Practical modalities necessary for a successful implementation of CRP point-of-care tests in Belgian general practices: a systematic literature review

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Introduction

Raising antibiotic resistance remains an urgent global health threat according to the World Health Organization. The World Health Organization has declared it one of the top 10 current global health threats(1). Methods for safely reducing unnecessary antibiotic prescribing are thus urgently needed especially in primary care, since 90% of antibiotics are prescribed by general practitioners (GPs) and 70% of these are for respiratory tract infections (RTIs) (2-4). The vast majority of RTIs are self-limiting and are caused by a virus. It is difficult to make the distinction between self-limiting acute bronchitis and pneumonia only based on clinical symptoms and signs (5). This leads to unnecessary antibiotic prescriptions that have no benefit for the patient and may even cause harm due to side effects and increased microbial antibiotic resistance (4). A UK study found that between 8.8% and 23% of antibiotic prescriptions from primary care are unnecessary, with a majority being prescribed for RTIs (6).

One of the methods for reducing antibiotic prescribing for RTIs is the measurement of the patient's **C-reactive protein** (CRP) level. CRP is an inflammatory marker that raises rapidly in severe bacterial infections and raises more slightly in uncomplicated infections (7, 8). Determining CRP levels is recommended in national guidelines in some European countries when a clinician is unsure whether to prescribe an antibiotic after his clinical examination (9-11). CRP can be measured in a standard blood analysis or with a **point-of-care test (POCT)** (9-11). A POCT is a rapid test that requires one drop of blood from a finger prick sample and that allows the quick availability of results in a matter of minutes (12). This bypasses the need of sending recipients to a central laboratory and only getting results hours or a day later. POCTs make it possible to have a discussion with the patient about the test result during the initial consultation, eliminating the need for a later discussion over telephone or a follow-up consultation (12).

CRP POC testing has been associated with a **reduction in antibiotic prescribing** for acute RTIs, as also confirmed by a recent Cochrane review (7, 13-15). Since the development of CRP POC testing machines in Norway and Finland in 1993, they have been widely used in primary care in the Scandinavian countries with almost every GP practice owning a CRP analyser (15-18). These countries also have some of the lowest rates of antibiotic prescribing (8, 15). Across other European countries, there is a high **variation in the availability** of CRP POCTs. They are highly accessible in the Netherlands, Scandinavian countries, and Switzerland. In the Netherlands, the use of CRP POCTs by GPs has been recommended in clinical guidelines since 2011, which has since led the Dutch Healthcare Authority to reimburse CRP POCTs. In England the NICE guideline on pneumonia in adults has since 2014 recommended using CRP POCTs but it did not gain reimbursement and the uptake by GPs was very low. In Belgium, CRP POCTs are currently used within hospitals, mostly in emergency and intensive care departments. But the tests are scarcely used in primary care, since there is still no reimbursement nor legal framework outside the hospital (19).

Despite the high availability of research about the effects of CRP POCTs (on antibiotic prescribing rates, on quality of patient care), and despite their high uptake in some European countries, there is limited research into practical aspects of its implementation. Therefore, we currently will perform a systematic scoping review of the practical aspects concerning the implementation of CRP POCTs in high- and middle-income countries. We will focus on flow of goods, quality control measures to be taken, registration of results, involvement of clinical laboratories, effects on patient flow, organization of the user training, different funding mechanisms and the effect thereof on uptake of the tests, mapping of different stakeholders and best methods of approaching and involving them in the implementation

process. We will conclude with a recommendation of implementation strategies for the Belgian context.

Materials and methods

Data sources and searches

For this systematic review the following databases were searched: Medline via Pubmed, Embase, Scopus, Web of Science, the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Services Economic Evaluation Database (NHS EED), the NHS Health Technology Assessment Database (NHS HTA). With help from the biomedical library of the University of Leuven (KU Leuven), a search strategy for each database was prepared by using Medical Subject Headings (MeSH terms), keywords and equivalent terms.

The search was based on the combination of following concepts:

1. CRP
2. Point-of-care test
3. Organisational aspects:
    - Logistics: chain of delivery, storage, waste management, effects on patient flow
    - Price, funding mechanism (device, cartridges), reimbursement methods
    - Effect of funding mechanisms on uptake of the tests
    - Quality control procedures (how, by whom, frequency)
    - User training (what, how, by and to whom, frequency)
    - Registration of results
    - Involvement of clinical laboratories
    - Implementation, uptake
    - Stakeholder mapping, and best methods of involving them in the implementation process

We searched the literature for articles from 01/01/1990 to 23/02/2023. The search strategy itself can be found in *Supplementary materials 1*.

Selection of studies

Once all searches were completed, the resulting articles were uploaded into Endnote® and duplicates were removed. Then, using the Rayyan® screening tool, two researchers independently screened the title and abstract of all articles for relevance. Conflicts were resolved through discussion during several meetings. When uncertain as to whether an organisational aspect had been addressed within the article, the article was included for evaluation during the full-text screening process. The reasons for exclusion were noted.

Inclusion criteria

Included studies had to involve the aspects outlined above in 'data sources and searches'. Each included study had to involve CRP POCT, and at least one of the described managerial aspects. The studies also had to involve primary care settings.

Exclusion criteria

Criteria for exclusion were: animal studies, low income countries, no English, Dutch or French text available, studies concerning the use in hospitals (since the focus of the present study is in primary care) and studies concerning the use in children.

Data extraction and analysis

After the title/abstract screening, full text screening and data extraction were performed in Microsoft Excel®. Each article was analysed by two researchers independently. During this step the reasons for exclusion were captured.

Aspects evaluated in the data extraction table included:

- Aspects of the individual papers (author, date, institution, country, journal, funding, conflicts of interest)
- Logistics (delivery, storage, disposal, which analyser is used, placement of the analyser, performer of the test, other logistical aspects)
- Patient flow (time needed to perform the test, effects of using POCT in general practice on patient flow in the practice)
- Economic aspects (price of the analyser and consumables, funding mechanisms of analyser and consumables, reimbursement, influence of reimbursement on uptake of the tests)
- Quality control (who performs quality control, how is it conducted, at what frequency is it conducted, validation of results through laboratory services)
- Registration of results
- User training (what entails user training, who administers the training, who should receive training, at what frequency is training conducted, other training aspects)
- Implementation (factors that are involved in the implementation process, uptake of the tests)
- Stakeholder mapping (who are the different stakeholders, how to involve different stakeholders)

Additional articles were acquired through snowballing methods and by searching for relevant articles in grey literature.

The results will be presented as a narrative synthesis.

Results

The initial search resulted in 6430 articles (see PRISMA diagram, *Figure 1*). 2386 duplicates were removed through Endnote®, resulting in 4044 articles. After performing the title/abstract screening, 93 articles were retained, from which 49 remained after full text screening. Through snowballing and searching in grey literature, 28 more articles were added, bringing the total number of included articles to 77.

