-quality health economic evidence across a few dimensions of value does exist. This suggests that the low uptake of POCT in clinical practice is due to a combination of barriers and not (only) due to a lack of evidence.

Some additional barriers could be associated with aspects around organization of care, support of clinicians and quality management. In Chapter 4, the healthcare system of the Netherlands, England, Australia and Norway are evaluated to investigate whether the current organization of care is capable of supporting the implementation of POC testing. After comparing these countries' health networks in terms of seven previously published factors that support the successful implementation, sustainability and scale-up of innovations, it was found that the lack of effective communication within the health network as well as the high workload for GPs aiming to implement POCT were among the biggest challenges for countries with low POCT uptake. In Norway, it was observed that when a country assigns a single national authority to govern the task of POCT roll-out and management, the full benefits of POCT are easier to realize. Such a national authority is especially beneficial since the workload and direct costs for GPs (associated with the implementation and management of POCT) can be reduced when they receive the necessary assistance with set-up, quality control, training, and maintenance.

In Chapter 5, the potential impact of implementing an at-home POC blood sampling device is investigated. In this evaluation, it was found that the majority of chronic care patients suffering from diabetes mellitus, cardiovascular diseases, chronic kidney disease, and thyroid diseases prefer to use an at-home blood-sampling device instead of venous phlebotomy at another location to monitor their disease. It was also found that, even though the wide-scale implementation

of such a device would increase phlebotomy costs (by €27.25) per patient per year, it would still reduce the overall societal costs by €24.86 per patient per year, mainly due to limiting productivity loss. This Chapter confirmed that an at-home POC device would not only increase patient satisfaction, but can also be cost-saving as it is expected to reduce societal costs.

It has been shown that, when successfully implemented, innovative technologies in healthcare (such as POCT) can improve patient outcomes, improve patient satisfaction and reduce healthcare costs. Although POCT has been widely implemented in some countries, such as Norway, there are still many countries where the uptake is quite slow. The findings from this research suggest that there is high-quality evidence available to support the implementation of POCT, even though this evidence might not always be relevant to those who are going to use the test (such as GPs) or to the stakeholders and policy-makers responsible for wide-scale implementation. This research also found that the healthcare systems currently in place often fail to provide sufficient support to the healthcare providers who want to make use of POCT. In order to encourage the wide-scale implementation of POCT, improved communication- and leadership structures need to be constructed that are dedicated to the roll-out and management of healthcare innovations such as POCT. With enough support available, healthcare providers will be more inclined to make use of innovative health technologies, thereby positively contributing to the patient's experience, as well as the quality and efficiency of the healthcare system.

Samenvatting

SAMENVATTING

De steeds meer vergrijzende bevolking, alsook de groeiende vraag naar patiëntgerichte gezondheidszorg, blijven de efficiëntie van het zorgstelsel op de proef stellen. Diagnostiek is een waardevol hulpmiddel op vlak van het ziektebeheer en ook wordt diagnostiek steeds belangrijker om patiëntenzorg te verbeteren door middel van het maken van weloverwogen beslissingen betreffende de behandeling van patiënten. Een vorm van diagnostische testen die mogelijk de efficiëntie van het gezondheidssysteem kunnen verhogen zijn de zogenoemde point-of-care testen (POCT). Deze worden in de buurt van de patiënt uitgevoerd, vereisen slechts een kleine hoeveelheid bloed, en leveren de nodige testresultaten op het moment van de klinische besluitvorming. Bij een correct gebruik kunnen deze nauwkeurige POCT de patiëntenzorg verbeteren, alsook de efficiëntie van de gezondheidszorg verhogen, doordat de diagnostiek snel testresultaten oplevert. Dit resulteert er in dat behandelbeslissingen eerder genomen kunnen worden zonder dat men hoeft te wachten op de resultaten van het centraal laboratorium. Hoewel het aantal in de handel verkrijgbare POCT blijft toenemen, zijn er slechts enkele POC-T op grote schaal toepasbaar. De belangrijkste belemmeringen voor de adoptie van POCT betreffen het gebrek aan betrouwbaar gezondheidseconomisch bewijs, heel wat bezorgdheden over de kwaliteitscontrole en –borging, kosten en vergoedingen, en tot slot ook de hoge werkdruk en de gecompliceerde processen die gepaard gaan met de implementatie van POCT.

