A qualitative process evaluation of the introduction of procalcitonin testing as an antimicrobial stewardship intervention.

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Abstract

Background

Successful antimicrobial stewardship interventions are imperative in today's environment of antimicrobial resistance. New antimicrobial stewardship interventions should include qualitative analysis such as a process evaluation to determine which elements within an intervention are effective and provide insight into the context in which the intervention is introduced.

Objective

To assess the implementation process and explore the contextual factors which influenced implementation.

Setting

An academic teaching hospital in Cork, Ireland.

Methods

A process evaluation was conducted on completion of a feasibility study of the introduction of a procalcitonin antimicrobial stewardship intervention. The process evaluation consisted of semi-structured face-to-face interviews of key stakeholders including participating (senior) doctors (5), medical laboratory scientists (3) and a hospital administrator. The Consolidated Framework for Implementation Research was used to guide data collection, analysis, and interpretation.

Main outcome measures

Qualitative assessment of the intervention implementation process, the contextual factors which influenced implementation and identification of improvements to the intervention and its implementation and determine if proceeding to a randomised controlled trial would be appropriate.

Results

Analysis of the interviews identified three main themes. (i) The procalcitonin intervention and implementation process was viewed positively to support prescribing decisions. Participants identified modifications to procalcitonin processing and availability to improve implementation and allow procalcitonin to be "*more of a clinical influence"*.

ii) In the antimicrobial stewardship context the concept of fear of missing an infection and risks of potentially serious outcomes for patients emerged.

(iii)The hospital context consisted of barriers such as available resources and facilitators including the hospital culture of quality improvement.

Conclusion

This process evaluation provides a detailed analysis of the implementation of procalcitonin testing as an antimicrobial stewardship intervention. The positive findings of this process evaluation and feasibility study should be built upon and a full randomised controlled trial and economic evaluation should be conducted in a variety of hospital settings to confirm the effectiveness of procalcitonin as an antimicrobial stewardship intervention.

Impact on practice

- Procalcitonin is a useful additional antimicrobial stewardship intervention
- The fear of missing infections and the risk of negative clinical outcomes for patients significantly influences antimicrobial prescribing decisions and must be considered when designing antimicrobial stewardship interventions.
- A culture of quality improvement within a hospital is an important facilitator of antimicrobial stewardship programmes

Keywords

Antimicrobial stewardship

Respiratory tract infections

Procalcitonin

Process evaluation

Consolidated Framework for Implementation Research

Introduction

Antimicrobial resistance(AMR) is a significant risk to human health and we face the very real possibility of a "post antibiotic era in which common infections could once again kill"[1]. Antimicrobial stewardship(AMS) programmes are well established and include interventions to improve antimicrobial prescribing[2-4]. Some AMS interventions can lack sustainability[5] which may be related to contextual factors of those interventions, but these have been poorly investigated particularly their role in the effectiveness of interventions and sustainability on a larger scale[6]. This has prompted the suggestion that interventions should look to include components that enhance enablement for the implementation of evidence-based practice,[6] defined as *"increasing means or reducing barriers to increase capability or opportunity"*[6, 7]. Furthermore a recent Cochrane review of interventions to improve antimicrobial prescribing for hospital patients[8] has advocated for greater use of qualitative research such as a process evaluation(PE) of a trial to determine which elements within an intervention are effective.

A qualitative PE[9] assesses the fidelity and quality of implementation, providing insight into the context into which the intervention is introduced, clarifies causal mechanisms of the intervention without assuming that the intervention itself leads to the outcome and builds the evidence base to support the intervention that will inform policy makers and practice[10]. A PE is important in complex interventions in the healthcare setting as a means to identify the underlying cause of the success or failure of interventions because occasionally even highly successful quality improvement interventions[11] have proven difficult to replicate in different contexts due to fundamental differences in how the intervention was delivered[12]. A PE is an important element of implementation research and should incorporate a theoretical framework to guide data collection, analysis and interpretation. Theoretical frameworks have a predictive capacity to identify or explain causal mechanisms of

implementation. This allows for identification of contextual factors that influenced implementation and so aids our ability to generalise study findings.[13].

Greater utilisation of rapid diagnostic tests and biomarkers has been highlighted as an important factor in addressing AMR by improving infection diagnosis, supporting prescribing decisions and AMS programmes[14]. Procalcitonin is a biomarker which has been shown to support prescribing decisions and reduce antimicrobial use safely in patients with respiratory tract infections[15-18]. The findings of a recent Cochrane review[17] supports its use in the context of AMS in safely reducing antimicrobial consumption by 2.4 days in patients with respiratory tract infections. We have previously reported the positive influence of procalcitonin on antimicrobial prescribing following the introduction of procalcitonin testing in a feasibility study[19]. The study identified some variability in the use and interpretation of procalcitonin levels suggesting a range of factors influenced implementation and should be explored to improve the effectiveness of intervention implementation in the future.