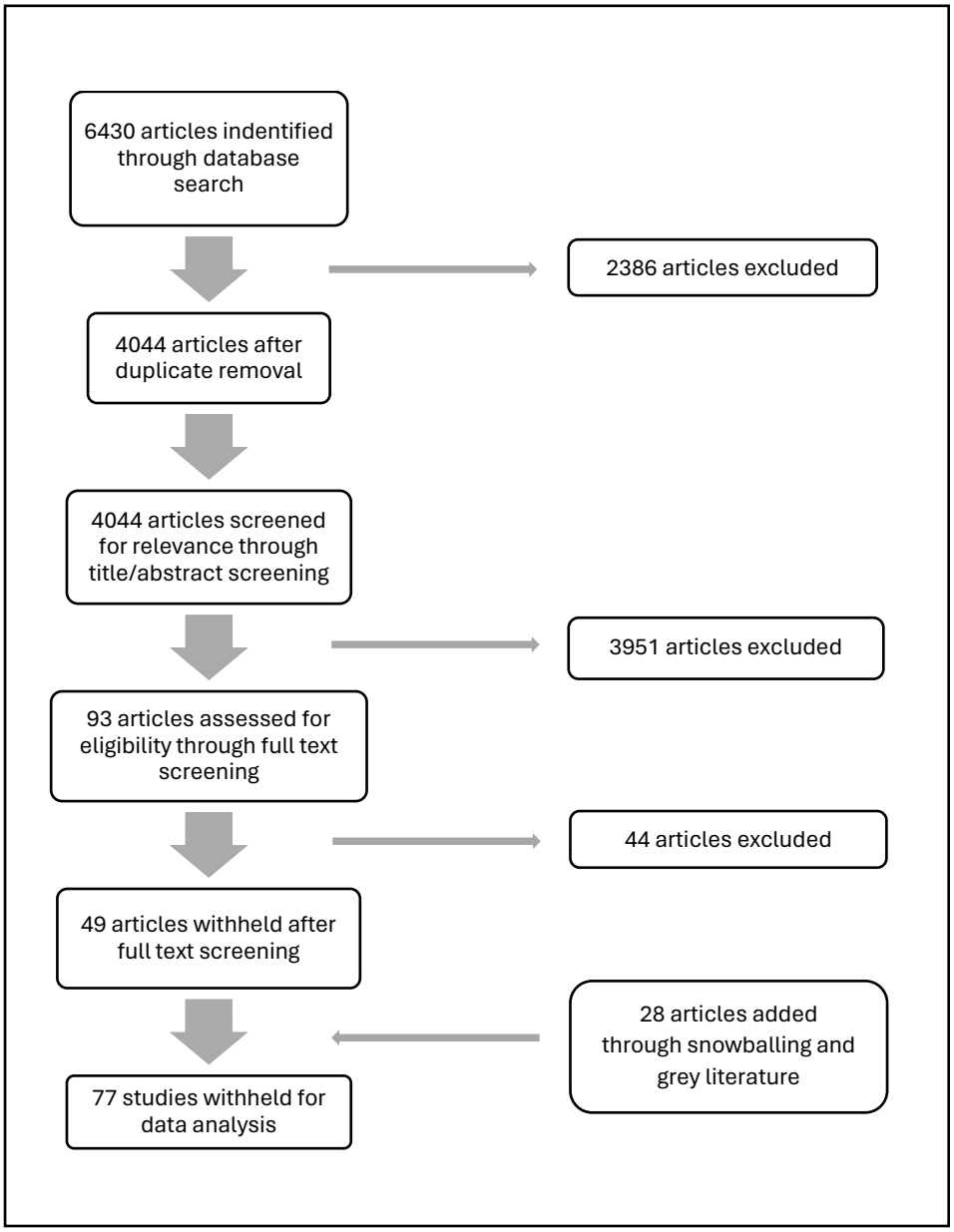


Figure 1: PRISMA diagram of included studies

1. Logistics

1.1 Different CRP POC devices

Most frequently used quantitative CRP POCT devices are the QuickRead go by Aidian diagnostics, the Afinion AS100 or 2 by Alere and the NycoCard reader by Abott Diagnostics (5, 11, 13, 20-26). Devices lesser used, are the i-CHROMA (Boditech Med Inc., South Korea) and the Cobas b101 (Roche) (11, 27, 28).

Semi-quantitative CRP POC devices are also available. In contrast to the quantitative devices which require an analyser, semi-quantitative devices use a test strip, dipstick or single-use disposable device, as for example the SureScreen lateral flow assay (11, 29). GPs have expressed interest in using these during home visits (30).

During the current literature review it was notable that the by far most commonly used devices were the Afinion AS100/2 and the QuickRead go. In Norway, where the tests are widely used, the Afinion AS100 and the QuickRead go are recommended by the Norwegian Quality Improvement of Primary Care Laboratories (26). This Norwegian institution decided in a commutability study that Afinion AS100 and QuickRead go showed the lowest systemic deviations from control measurements (26). Also in the Netherlands, recommended devices are the Afinion AS100 and QuickRead go (21, 22). Although studies on analytical performance at the point of care are rare, the smallest bias in accuracy (<5%) was found for the Afinion device compared to the others (11). All tests scored adequate for analytical performance. It was also concluded that the Afinion device was the least susceptible to flaws in preanalytical and analytical handling, QuickRead scored moderately, and NycoCard scored poorly. Concerning ease of use, all devices prompted some concerns. The QuickRead go has complex preanalytical steps, and there are reports of issues with putting the cap on the cuvette. The same applies to QuickRead 101. The Afinion CRP testing machine gives error codes relatively often because the sample dried out (due to the smaller sample size), and is not portable when turned on (11).

The available CRP POCT devices have a variable weight, ranging from 1 to 35 kg. The Afinion AS100 Analyser weighs 5 kg (measurements are 17 x 19 x 34 cm), the Afinion 2 analyser weighs 3.4 kg (20 x 19 x 33 cm), the QuickRead go device weighs 1.7 kg (14.5 x 15.5 x 27 cm), the QuickRead 101 weighs 1 kg (8 x 14 x 22 cm), the NycoCard Reader II weighs 0.54 kg (20 x 17 x 7 cm) and the i-CHROMA weighs 1.3 kg (18.3 x 8 x 25 cm) (11).

1.2 Testing procedures

QuickRead go (Aidian diagnostics, Finland)

The pre-analytical handling comprises of collecting a blood sample in the capillary sample collector, placing the collector in the pre-filled cuvette that has reached room temperature and within two minutes of opening the cuvette, then closing the cuvette which makes the reagent mix in. Then the cuvette can be inserted into the instrument (11, 31).



Figure 2: The QuickRead go's pre-analytical process (31).

QuickRead 101 (Aidian diagnostics, Finland)

Same pre-analytical process as the QuickRead go (11, 32).

Afinion AS100/2 (Alere, US - acquired by Abbott in 2017)

This device requires short pre-analytical handling and no manual mixing of reagents. The few pre-analytical steps to be taken are: getting a blood sample with the plunger and then placing the plunger into the test cartridge within one minute, because the small sample volume makes it susceptible to drying out. Then the cartridge can be placed in the instrument (11).



Figure 3: The Afinion AS100's pre-analytical process (33)

NycoCard reader (Abott diagnostics, US)

The preanalytical handling comprises of firstly manually adjust and white calibrate the reader pen, then taking a capillary sample and adding this to the test tube, then manually mixing them and let it sit for minimum two and maximum three minutes (timer required). The next step is a short remixing and applying this sample to the test device. Then a short wait time of ten seconds before applying a washing solution to the test device. Within five minutes the result can be read by the NycoCard Reader (11, 34).



Figure 4: the NycoCard reader's analytical process (34)

i-CHROMA (Boditech Med Inc., South Korea)

For the use of the i-CHROMA device, users need to first open the buffer tube, take a blood sample and add this to the buffer tube, then mix these well by shaking at least ten times. After, they should add two drops to the test cartridge after discarding the first two drops of the buffer tube. Lastly, the test cartridge can be inserted into the machine for analysis (35).

It should be noted though that in the product information sheet, the manufacturer does not mention an incubation period to allow adequate binding of the antibodies to the antigens, which however is done for ten minutes in the original validity study (27).

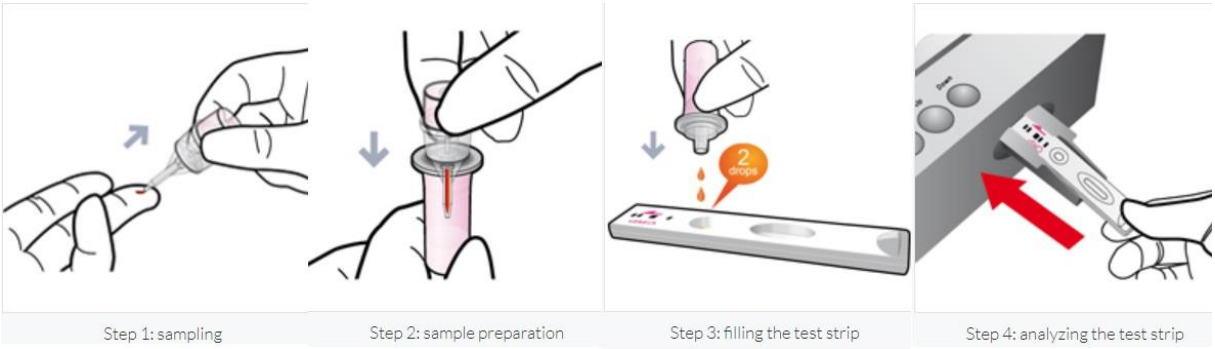


Figure 5: i-CHROMA's pre-analytical process (35)

1.3 Storage conditions

Most CRP testing kits have specific storage conditions, mainly keeping them refrigerated at 2-8°C and bringing them to room temperature prior to use (11, 15).

- QuickRead go:
    - The different parts of the QuickRead go testing kit require different storage conditions.
    - CRP reagent caps: storage at 2-8 °C makes the caps hold until expiry date. It is possible to keep them out of the refrigerator for certain hours per day, however this will make them expire sooner (24 hours per day at 15-25°C: 1 month, 7,5 hours per day at 15-25°C: 3 months).