Een grootschalige implementatie van POCT zou (mede) leiden tot een verschuiving van het huidige diagnostische onderzoek, en dan met name van het centrale laboratorium naar de eerste lijn. Dit zou leiden tot een hogere werkdruk (en in sommige landen ook hogere kosten) voor zorgverleners werkzaam in de eerstelijnszorg. Concreet zou dit invloed hebben op de opzet, de trainingen, en de algemene organisatie en bedrijfsvoering. Het doel van dit proefschrift is daarom het bestuderen van het gezondheidseconomisch bewijs en de organisatorische factoren die de langzame implementatie van de POCT binnen de eerstelijnszorg zouden kunnen verklaren. Zo zouden er inzichten verkregen kunnen worden in factoren die vervolgens het potentiële gebruik en de impact van de POCT kan verbeteren.

Hoofdstuk 2 en 3 geven een overzicht van het reeds beschikbare gezondheids- en economische bewijs van POCT. Hiermee zal onderzocht worden of er voldoende bewijs is dat de implementatie van deze testen mogelijk is. Een systematische review, te lezen in hoofdstuk 2, laat zien dat de meeste studies zich richten op het evalueren van de POCT, maar niet rapporteren over bekende aspecten die huisartsen belangrijk vinden tijdens beslissingen omtrent de implementatie van POCT in de praktijk. In de evaluaties betreffende 83 geïdentificeerde POCT was er een duidelijke inconsistentie tussen wat in de onderzoeken werd gerapporteerd en wat de huisartsen belangrijk vonden. Concreet zien huisartsen de klinische bruikbaarheid als het belangrijkste aspect bij het overwegen van het gebruik van de POCT terwijl slechts 8% van de geëvalueerde studies in de review dit aspect opnamen in de analyse of discussie. De resultaten van deze review benadrukken het belang van het niet enkel opnemen van de technische prestatieaspecten van de test, maar ook de aspecten die betrekking hebben op hun klinische bruikbaarheid en risico's.

Vervolgens illustreert hoofdstuk 3 dat het gebrek aan bewijs over de POCT niet de primaire barrière vormt voor de implementatie ervan. In de systematische review beveelt meer dan 75% van de opgenomen gezondheidseconomische evaluaties van de POCT de implementatie ervan aan. Hoewel de volledige en langetermijnvoordelen van de testen niet altijd aan bod kwamen in de gezondheidseconomische evaluaties, was het duidelijk dat er een kwalitatief hoogstaand gezondheidseconomisch bewijs bestaat voor heel wat waardedimensies. Dit suggereert bijgevolg dat de lage opname van POCT binnen de klinische praktijk te wijten is aan een combinatie van barrières, en dus niet (enkel) aan een gebrek aan bewijs.

Enkele bijkomende barrières kunnen verband houden met aspecten rond de organisatie van zorg, de ondersteuning van clinici, alsook het kwaliteitsmanagement. In hoofdstuk 4 wordt daarom het zorgstelsel van Nederland, Engeland, Australië, en Noorwegen geëvalueerd om te onderzoeken of de huidige zorgorganisatie een dergelijke implementatie van POCT zou kunnen ondersteunen. Na vergelijking van de gezondheidsnetwerken van deze landen, dit met zeven eerder gepubliceerde factoren die een succesvolle implementatie, duurzaamheid, en opschaling van innovaties ondersteunen, bleek dat het gebrek aan effectieve communicatie binnen het gezondheidsnetwerk en de hoge werkdruk voor huisartsen om deze POCT te implementeren, behoorden tot de

grootste uitdagingen, althans bij landen die momenteel een lage POCT-opname hebben. In Noorwegen kon worden opgemerkt dat, indien een land één enkele nationale autoriteit aanwijst om de taak van de uitrol en het beheer van de POCT te regelen, alle voordelen van POCT makkelijker te realiseren zijn. Een dergelijke nationale autoriteit reduceert de werkdruk, alsook de directe kosten voor huisartsen (geassocieerd met de implementatie en het beheer van POCT), doordat huisartsen de nodige hulp krijgen tijdens het opzetten, de kwaliteitscontrole, trainingen, en het onderhoud.