Feasibility studies should be complemented by a qualitative PE[9] to facilitate improved development and implementation of interventions[20]. This is particularly relevant when introducing new diagnostic tests to support AMS to assess how best to use such new tests[21] and reporting of qualitative analysis of procalcitonin implementation has been limited[22, 23].

Aim of the study

To explore how and why the introduction of a procalcitonin intervention worked or did not work in an Irish hospital setting. The study objectives were to gain an understanding and assessment of the fidelity and quality of the implementation process, explore the contextual factors which influenced implementation, identify the barriers and facilitators to

implementation and inform improvements to the intervention and its implementation if proceeding to a randomised controlled trial was deemed appropriate.

Ethics

The study was approved by the Clinical Research Ethics Committee of University College Cork and the Cork Teaching Hospitals (reference code ECM 4 (w) and ECM 3 (III)). Written informed consent was obtained from all participants prior to the interviews and confidentiality of the participants was assured.

Methods

The Standards for Reporting Qualitative Research were used to guide the development of this manuscript[24].

A qualitative PE was conducted of a single centre, randomised, open-label feasibility study[19] of the introduction of procalcitonin testing in patients admitted to hospital with a lower respiratory tract infection, under the care of the respiratory medicine team, during on-call acute unselected general medical take. The feasibility study ran from June 1st 2017 to May 31st 2018 and was conducted in a single, 321 bed model 3 (smaller general)[25] inner city, voluntary acute University Teaching Hospital, which is part of the South/South West Hospital Group[26] in the Republic of Ireland. The PE was conducted following completion of the feasibility study.

The Consolidated Framework for Implementation Research(CFIR) [27] was used to guide data collection, analysis, and interpretation. It is a meta-theoretical framework based on existing determinant frameworks and multiple implementation theories which provides a roadmap of constructs to monitor the implementation process[27] by recognising that implementation is a multidimensional phenomenon with multiple interacting influences from the individual to the organisation and beyond[28]. The CFIR was chosen because it can be applied at any stage

of the evaluation process of an intervention, it provides a framework to investigate and assess the complex multi-level nature of implementation in the healthcare setting including barriers and facilitators to effective intervention implementation[13] and provides a way in which to organise and communicate findings.

Participants

An invitation to participate in the study was issued in person or by email to key stakeholders involved in the feasibility study or would be involved in the decision to implement procalcitonin testing in the hospital in the future. All agreed to participate but one medical doctor later withdrew due to scheduling constraints. Participants included five medical doctors (DR1-5) (3 respiratory clinicians and 2 general clinicians), three medical laboratory scientists (MS1-3) and a hospital administrator (ADM). The interviews ranged in length from 6 to 29 minutes with a mean duration of 16 minutes.

Data collection

Semi-structured face-to-face interviews were conducted by the primary researcher. Interviews took places in the hospital where the study was conducted at a date and time that was convenient for participants. The interview topic guide was developed by two researchers (FOR and AF), both pharmacists with experience of AMS. The interview topic guide was informed by the most relevant CFIR constructs[27] which were used as a 'check-list' of variables for consideration. The topic guide was refined following a pilot interview with a medical doctor who participated in the feasibility study. Pilot interview data were included in the study due to the limited number of medical doctors participating directly in the feasibility study.

Interviews with medical laboratory scientists focused on the provision of procalcitonin testing in the laboratory, the interviews with doctors focused on the use of procalcitonin in making

antimicrobial prescribing decisions while the interviews of participants with managerial responsibilities and the hospital administrator focused on implementation of procalcitonin testing on a larger, ongoing scale in the hospital. Issues and opinions on AMS and the hospital context for change and quality improvement were asked of all participants.

All interviews were digitally recorded and transcribed verbatim by a professional transcription service. The accuracy and quality of the transcripts was checked against the original recordings and any identifiable data was removed from the transcripts (by FOR).

Data analysis

Interview analysis used the framework method[29, 30] which provides a systematic step-wise approach to produce structured outputs of summarised data and is most commonly used for the thematic analysis of semi-structured interview transcripts[29]. It consists of the following steps 1. Transcription of the interviews, 2. Familiarisation with the interview data 3. Coding of the data using the CFIR constructs as deductive codes (open coding was applied when themes emerged during the familiarisation process that did not fit within the definitions of the CFIR constructs) 4. Charting and indexing of the data using a thematic framework 5. Interpretation and analysis of the data.