    - Prefilled cuvettes: In unopened foil pouches they can be stored at 2-25°C until the expiry date. Once the foil pouch is opened, their shelf life reduces to 6 months at 2-8°C or to 3 months at 18-25°C.
    - It will take 15 minutes for a refrigerated cuvette to reach room temperature (11).
- Alere Afinion:
    - The test cartridge must be kept refrigerated and brought to room temperature (15-30°C) before use by leaving the cartridge in an unopened foil package on room temperature for at least 15 minutes (11).
    - Once the cartridges have reached room temperature, the shelf life is reduced to 4 weeks (33).
- NycoCard:
    - The test tubes with dilution liquids must be stored in the refrigerator and be brought to room temperature before use (11, 36). The manual however notes that the dilution liquid can also be stored at room temperature (34).
    - The test device, the conjugate solution and the washing solution can be stored refrigerated until their expiration dates or they can be stored at room temperature for 6 weeks. The recommendation is to refrigerate them at the end of each working day (34).
- i-CHROMA:
    - The test tubes with detection buffer have to be stored in the refrigerator (2-8°C) and be brought to room temperature before use by keeping it out of the refrigerator for 30 minutes.
    - The cartridges can be stored at 4-30°C (11).

The most common irregularities included incorrect storage conditions, such as being kept out of the fridge for too long, exposure to sunlight, and other similar factors (22).

The Alere Afinion test kits are individually packaged and the QuickRead go kits are packaged per 25. Bigger packages could pose a problem in practices where the CRP machines are infrequently used, by making it more difficult to monitor the expiry period when the reagents are alternately placed in and out of the refrigerator (21). This finite shelf life caused Peirce et al. in a UK study to consider not to distribute CRP tests to practices with an infrequent usage, as distributing to such practice would reduce cost-effectiveness of implementation (20).

1.4 Device maintenance

The QuickRead analysers are designed to be free of maintenance and have automatic self-check methods. Similarly, te Afinion analysers do not require user calibration. It does need a once-monthly cleaning of the cartridge chamber with a swab. The i-CHROMA analyser requires regular cleaning of the pen tip, and regular checking of the pen tip and white calibration device for dirt or damaged. If either is present, they should be replaced (11).

1.5 Disposal

The implementation of CRP POCT will result in increased clinical waste. All test materials should be disposed of following the usual regulations. A key point is the necessity of sufficiently sized waste receptacles for potentially biohazardous waste. Usually, the waste disposal costs are the responsibility of the GP practice (11).

1.6 Delivery

In the Netherlands, where CRP POC tests are widely used, delivery of the device is managed by the laboratories. They achieve better pricing than individual practices by centralizing the purchases (21, 22, 37). It has been proposed by Van Hoof et al. that in Belgium, in case of global introduction of CRP POCT to primary care facilities, it would preferably be the laboratory that would be responsible for ordering, distributing and storing of reagents, since it is already familiar with these aspects in hospital context (19).

In individual studies, the devices and consumables are primarily delivered by the manufacturer of the device (38-41).

1.7 Other practicalities

As mentioned above, the most common irregularities observed during studies about using CRP POCTs in general practice comprised of wrong storage conditions. This underlines the importance of having a mechanism in place to keep track of the shelf-life of the test cartridges (42, 43). It has been recommended that one POC coordinator per practice keeps track of the shelf-life of consumables (43).

Other concerns that arised from frequent usage in the Netherlands were an underreporting to the laboratories of error messages, the wrong interpretation of error messages (interpreting the error message as a numeric CRP result), wrongfully linking the test result of one patient to another patient and (oral) communication errors to the GP when the test was performed by a practice assistant (22).

On all times it must be clear which samples (by lot number) are in use in any clinical practice, so the laboratories have this information in case of systemic deviations (11). The identification of sample lot numbers might require a barcode scanner to transfer this information to the laboratory information system (11).

2. Patient flow

2.1 Device placement

There is a high variation of where practices place their analyser. Observed placements are in the GP's consultation office, in a separate room so all GPs could access the device, in the nurse's room, in the pharmacist's room, a separate room in long term care facilities or portable on a trolley (44). It should be noted however that the Afinion analyser is not portable when turned on (11).

One study showed that it has negative effects on uptake of CRP POC testing when the device is placed further from a GP's office, or when the GP has to cross the waiting area to reach the testing machine (45). Placement in one GP office when there are multiple GPs working on-site limits access to the machine (45). A study concerning implementation of CRP POC testing in nursing homes also described difficulties when the analyser is placed far away, since on multiple occasions the sample dried out before reaching the analyser (46).

One UK study considered whether it would be cost-saving to base locations of CRP POC testing on a mathematical model which provides a CRP POCT machine within 500 meters travel distance of any GP practice (47). This option seemed to greatly reduce the number of POCT machines required and thus a significantly lower healthcare cost, with little travel impact for patients and also alleviating the time pressure on GPs performing the tests. In this scenario the POC machines would be accessible at certain GP offices and pharmacies. The largest savings according to this model were acquired when a maximum travel distance of 2000 meters was allowed to get access to testing. It was also considered to only provide testing at community pharmacies, but this method was deemed to greatly limit the access of some patients to testing, especially in rural areas (47).

2.2 Time needed to perform the test

The time needed to perform a CRP POCT differs per device ranges from 3 minutes to more than 13 minutes (11). The reported average time that is needed for handling of CRP POCT in individual studies is 4 minutes (3-5 minutes) (5, 22, 40, 42, 44, 45, 48). This includes the pre-analytical (taking and preparation of the sample) and analytical (the analysis by the machine itself) handling.

Preanalytical and analytical handling times per device are respectively:

- QuickRead go: 4.5 minutes (2.5 min + 2 min)
- QuickRead 101: 5.5 minutes (2.5 min + 3 min)
- Afinion AS100: 4.25 minutes (0.5 min + 3.75 min)
- Alere 2: 3.30 minutes (0.5 min + 3 min)
- NycoCard: 8.35 minutes (3.35 min + 5 min)

The warm-up time of the analysers also differs: QuickRead go takes 50 seconds, QuickRead 101 takes 30 seconds, Afinion AS100 takes 3 minutes, Alere 2 takes 1.5 minutes, NycoCard takes 25 seconds (11).

2.3 Test administrator

The CRP POC tests are mostly administered by practice assistants or nurses, or by the GPs themselves (11, 16, 22, 42, 44-46, 49-52). The literature provides no information about the differences between countries, since the choice of executor depends mostly on preference of the practitioners (44, 50). Although the general working pathway in the Netherlands is that the tests are administered by practice assistants at the request of the GP, some GPs still prefer to administer the tests themselves (22, 45).

In the UK the tests are sometimes also administered by pharmacists, since some UK practices have a pharmacist employed on-site (44, 50). Further, implementation studies have been conducted where the tests are administered in community pharmacist offices, during a consultation for a respiratory tract infection with the pharmacist (41, 53, 54). The working protocol in this case is as follows: Pharmacists first decide whether to refer the patient to their GP immediately (due to red flags, signs of serious illness or complications) and then determine whether a CRP test is necessary. If not, the pharmacist gives advice on self-care. If a test is performed, the pharmacist interprets the result based on set protocols (<20 mg/L means self-care, 20-100 mg/L watch and wait approach with advice on self-care, >100 mg/L referral to GP) (41, 53). The time necessary for a pharmacist consultation for RTI was 15 minutes (41, 54).

2.4 Effects on patient flow

In individual studies, the use of POC testing reduced the need for follow-up telephone consultations, which are still necessary after taking a venous blood sample for CRP that was then sent to the laboratory (38). The usage in GP practices does however require changes to working processes within the practice. An extensive health technology assessment report from Ireland describes possible treatment pathways in the GP practice, which are illustrated in *Figure 6* below (11). Instances where the GPs administer the test themselves have the greatest impact on workload (42).

In the Netherlands, the general working pathway is tests being administered by practice assistants at the request of the GP after the consultation, The assistant then communicates the result to the GP, who continues the consultation. While the test is being administered, the GP sees another patient (22). This working pathway is also described in other studies (42, 44, 51, 55). Another option is that the GP only sees the patient again if the test results are out of the normal range (48).

Some studies proposed a positive correlation between the use of CRP POCTs and reconsultation rates within 30 days (56, 57), but this correlation was not statistically significant in any of the studies nor in a pooled meta-analysis(11). One study showed a reduction of consultations for respiratory tract infections in the 3.5 years following the introduction of CRP POC testing (14). The use of CRP POC testing in GP practices does not seem to significantly influence the number of hospital referrals (11, 56).