Binnen hoofdstuk 5 wordt vervolgens de potentiële impact onderzocht van het implementeren van een POC-bloedafnameapparaat zodat dit ook voor thuisgebruik mogelijk wordt. Uit deze evaluatie is gebleken dat de meerderheid van de chronische zorgpatiënten die lijden aan diabetes mellitus, hart- en vaatziekten, chronische nieraandoeningen, alsook schildklieraandoeningen, de voorkeur geven aan een thuisbloedafnameapparaat in plaats van een veneuze flebotomie op een andere locatie, met name wegens hun ziekte. Verder werd er ook vastgesteld dat, hoewel de grootschalige implementatie van een dergelijk apparaat de aderlatingskosten (met €27,25) per patiënt, per jaar, zou verhogen. De totale maatschappelijke kosten nog steeds met €24,86 per patiënt, per jaar, zouden afnemen, voornamelijk als gevolg van de beperking van productiviteitsverlies. Dit hoofdstuk heeft uiteindelijk kunnen bevestigen dat een POC-apparaat voor thuisgebrek niet enkel de tevredenheid van patiënten zou kunnen verhogen, maar dit ook kostenbesparend zou zijn. Dit komt voornamelijk doordat het de maatschappelijke kosten kan verlagen.

Er is aangetoond dat, indien succesvol geïmplementeerd, innovatieve technologieën binnen de gezondheidszorg, zoals POCT, de patiëntenzorg kunnen verbeteren, de patiënttevredenheid verhogen, alsook de zorgkosten kunnen verlagen. Hoewel POCT in sommige landen, zoals Noorwegen, reeds op grote schaal zijn geïmplementeerd, zijn er nog steeds veel landen waar deze implementatie vrij traag verloopt. De bevindingen uit dit onderzoek suggereren uiteindelijk dat er hoogwaardig bewijs beschikbaar is om de implementatie van POCT te ondersteunen, al is dit bewijs niet altijd relevant voor degenen die de testen uiteindelijk zullen gebruiken (zoals huisartsen, belanghebbenden, en beleidmakers die verantwoordelijk zijn voor grootschalige implementaties). Verder bleek ook uit dit onderzoek dat de huidige zorgstelsels vaak onvoldoende ondersteuning bieden aan de zorgverleners die gebruik willen maken van POCT.

Om de grootschalige implementatie van POCT te stimuleren, moeten er verbeterde communicatie- en leiderschapsstructuren worden opgebouwd die gericht zijn op de uitrol en het beheer van zorgzinnovaties, zoals POCT. Bij voldoende draagvlak zullen zorgaanbieders eerder geneigd zijn om gebruik te maken van innovatieve gezondheidstechnologieën en daarmee een positieve bijdrage leveren aan de beleving van de patiënt, alsook aan de kwaliteit en efficiëntie van het zorgstelsel.

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Curriculum Vitae
and Publications

CURRICULUM VITAE

Deon Lingervelder was born on the 11th of November in Cape Town, South Africa. Directly after graduating from secondary school in 2010 at Bellville High School, he started as a bachelor student in the Industrial Engineering program at Stellenbosch University. His final year project "*Determining the optimum staffing levels for retail outlets*" was awarded the best optimization project by the Faculty of Industrial Engineering. Directly after graduating in 2013, he started with his master's degree in Industrial Engineering with a specialisation in Supply Chain Management. In 2017 he defended his master thesis Cum Laude, with the topic "An analysis of the upstream supply chain for second-line drugs for multidrug-resistant tuberculosis".

After obtaining his master's degree, Deon moved to the Netherlands where he started as a PhD candidate at the Department of Health Technology and services research at the University of Twente. His PhD project concerned the health economic evidence and organisational factors surrounding the adoption of point-of-care testing in primary care. The results of this project are described in this dissertation.

LIST OF PUBLICATIONS

Lingervelder D., Bam L., Bam W., 2016, A Systematic Comparison of Donor Funded Supply Chain and Commercial Supply Chain Characteristics, Proceedings of the 27th Annual Southern African Institute for Industrial Engineering Conference, South Africa.

Lingervelder D, Koffijberg H, Kusters R, IJzerman MJ. Point-of-care testing in primary care: A systematic review on implementation aspects addressed in test evaluations. Int J Clin Pract. 2019 Oct;73(10):e13392. doi: 10.1111/ijcp.13392. Epub 2019 Aug 19. PMID: 31313873; PMCID: PMC6790572.

Lingervelder, D., Koffijberg, H., Kusters, R. et al. Health Economic Evidence of Point-of-Care Testing: A Systematic Review. PharmacoEconomics Open 5, 157–173 (2021). https://doi.org/10.1007/s41669-020-00248-1.

Lingervelder D, Koffijberg H, Emery JD, et al. How to realize the benefits of point-of-care testing at the general practice: a comparison of four high-income countries. International Journal of Health Policy and Management, 2021 doi:10.34172/ijhpm.2021.143