The interview transcripts were coded independently by two researchers (FOR and AF) using the CFIR constructs and open coding by thematic analysis. All 39 constructs of the CFIR were used as the a priori codebook for this qualitative study. Important domains and constructs were identified based on the frequency of their appearance in the interviews, the degree of importance articulated by the participants or the researchers, or both. Emergent themes were reviewed throughout the interview process and the team made an assessment as to when data saturation had occurred. All authors reviewed the final codes. Discrepancies were resolved through discussion.

Results

Nine interviews were conducted with hospital staff to explore the different aspects of the procalcitonin intervention implementation in the hospital setting. Participants roles in implementation are contained in Table 1 below. The results have been informed by the CFIR and are categorised into three themes. 1. The procalcitonin intervention and the implementation process, 2. The AMS/AMR context and 3. The hospital/organisational context. Within these themes participants described a range of factors that interact with each other and the intervention to produce an effect as a facilitator or barrier to implementation. The CFIR constructs identified in the themes are listed in Table 2 below. They are supported by qualitative excerpts from the interviews (Tables S1, S2 and S3 available as supplementary data). The constructs of the CFIR are highlighted in bold in the text.

Theme 1: Procalcitonin intervention and implementation process

Participants described the procalcitonin intervention as having a well-established evidence base to support its use and clinical situations where it could act as an "*extra marker"* to support antimicrobial prescribing decisions. These decisions require clinicians to balance the need to adequately treat patients while also safely minimising antibiotic exposure and is a situation where "*procalcitonin would actually play a very useful role."* The feasibility study design and accompanying PE aligned with the **trialability** construct by providing participants the opportunity to test procalcitonin on a smaller scale, develop experience, reflect on the intervention, suggest changes to improve the intervention and adaptation in the future. Participants provided specific examples of clinical situations where procalcitonin supported antimicrobial prescribing decisions along with examples of where it was considered of less benefit. Overall participants felt more confident in the role of procalcitonin in the acute

infective setting and less confident in the reliability of procalcitonin in patients with underlying chronic lung disease. (Indicative quotations are shown in Table S1)

Several elements of the '**adaptable periphery**' [27] emerged which could be modified to improve the processing of samples in the laboratory and the subsequent availability of the procalcitonin results to clinicians. They included processing of the test more efficiently as part of a patients biochemistry profile by the biochemistry laboratory rather than processing samples in the microbiology laboratory (which occurred in this study). This would facilitate more prompt availability of results as part of the standard admission point of care blood test results. The changes suggested to the laboratory processing of the results were due to the elements of the intervention which aligned to the **complexity** construct and were considered barriers to implementation. (Indicative quotations are shown in Table S1)

Participants commented positively on the education and training provided and were engaged with the intervention and its intended purpose of improving antimicrobial prescribing. (Indicative quotations are shown in Table S1)

Participants suggested several other general recommendations to facilitate implementation of procalcitonin testing which aligned to the **reflecting and evaluation** construct. They included recommendations for a *"multi-modal"* educational plan, the need to identify the role of procalcitonin, *"it's place in the hierarchy"* and to consider potential unintended consequences of its use. Participants also highlighted the need to gain support and endorsement from hospital management and senior clinicians and using public forums within the hospital such as *"grand rounds"* to facilitate this objective and engage **champions** (individuals) who actively associate themselves to support the intervention during implementation.

Several potential barriers to implementation were also identified by participants. One participant highlighted that procalcitonin "*has been around for quite some time"* and questioned it's **relative advantage** over C—reactive protein as an indicator of viral infections. The barrier of additional costs and availability of resources to support new interventions in the hospital means they would require "*a really strong business case to suggest why we should add a resource".* The **opportunity cost** associated with implementing a procalcitonin intervention was also raised with the suggestion that alternative AMS interventions may be a more beneficial use of resources but this would require an economic assessment to determine the most cost-effective intervention..

The respiratory specialist participants in the study expressed a strong sense of **self-efficacy** and confidence in their professional knowledge and clinical experience of treating respiratory tract infections and making antimicrobial prescribing decisions *"it's very much linked to what we do"*. They highlighted situations where they have come into conflict with the AMS team in relation to compliance with antimicrobial guidelines highlighting they "*don't inappropriately apply the guidelines as opposed to that we ignore them"*. These findings were considered a potential barrier to implementation of AMS interventions.