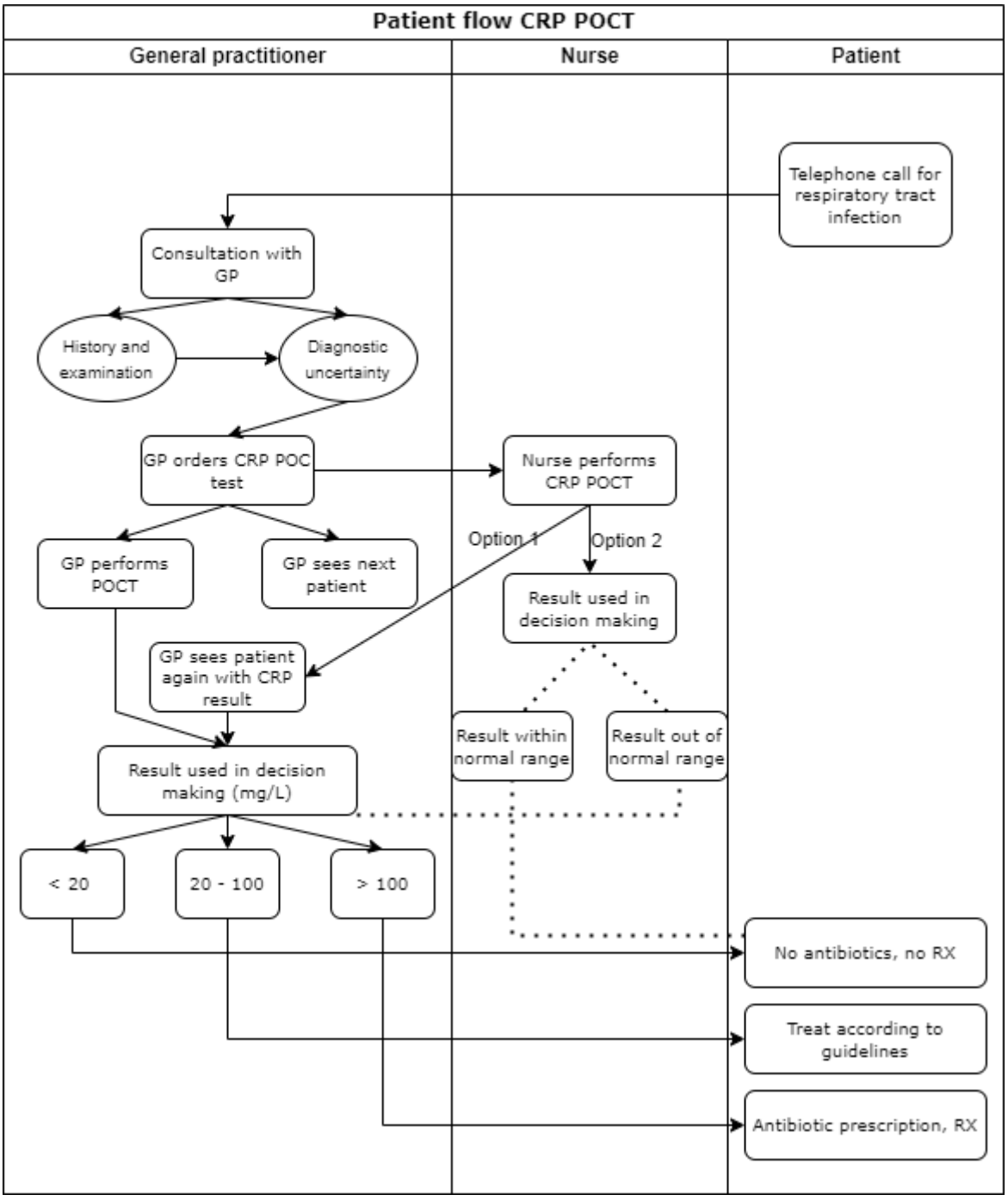


Figure 6: Sample patient flow for CRP POCT, adapted from (11)

3. User training

3.1 Required user training

Implementation studies describe the need for basic training of healthcare providers in using a CRP POCT. This training should include sample handling according to health and safety regulations, storage of materials, operation of the device, understanding and handling of error messages, calibration requirements, quality control measures, appropriate record keeping and the training of new recruits (11, 22, 26, 41, 43, 46, 58, 59).

In the Netherlands, user training is compulsory for acquiring and retaining accreditation for the use of CRP POCT (21, 22, 59). The training course, based on national practice guidelines, can be accessed by any GP on www.acutehoest.be. This course discusses indications for testing, principles of rational diagnostics, interpretation of the test results, the practical methods of using the test in daily practice and adequate communicative skills (22, 59). The certificate also requires training in safely recording incidents and conducting risk analysis (59). Practice assistants also require training for acquiring the certification. Their training comprises practical usage and maintenance of the analyser, method of drawing blood by finger prick, registration of the test results and quality control methods (22).

User training requirements for participation in individual clinical studies usually consisted of an introductory session covering test and device handling and internal quality control (36, 38). Additionally, most studies included a medical training session in which users were informed about indications for testing, current guidelines and cut-off values (4, 11, 25, 30, 39-41, 46, 49, 53, 54, 56, 58, 60, 61). Some studies also provided training on how to discuss the test result with patients (13, 49). Researchers occasionally offered follow-up training modules, sometimes monthly (24, 26). In some cases, parts of the training courses were delivered as online modules (13, 25, 49, 58, 62, 63). Digital education was deemed more effective and possibly more cost-effective than in-person training (58).

3.2 User training executer

In the Netherlands, training is given by members of the supporting laboratories (15, 37, 62). Initial training concerning use of the machine is often offered by manufacturers, but the support from laboratories is important concerning quality control, quality insurance, extra training and support when technical issues arise (11, 19). In Norway, the Norwegian Quality Improvement of Primary Care Laboratories (Noklus) covers the training by giving courses, making site visits, and offering telephone consultations. Noklus also actively contacts users who show poor analytical performance and offers those users support (26).

4 Quality control

4.1 Quality control procedures

Internal Quality Control

Internal quality control (IQC) comprises the testing of a control material with a specified concentration of analyte and comparing the user's test result to the specified acceptable concentration ranges (64). Samples for IQC can be purchased from the manufacturers of the devices (64).

There is no international consensus on the necessary frequency of IQC checks (64). However, performing IQC at least weakly is associated with optimal test performance (11, 24, 26). The UK's Medicine and Health products Regulatory Agency has concluded in their NHS Health Check Programme that IQC should be done daily when the machine is in use (64).

External Quality Control

External quality control (EQC) comprises the testing of a sample and comparing the user's test result to the result that was measured by the local laboratory on the same sample. Thus, the EQC samples must be obtained from an external party (64).

In Norway, Noklus performs external quality control (EQA) bi-annually by providing GP practices and nursing homes with 2 samples of in-house produced stabilized blood containing different analyte concentrations with ranges between 8-92 mg/L (26, 65). They actively contact users exhibiting poor analytical performance and offered them support and extra training. Their method showed to improve over-all performance in participants of the Noklus quality improvement system (26).

In the Netherlands a study found that monthly EQC with 2 samples (with a low (<20 mg/l) and high (>60 mg/l) analyte concentration provided extra information regarding systemic variations. They also recommended adding a EQC sample with an analyte concentration of >100 mg/l (24).

4.2 Quality control executer

In Norway, Denmark, Sweden, and Wales there are separate organisations providing external quality assurance. These are SKUP and Weqas. SKUP is a Scandinavian co-operation between Noklus in Norway, Equalis in Sweden and DEKS in Denmark, which are funded by the government (11).

Most laboratories in the Netherlands have a POC team. When the full POC system in a GP practice is supported by an accredited laboratory, the quality assurance falls under the accreditation of the laboratory. However, when a GP practice uses its own machine and performs its own quality control checks, they must adhere to the Healthcare Institutions Quality Act and can get accreditation by NHG practice accreditation. The Healthcare Institutions Quality Act for now does not lead to regular inspections but can on occurrence of an incident lead to a public health inspection (66).

It is strongly recommended to have a cooperation between the GP practice and the supporting laboratory involving systematic quality control procedures (11, 19, 43, 64). Laboratories have expertise in the processing and handling of quality control results and in the handling in cases of systemic

deviations (11, 19, 64). Laboratories can also provide assistance and give advice on which POCT machine to buy (64). In the Netherlands, quality control is mostly managed by laboratories (24, 43, 62, 66). In Norway quality control is managed by Noklus, and in the UK laboratory management of quality control is also recommended by the Medecines And Healthcare Products Regulatory Agencies (26, 37, 42, 65).

Guidelines on POC testing in some countries recommend that POCT services should be ISO (International Standards Organisation) accredited, which leads to GPs having CRP results that they can trust (11). ISO has developed an international standard for POC testing in ambulatory care in 2022 (67).

A European systematic review highlighted the need for a POCT coordinator on every site where POC testing is available (43). This coordinator should bear the task of educating all users on the proper operation of the device and on handling and adequate storage of consumables. The coordinator should also overview the internal quality control processes and make sure that the maintenance and necessary documentation (e.g. on materials' shelf life and quality control dates) are in order (43).

5. Registration of results

Manual registration of results is not recommended, since this can lead to various mistakes such as mixing up of patient samples, communication errors between the POCT operator and the GP. Having a connection between the POCT result and laboratory information system (LIS) is preferred, because it eliminates the above mistakes and since then the test information is available to other health professionals for use in their evaluation of the patient, avoiding unnecessary double testing (11, 51, 66). The connection between the POCT machine and the laboratory also gives way to the option of the laboratory quickly noticing problems or suspicious results to trouble-shoot (66).

Most current CRP POCT machines have the option for connectivity to the laboratory information system (LIS) (11, 19). The QuickRead machines have this option built-in and can send patient identification, operator identification, date, time, and the test result (and if applicable error messages) to the LIS. They can also send this data to electronic patient files (11, 68). The Afinion analysers can send the data to electronic patient files but need the Alere Afinion Data Connectivity Converter for sending data to the LIS. This converter is included when buying the machine. The NycoCard analyser however has no option for data transfer to electronic patient files. The i-CHROMA has the option of sending data to the LIS indirectly over an online connection (11). An additional barcode scanner for the Afinion and QuickRead systems can be bought separately, which allows for the identification of samples to be less time-consuming.

A Dutch study from 2014 describes the automatic transfer between the testing machine and the patient files or LIS at that time was not possible due to limitations in both the testing machine and the LIS (62). In the meantime, they had provided a structure for integrating the results into the LIS by having practice assistants sending the test results to the laboratory over the 'Zorgdomein®' internet application and the laboratory then integrating the result into the LIS (and subsequently having the opportunity to declare reimbursement to the health insurer) (62). As of now, ten years later, the bidirectional coupling of testing machines and LIS has been secured for most machines, rendering the described mechanism futile.

6. Economical aspects

Associated costs with a CRP POC test program include cost of the device itself, cost of materials and reagents, cost of training programmes for staff, cost of quality assurance and, if applicable, funding of the time needed for performing the test (43, 51, 69).

6.1 Cost of the device and cartridges

Costs of the POCT device ranges from €1100 to €3500 (62).

An article from the Netherlands notes that the QuickRead go device and cartridges are considerably less expensive than the Afinion AS100 (21). The total costs per year are estimated at €1462 and €2625 respectively for the QuickRead go and Afinion AS100 device. This equates to a total cost per test result of respectively €7,32 and €13,13 (21).

In the UK, the National Institute for Health and Care Excellence (NICE) in 2018 advised the cost of Alere Afinion AS100 to be £1200, and the cost of Alere test cartridges to be £3.50 per test (excluding VAT) (44).

A budget impact analysis of implementation of the CRP POCT machine was estimated in Wales, encapsulating the price of the machine, consumables, internal and external quality control, maintenance costs, connectivity, and laboratory team assistance. The prices were based on 2016-2017 data and the estimated lifetime of the analyser was 5 years. The price of the analyser itself (Afinion AS100) was £1500, with added costs of £125 for a barcode scanner, £250 for a results printer and £120 for a connecting service to the electronic health records of the GP practice. This comes to a total set-up cost of £1995 (70).

There are different options for purchase of the device (11):

- direct purchase by GP practices
- purchase by regional community health organisations
- block purchase by national health organisations
- purchase of devices by central or supporting hospital laboratories and then loaned or leased to GP offices
- loaned or leased by the manufacturer

6.2 Cost of user training and quality control

The costs of user training and quality control in different implementation studies vary.

A Wales study estimated the annual cost of user training, support, and quality control at £976.92 per year. This included internal quality control at £136, external quality assurance at £240, laboratory support (training, interpretation, quality and troubleshooting support) at £468.92 and maintenance costs at £280 (only to be paid after 3 years since the 3-year warranty of the Afinion AS100 covers this for 3 years) (11).

A UK study estimated the annual cost of quality assurance at £800. They however note that the QC costs vary in relation to the implementation requirements used (47).

An Australian study used a rental agreement with the GP practices involved in the study in which they rented a QuickRead go machine at $1250 per 6 months, which included warranty, training, test kits and control vials, but without ownership of the machine at the end of the study period. They estimated the cost of background and operational training of GPs to be $57 per six months, and the training of practice assistants to be $158.6 per six months (25).

6.3 Funding and reimbursement mechanisms

Belgium

In Belgium, there is currently no reimbursement provided for the use of CRP POCTs as there is no legal framework in place for POC testing in primary care (11, 19).

The Netherlands

In the Netherlands, CRP tests are partially reimbursed by the central government by a fee-for-service scheme at about €3.90-€7 per test depending on the health insurer (2, 30, 48, 62).

The Netherlands have a unique mechanism in which the central laboratory purchases the machine, which gives them a better price point than individual purchases by GP practices (2, 62). There is however no funding by the government for purchase of the machine itself (48, 66). This was solved by providing the reimbursement fee directly to the supporting laboratory instead of to the GP practice (37).

Norway

In Norway, CRP POCTs are financed by a fee-for-service system, in which the GP gets an additional fee of NOK 92 (approximately €12) per consultation in which a CRP test is used (17). Another study reported a reimbursement fee of NOK 42 per test (11). The device is paid for by the GPs themselves (2).

Denmark

GPs in Denmark receive reimbursement from the national health service for carrying out CRP POCT(71). The reimbursement rate in Denmark in 2022 was €10 per test (16).

Switzerland

In Switzerland, CRP tests do receive reimbursement at €10.33 per test (CHF 10) (2, 11).

Sweden

Although the tests are reported to be widely used in Sweden and they are included in national clinical guidelines, no information about reimbursement was found in the literature (55).

Ireland

There are no reimbursement schemes in place for CRP POCTs in Ireland (11, 51).

UK

Currently there are no reimbursement mechanisms in place in the UK for CRP POCTs. This leads to a mechanism where these tests are paid for in full by GP practices, since UK healthcare is funded through central taxation and no direct costs are to be paid by patients (2, 20, 48, 63). Patients do not pay for laboratory tests since these are paid for by the NHS (National Health Services) through Local Clinical Commissioning Groups (CGGs) (11).

A 2018 UK study examined the possible funding and policy incentives to encourage uptake of CRP POC testing (63). The proposition was to introduce an 'item of service' payment to GPs for using the test for LRTIs. This could be achieved by adding CRP POCT to one of the Locally Enhanced Services which are reimbursed by local Central Commissioning Groups (30, 63, 72). The Commissioning Groups can in turn achieve extra national funding if they reach the National Health Service's 'Quality Premium' target for reduced antibiotic prescribing in primary care. However, this implementation study regained little traction with the financially constrained Commissioning Groups and after the initial study period, only one has implemented the Locally Enhanced Services scheme and later removed this due to declining utilisation in response to operational barriers (63).

Australia

In Australia, CRP POCTs in general practice do not receive reimbursement (37).

Germany

Germany has a limited list of POCTs that are reimbursed, and only at a low reimbursement rate (2). The reimbursement rate in Germany is €1.15/test in a general laboratory and €4.90 in a special laboratory (11).

France

France has no reimbursement in place for CRP POCT in primary care (73).

Italy

It has been reported in one HTA that CRP POC tests are reimbursed in Italy at about €3.87 per test (11). On the other hand, an Italian study from 2023 reported that there was no reimbursement for CRP POC testing (2).

Spain

In Spain the same HTA reported reimbursement of CRP POC testing (11), although another study notes that Spain has no current reimbursement mechanisms in place (2). The use of CRP POCT is however recommended in their national guidelines (2, 11).

Hungary

In Hungary there seems to be no reimbursement for CRP POCT, although it is reported in the Irish HTA (11, 43).

6.4 Effects of the funding mechanisms on uptake of CRP POC testing

Uptake

Usage of CRP POCT in primary care varies a lot between counties. In 2013, 48% of primary care physicians report using CRP POCT in the Netherlands, versus 3% in Belgium, 15% in the UK and 3% in Australia (11, 23). In 2019 80% of Dutch GPs report using CRP POC testing (69). In Norway, Denmark and Sweden most GP offices have access to CRP POCT (15-18). In the UK there is still no routine use of CRP POCTs, even though they are recommended in NICE guidelines (20, 42, 50, 63).

The uptake of CRP POCT seems to be closely linked to available funding mechanisms (2, 48). It is also noted that when the reimbursement mechanism is overly complex, it has a negative impact on uptake (2).

Overconsumption of CRP POC tests

CRP POCT is extensively used in Norway, leading to reported cases of overconsumption, particularly in conditions such as sore throat, tonsillitis and otitis, where the test has no value (17). The introduction of CRP POCT in Scandinavian countries three decades ago did not go hand in hand with the development of guidelines and cut-off values, giving potential for over-use and misinterpretation of results (15). During daytime practice in Norway, CRP POCTs are used in as much as 60% of consultations for respiratory tract infections, and in 70% of out-of-hours consultations (18). Similarly, in Sweden overconsumption of CRP POC testing has been reported (55, 71). About 42% of Swedish patients with acute respiratory tract infections receive a CRP POCT when consulting their GP. Most of these are performed in patients with upper respiratory tract infections (71). Although current guidelines recommend conservative use, there seems to be a low adherence to these guidelines (55).

It has been suggested that the observed over-usage is partly due to economic incentive (42). In out-of-hours services, CRP POCTs are even more frequently used and costs during out-of-hours services

are fully covered by the municipalities. An important sidenote here is that in out-of-hours services, clinicians face more uncertainty due to not having had previous contact with the patients and having even more limited time for decision-making (17).

It has been suggested that overuse driven by financial incentives can be mitigated by linking reimbursement to clinical guidelines and thus only paying when the test is done in accordance with these guidelines (42). The cost-effectiveness of CRP POC testing decreases when it is used indiscriminately instead of in line with clinical guidelines (70).

7. Stakeholders

7.1 Stakeholder mapping

A European expert panel concluded that the most important stakeholders to engage with in an implementation process are GP organisations (local, national and/or international), health authorities (local and national), multidisciplinary groups of clinicians, and members from the industry, research and insurance (2). These stakeholders are also mentioned in other studies, supplemented with patients, laboratories, clinical biologists, IT consultants, POC experts, pharmacies, and nursing homes (19, 26, 42, 62, 63, 69, 74, 75). One study also included the media as a stakeholder (20).

It is highly recommended to set up a multidisciplinary POCT committee (2, 76). This committee can assure communication and cooperation between the different groups in a large healthcare system concerning appropriateness of testing, risk management, quality assurance, user training and the evaluation of instruments and testing procedures. The committee should include a director, manager and coordinator of POC testing, GPs, emergency medicine physicians, nurse practitioners, representatives from infection control and public health, representatives from the supply chain, an IT consultant, a consultant from biomedical engineering and laboratory representatives (76).

For the UK it has been recommended to involve representatives from industry, from health insurance companies, members from Clinical Commissioning Groups, members from the clinical guidelines development group, members from the NHS quality improvement program and GPs (69).

7.2 Engaging different stakeholders

One of the most important factors for a successful implementation seems to be the inclusion of CRP POC testing in local clinical guidelines, associated with clear cut-off values (2, 4, 11, 42, 56, 69).

A European expert panel recommended that GPs be motivated through ongoing education on POC testing, its impact on antibiotic prescribing and the way a test result can best be translated to the patient. They also suggest that local effects of the intervention on antibiotic prescribing should be communicated back to the GPs. Additionally, a decision aid that uses CRP POC testing when necessary, can be useful (2). Other studies highlighted the importance of environmental cues such as clinician handouts, desk reminders with the CRP cut-off values, patient leaflets, waiting room posters and a clear website with information for users (4, 30, 54, 56, 60).

Providing GPs with up-to-date evidence about the clinical and health economic effects of the intervention is considered beneficial to its implementation. (2, 43).

Studies have also described a positive effect of having clear quality assurance mechanisms in place as well as an exemplary model of the adaptations to patient flow in GP practices (11, 26, 37, 43). A positive effect on uptake can also be achieved by having a direct helpline for when issues with testing arise (11, 26, 60).

Having clear and transparent reimbursement mechanisms also plays a key role in the implementation phase of POC testing (20, 43).

Different studies recommend having one CRP POCT champion per GP practice to coordinate administration, internal QC,… The position should be longer-term and economically supported (30, 43, 46).

Engaging policymakers and industry-members can be enhanced by the development of visually appealing research findings before, during and after the implementation's pilot phase (77). An early cost-effectiveness evaluation is also recommended (20, 77).

A media campaign has potential for raising awareness among the general public about the rising antimicrobial resistance and the positive role CRP POC testing could play in this scenario (11, 61).

8. Implementation strategies

A Hungarian study designed a roadmap for the successful implementation of CRP POC testing in European countries (43). According to this study, successful implementation starts with raising public and professional awareness by early adopters sharing their experiences and by publishing articles. Early adopters of the service can be motivated by setting up pilot projects that can generate literature evidence (11, 43). This should start a healthy discussion among different stakeholders which should then lead national organisations to develop national guidelines. As such, policy makers will have plenty of information to consider funding mechanisms, motivated by the fight against antimicrobial resistance. On top of funding mechanisms, a protocol for quality control should be developed (43). The setting up of a multidisciplinary POCT committee is highly recommended, as is described above (76).

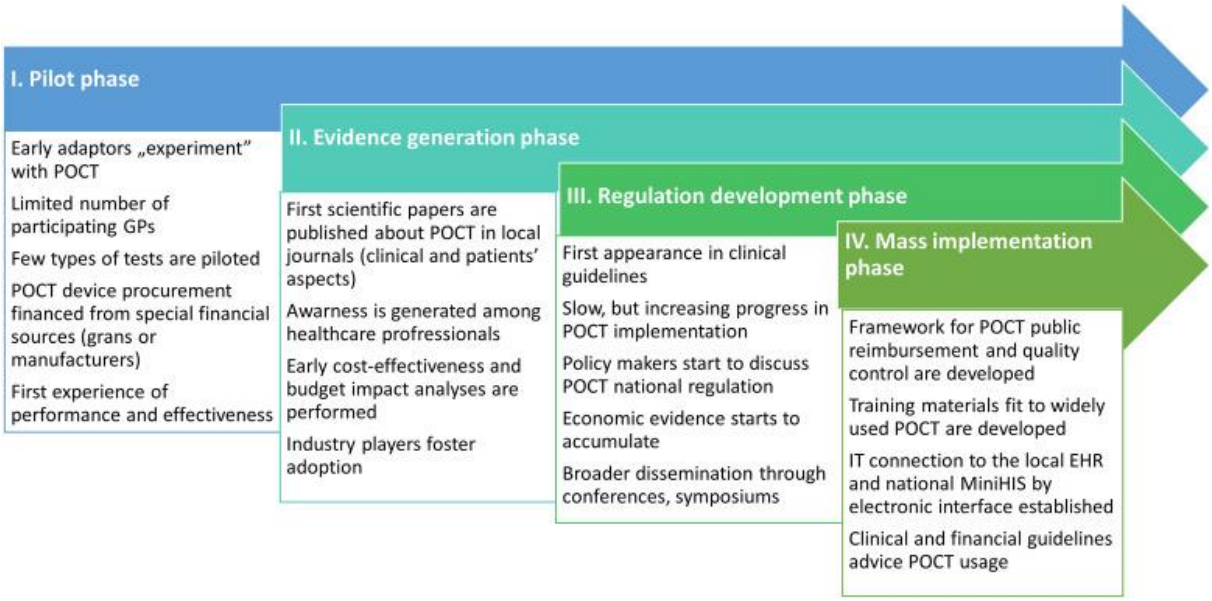


Figure 7: Proposed POCT implementation pathway by Dózsa et al. (84)

There are a lot of similarities between this roadmap and the implementation process that happened in the Netherlands. The Dutch Royal College of GPs produced a clinical guideline in 2011 in which the CRP POCT should be used and then the Dutch Healthcare Authority made the decision to reimburse CRP POC tests in primary care. An important role was played by the early adopters by engaging with all relevant stakeholders (48).

Discussion

1. Summary of findings

1.1 Implementation aspects

CRP POC testing has been proven to have a positive impact on reducing unnecessary antibiotic prescriptions for RTIs in primary care (7, 15). Its use has been included in national guidelines in the Netherlands, Scandinavian countries, and the UK (9-11). UK NICE guidelines have recommended using CRP POCTs for diagnosing pneumonia since 2014 (10). The tests have been recommended in Dutch primary care guidelines for pneumonia since 2011 and have now also been added to the guideline concerning diverticulitis to differentiate between complicated and non-complicated diverticulitis (9, 21).

There is a high variation between countries in the availability and reimbursement mechanisms of CRP POCTs. In the Netherlands, using the tests gained significant momentum after its introduction into primary care guidelines in 2011 which then led to its reimbursement (19, 21). The tests are now widely used across the Netherlands with 80% of Dutch GPs reporting using them (69). This is in stark contrast with the situation in the UK, where CRP POC testing is also recommended in NICE guidelines but without reimbursement mechanisms in place and only 15% of GPs reporting using the tests (11, 23). It has also been reported that overly complex reimbursement mechanisms have a negative impact on uptake (2). This seems to suggest that reimbursement plays a big role in the uptake of POC CRP testing.

In Belgium there is currently no reimbursement nor a policy concerning CRP POC testing in primary care. In hospitals however, the tests are being used and for in hospital environment there is a policy where testing is supported and accounted for by the hospital's laboratory. As a result of the lack of policy in primary care, there is no required quality control for CRP POC testing nor a limited price that could be charged to the patients (19).

1.2 Practical aspects

The tests are mainly administered by practice assistants instead of the GPs themselves, which minimizes workload for GPs (11, 22, 42, 44, 51, 55). A working protocol has been developed which is shown in *Figure 6* (11). A great benefit of using a POCT instead of a classic blood analysis is that the result is available at the time of consultation to be discussed with the patient and thus the reduction of follow-up telephone calls (38). All users should receive training as described in the result section. In the Netherlands this training is linked to the retainment of accreditation for using CRP POCTs (21, 22, 66). Digital education was deemed more effective and possibly more cost-effective than in-person training (58). The training courses are mostly provided by members of supporting laboratories which also have expertise concerning necessary quality control procedures (11, 19, 62). Laboratory support is important, and laboratories are heavily involved in countries where the use of CRP POCTs is successfully implemented (24, 26, 37, 62, 65).

Most common practical irregularities comprised of wrong storage conditions of reagents, since different parts require different storage conditions. It is important to have a practice protocol in place to adequately keep track of storage conditions and shelf life (22, 42, 43). Another practical irregularity to consider is the errors with manually entering test results into the patient health record (11, 43, 66). Most analysers currently have the ability to register results automatically into the patient records, as do the QuickRead and Afinion analysers. The NycoCard analyser lacks this option (11). The registration into patient records happens through the laboratory information system, giving the added bonus of having results visible for other health care providers and of giving laboratory personnel automatic access to results for quality control (66).

2. Recommendations

After reviewing the above-mentioned literature, the author of this paper decided on following recommendations for a successful implementation of CRP POC testing in the Belgian context:

The initial phase of implementation should raise professional awareness of the option to use a CRP POCT for RTIs, ideally through the execution of **pilot studies** (11, 43). These pilot studies can then be published in local and national literature which will engage different stakeholders to discuss different methods of a wider implementation. It is deemed beneficial to make visually appealing research findings for policymakers in different phases of the implementation process (77). We recommend to also communicate local effects on antibiotic prescribing of these pilot studies to the local GPs, for example through out-of-hours posts or GP meeting groups. We also recommend developing visual aids for clinicians and patients to motivate and help patients and clinicians during the implementation process. A decision aid and clear website for users would be beneficial.

Ideally, a **multidisciplinary POCT committee** should be set up including different stakeholders, especially GPs, laboratory personnel, policy makers and representatives from the manufacturer of the device (48, 76). This committee can mitigate practical aspects of the implementation phase and have discussions about the legal framework that needs to be developed for using CRP POCTs in primary care (19).

A clear **quality assurance mechanism** should be developed where GP practices collaborate with the local or hospital laboratories (20, 43). There should be a clear line of communication between the users of the tests and the collaborating laboratory for trouble-shooting and external quality control. Whether local or hospital laboratories should be involved will have to be determined.

We recommend that continued **user training** is provided for by the involved clinical laboratory and that this training is compulsory. The training can be linked to acquiring and retaining accreditation for use of the tests, like in the Netherlands (21, 22, 66). This training should at least include indications for testing, principles of rational diagnostics, interpretation of results and the practical handling of the device (with principles of internal quality control) in basic practice (21, 22, 66). We would deem it beneficial to include a section to the training materials about how to discuss the test results with patients. This user training could be provided as online learning modules.

It is advisable to have a **POCT coordinator on-site** at every practice where POC testing is performed, to keep track of shelf life and storage conditions of reagents and to assist other test users when practical problems arise. This coordinator should also be the performer and manager of internal quality control, maintenance and should keep the necessary documentation in order (quality control

dates, shelf life of materials,…) (43). This coordinator could be a GP or a practice nurse and should be economically supported (30, 43, 46).

Our research suggests that the availability of **reimbursement** mechanisms play a crucial role in the adaptation of the service. We recommend implementing a set reimbursement rate per performed test. This reimbursement could be paid directly to the performing GP practice, or to the involved clinical laboratory. This last option is applied in the Netherlands, where the laboratories purchase the analyser and consumables (2, 62). The reimbursement rates in different countries are mentioned above in the result section, but a cost-benefit analysis in the Belgian healthcare setting is advised to help determine the necessary reimbursement rate. Overconsumption of the tests, as has been reported in Norway and Sweden, can be mitigated by linking reimbursement to the adherence to clinical guidelines (42).

Summary of recommendations	
Test administrator	The tests can be administered by trained practice assistants instead of the GPs themselves by following a working protocol shown in *figure 6*.
Storage conditions	Appointing one POC coordinator per practice to keep track of shelf-life and storage conditions of reagents following a protocol
Result registration	Using the QuickRead or Afinion analysers, since these have the option to automatically register results into patient files and into the laboratory information systems
User training	User training provided by the supporting laboratory
	Making user training compulsory for having access to reimbursement
	User training could be partly provided as online learning modules
Quality control (QC)	Development of a standard quality assurance mechanism
	Internal QC performed by one appointed POC coordinator per practice, standardized, logged
	External QC provided by the supporting laboratory
	Establishing a clear line of communication between practices and the supporting laboratory for trouble-shooting
Engaging stakeholders	Formation of a multidisciplinary POCT committee to start a healthy discussion among different stakeholders and to guide the implementation phase
	Performing pilot studies and publishing the results in local and national literature, also publishing local effects of the intervention on antibiotic prescribing to engage GPs and policy makers
	Developing visual aids for patients and GPs to aid shared-decision making based on CRP POCT results
	Developing a clear website and decision aid using CRP POCT for GPs
Reimbursement	Development of a legal framework for POC testing in the Belgian context
	Introduction of a fixed reimbursement fee for using the test
	Linking the reimbursement fee to the adherence to clinical guidelines
	Reimbursement mechanisms should be clear and transparent

Table 1: Summary of recommendations

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Supplementary materials

Supplementary material 1: Search strategy

PubMed

Concept 1 = POCT

"Point-of-Care Systems"[Mesh] OR “POCT"[tiab] OR "point of care"[tiab]

OR (("near patient"[tiab] OR poc[tiab] OR rapid[tiab] OR bedside[tiab] OR "bed side"[tiab]) AND (test*[tiab] OR analys*[tiab] OR immunoassay*[tiab] OR technique*[tiab] OR immunofluorescen*[tiab] OR "fluorescent antibod*"[tiab]))

Concept 2 = CRP

"C-Reactive Protein"[Mesh] OR "c reactive protein"[tiab] OR "crp"[tiab]

Concept 3 = Logistics (storage, disposal, impact on patient flow), training for users, quality assurance, funding mechanisms, stakeholder mapping

"Practice Management/organization and administration"[Mesh] OR "Practice Management/supply and distribution"[Mesh] OR “Management”[tiab] OR "logistic*"[tiab] OR "Medical Waste Disposal"[Mesh] OR "storage"[tiab] OR “storing”[tiab] OR “waste”[tiab] OR “disposal”[tiab]

OR "Total Quality Management"[Mesh] OR "Quality Improvement"[Mesh] OR "Quality Control"[Mesh] OR “Quality”[tiab] OR "Process Assessment, Health Care"[Mesh] OR “Process Assessment*”[tiab] OR "Technology Assessment, Biomedical"[Mesh] OR “technology assessment*”[tiab] OR “process assessment*”[tiab] OR "Program Evaluation"[Mesh] OR “Program Evaluation*”[tiab] OR "Efficiency, Organizational"[Mesh] OR “efficiency”[tiab] OR “patient flow*”[tiab] OR “crowding”[tiab]

OR "Inservice Training"[Mesh] OR "Education, Nursing, Continuing"[Mesh] OR "train*"[tiab] OR “educat*”[tiab] OR “inservice”[tiab] OR "in service"[tiab] OR “on-the-job”[tiab]

OR “rollout”[tiab] OR “roll-out”[tiab] OR “implement*”[tiab] OR “adopt*” OR "Implementation Science"[Mesh] OR "Stakeholder Participation"[Mesh:NoExp] OR "stakeholder*"[tiab] OR "Policy Making"[Mesh] OR “Polic*”[tiab] OR “barrier*”[tiab] OR “facilitator*”[tiab]

OR "funding"[tiab] OR "Financ*"[tiab] OR "Healthcare Financing"[Mesh] OR "Fees, Medical"[Mesh] OR “Medical Fee*”[tiab] OR "economic*"[tiab] OR cost*[tiab] OR "Cost-Benefit Analysis"[Mesh] OR "Costs and Cost Analysis"[Mesh] OR "Reimbursement, Incentive"[Mesh] OR “Pay for Performance”[tiab] OR “reimbursement”[tiab] OR “incentive*”[tiab]

OR "Physician-Patient Relations"[Mesh] OR "Nurse-Patient Relations"[Mesh] OR "Attitude of Health Personnel"[Mesh:NoExp] OR "Qualitative Research"[Mesh:NoExp] OR "Focus Groups"[Mesh] OR "Interviews as Topic"[Mesh] OR "Interview"[Publication Type] OR "Health Care Surveys"[Mesh] OR

"Patient Satisfaction"[Mesh] OR “qualitative”[tiab] OR “interview*”[tiab] OR “focus group*”[tiab] OR “view*”[tiab] OR “Attitude*”[tiab] OR "Utilization Review"[Mesh]

OR “service report”[tiab] OR “service evaluation”[tiab]

Embase

Concept 1 = POCT

'point of care testing'/exp OR 'point of care system'/exp OR POCT:ti,ab,kw OR ‘point of care’:ti,ab,kw OR ((‘near patient’:ti,ab,kw OR poc:ti,ab,kw OR rapid:ti,ab,kw OR bedside:ti,ab,kw OR ‘bed side’:ti,ab,kw) AND (test*:ti,ab,kw OR analys*:ti,ab,kw OR immunoassay*:ti,ab,kw OR technique*:ti,ab,kw OR immunofluorescen*:ti,ab,kw OR ‘fluorescent antibod*’:ti,ab,kw))

Concept 2 = CRP

'C reactive protein'/exp OR ‘c reactive protein’:ti,ab,kw OR CRP:ti,ab,kw

Concept 3 = Logistics (storage, disposal, impact on patient flow), training for users, quality assurance, funding mechanisms, stakeholder mapping

'logistics'/exp OR logistic*:ti,ab,kw OR 'waste management'/de OR 'waste disposal'/de OR ‘waste’:ti,ab,kw OR disposal:ti,ab,kw OR 'storage'/exp OR storage:ti,ab,kw OR storing:ti,ab,kw OR 'health care management'/exp OR 'resource management'/exp OR management:ti,ab,kw

OR 'total quality management'/exp OR 'program evaluation'/exp OR 'quality control procedures'/exp OR quality:ti,ab,kw OR 'biomedical technology assessment'/exp OR ‘technology assessment*’:ti,ab,kw OR ‘process assessment*’:ti,ab,kw OR ‘program evaluation*’:ti,ab,kw OR 'organizational efficiency'/exp OR efficiency:ti,ab,kw OR 'patient flow*':ti,ab,kw OR ‘crowding’:ti,ab,kw

OR 'education'/de OR 'in service training'/exp OR 'paramedical education'/exp OR 'continuing education'/exp OR train*:ti,ab,kw OR educat*:ti,ab,kw OR inservice:ti,ab,kw OR ‘in service’:ti,ab,kw OR ‘in-service’:ti,ab,kw OR ‘on-the-job’:ti,ab,kw

OR rollout:ti,ab,kw OR ‘roll-out’:ti,ab,kw OR implement*:ti,ab,kw OR adopt*:ti,ab,kw OR 'implementation science'/exp OR 'stakeholder engagement'/exp OR stakeholder:ti,ab,kw OR 'health care policy'/exp OR polic*:ti,ab,kw OR ‘barrier*’:ti,ab,kw OR ‘facilitator*’:ti,ab,kw

OR 'funding'/exp OR financ*:ti,ab,kw OR 'economics'/de OR 'economic model'/exp OR ‘economic*’:ti,ab,kw OR cost*:ti,ab,kw OR 'health economics'/exp OR 'health care financing'/exp OR 'national health organization'/exp OR 'economic evaluation'/exp OR 'cost benefit analysis'/exp OR 'reimbursement'/exp OR reimburs*:ti,ab,kw OR incentive*:ti,ab,kw OR 'certification'/exp

OR 'patient satisfaction'/exp OR 'professional-patient relationship'/exp OR 'health personnel attitude'/exp OR 'qualitative analysis'/exp OR qualitative:ti,ab,kw OR 'questionnaire'/exp OR ‘focus group*’:ti,ab,kw OR 'interview'/exp OR interview:ti,ab,kw OR viewpoint*:ti,ab,kw OR attitude*:ti,ab,kw

OR ‘service report’:ti,ab,kw OR ‘service evaluation’:ti,ab,kw

NOT 'conference abstract':it

Web Of Science

Concept 1 = POCT

TS=(POCT) OR TS=(point of care) OR ((TS=(“near patient”) OR TS=(POC) OR TS=(bedside)) AND (TS=(test*) OR TS=(analys*) OR TS=(immunoassay*) OR TS=(technique*) OR TS=(immunofluorescen*) OR TS=(“fluorescent antibod*”)))

Concept 2 = CRP

TS=(crp) OR TS=(c reactive protein)

Concept 3 = Logistics (storage, disposal, impact on patient flow), training for users, quality assurance, funding mechanisms, stakeholder mapping

TS=(supply) OR TS=(distribution) OR TS=(logistic*) OR TS=(management) OR TS=(storage) OR TS=(storing) OR TS=(waste) OR TS=(disposal)

OR TS=(quality) OR TS=(“process assessment*) OR TS=(“technology assessment*) OR TS=(“process assessment*) OR TS=(“program evaluation*) OR TS=(efficiency) OR TS=(“patient flow*) OR TS=(crowding)

OR TS=(“in service”) OR TS=(train*) OR TS=(“on the job”) OR TS=(educat*)

OR TS=(rollout) OR TS=(“roll out”) OR TS=(implement*) OR TS=(adopt*) OR TS=(stakeholder*) OR TS=(polic*) OR TS=(barrier*) OR TS=(facilitator*)

OR TS=(funding) OR TS=(financ*) OR TS=(“medical fee*”) OR TS=(economic*) OR TS=(cost*) OR TS=(“pay for performance”) OR TS=(reimbursement*) OR TS=(incentive*)

OR TS=(qualitative) OR TS=(interview*) OR TS=(“focus group*) OR TS=(view*) OR TS=(attitude*)

OR TS=(“service report”) OR TS=(“service evaluation”)

Scopus

Concept 1 = POCT

TITLE-ABS(POCT OR "point of care" OR (("near patient" OR poc OR rapid OR bedside OR “bed side”) AND (test* OR analys* OR immunoassay* OR technique* OR immunofluorescen* OR "fluorescent antibod*"))) OR

AUTHKEY(POCT OR "point of care" OR (("near patient" OR poc OR rapid OR bedside OR “bed side”) AND (test* OR analys* OR immunoassay* OR technique* OR immunofluorescen* OR "fluorescent antibod*")))

Concept 2 = CRP

TITLE-ABS("c reactive protein" OR CRP) OR AUTHKEY("c reactive protein" OR CRP)

INAHTA

Concept 1 = POCT

(POCT OR "point of care" OR (("near patient" OR poc OR rapid OR bedside OR “bed side”) AND (test OR testing OR tests OR analysis OR analyses OR immunoassay OR immunoassays OR technique OR techniques OR immunofluorescence OR immunofluorescent OR "fluorescent antibody" OR “fluorescent antibodies”)))[title]

OR (POCT OR "point of care" OR (("near patient" OR poc OR rapid OR bedside OR “bed side”) AND (test OR testing OR tests OR analysis OR analyses OR immunoassay OR immunoassays OR technique OR techniques OR immunofluorescence OR immunofluorescent OR "fluorescent antibody" OR “fluorescent antibodies”)))[abs]

OR (POCT OR "point of care" OR (("near patient" OR poc OR rapid OR bedside OR “bed side”) AND (test OR testing OR tests OR analysis OR analyses OR immunoassay OR immunoassays OR technique OR techniques OR immunofluorescence OR immunofluorescent OR "fluorescent antibody" OR “fluorescent antibodies”)))[keywords]

OR “models, economic”[mhe]

Concept 2 = CRP

("c reactive protein" OR CRP)[title]

NHS EED

Concept 1 = POCT

(POCT OR point of care OR ((poc OR rapid OR bedside OR bed side) AND (test* OR analys* OR immunoassay* OR technique* OR immunofluorescen* OR fluorescent antibod*)))

Concept 2 = CRP

(c reactive protein OR CRP)