Theme 2: Antimicrobial stewardship and antimicrobial resistance context

The need to address the problems associated with AMR were seen as facilitators to AMS interventions. Patient safety was seen as a priority but participants highlighted the increasing complexity and difficulties in managing patients with resistant infections. The management of patients with carbapenemase producing *Enterobacteriaceae* emerged as an example of the organisational approach to the problem of AMR and elements of this approach were considered as facilitators of implementation. The hospital *"eventually"* realised the problems associated with carbapenemase producing *Enterobacteriaceae* following communication

between national and local level management resulting in greater **leadership engagement** at local level to address the problem. These factors created a **tension for change** to respond to this problem within the organisation and the need to take a long term rather than a short term view to respond to the problem. (Indicative quotations are shown in Table S2)

The **culture** within the hospital in relation to antimicrobial prescribing emerged as a barrier to implementation of AMS interventions. The concepts of fear and risk aversion were a significant influence on antimicrobial prescribing decisions. Fear arose in relation to the *"possibility of missing infection"* in patients and the associated potential for negative clinical outcomes for those patients related to an inadequately treated infection and the associated feelings of clinical responsibility (indicative quotations are shown in Table S2). This fear was accompanied by the *"fear of litigious issues"* and the need for *"self-protection".* Clinicians described the risk-aversion and need for self-protection as motivating factors for the prescription of antimicrobial courses to patients "*even in times that maybe the front-line clinician themselves maybe isn't convinced fully that it's a bacterial infection"*. There was acknowledgement of antimicrobial over-prescribing but these risks were outweighed by the needs of the individual complex sick patient admitted to hospital. A possible explanation for this which emerged was that the longer term consequences of AMR "*aren't as apparent"* and may be perceived to be less important than the treatment of current patients. There was also an acknowledgement that the problem requires a significant amount of behavioural change as the *"habits of the prescribing hand are firm and hard to change".*

Theme 3: Hospital/organisational context

All participants described a range of factors which act as barriers or facilitators of implementation. A growing culture of quality improvement in the hospital was described by all participants aligning with the **culture** construct. There were some differing individual

perspectives on the degree of **leadership engagement** with quality improvement in the hospital with an acknowledgement that senior clinicians could be more engaged with it. The development of structural *"scaffolding"* to support a clinical lead with dedicated time to encourage and support quality improvement work was identified as a facilitator of future interventions. (Indicative quotations are shown in Table S3)

Communication was seen as an important facilitator of interventions aligning with the **networks and communication** construct. The hospital size was seen as a positive factor to encourage greater engagement with colleagues. Communication between medical teams and the AMS team was seen as good and had a positive influence on antimicrobial prescribing. However inter-departmental communication, and communication between senior clinicians and hospital management emerged as a barrier to implementation. (Indicative quotations are shown in Table S3)

Available resources emerged as a barrier to implementation in relation to the limitations of the funding model of Irish healthcare where despite the intensions of staff there is limited opportunities to *"invest to get future success"*. Participants also raised issues related to the perception of how resources are distributed within the hospital "*it does seem to be he who shouts loudest"*.

Discussion

This study provides a detailed PE of the introduction of procalcitonin testing as an AMS intervention. The CFIR guided a systematic assessment of the intervention and implementation process, identification of barriers and facilitators of implementation, and provided an insight into the contextual factors which influence AMS in the Irish hospital setting. The findings provide actionable recommendations to successfully implement a procalcitonin intervention.

The main findings of this study identified the positive elements of the intervention and implementation process while also exploring the barriers to implementation related to the intervention and the contextual barriers of the study setting to be overcome to successfully implement a procalcitonin intervention. Participants engaged with the intervention, the education provided, assessed the supporting evidence for the intervention, gained experience of the intervention, reflected on its clinical value and proposed modifications to the intervention delivery which would improve implementation in a future randomised controlled trial. All these elements promote successful adaptation of interventions[27] and it has also been shown that previous experience of procalcitonin testing leads to greater confidence in the application of procalcitonin as an AMS intervention[31].

The adaptability and trialability constructs identified the most relevant factors to improve the delivery and selection of patients to maximise the benefits of the intervention. Procalcitonin levels were tested in the microbiology laboratory during this study and while the test itself was relatively quick to process there were several factors which led to delays in the availability of the results. These delays in availability resulted in clinicians feeling that *"hearing afterwards it was something that you know, you felt almost it was a feedback after the decision had been made"* rather than contributing to the clinical decision-making process.

317 Processing of the procalcitonin level in the biochemistry laboratory emerged as a solution to
318 this problem and the procalcitonin levels should be available as part of the admission list of
319 blood results at the point of care to allow the results to be "*more of a clinical influence"* on
320 prescribing.
321 The participating respiratory clinicians expressed a strong degree of self-efficacy in relation
322 to their expert knowledge and clinical experience in treating respiratory tract infections while
323 also acknowledging the diagnostic difficulties associated with respiratory tract infections.
324 These findings suggest that respiratory clinicians could be perceived as barriers to
325 implementation of AMS interventions and are similar to those found in a recent study which
326 highlighted the barriers to integrating AMS processes within respiratory medicine[32]. The
327 perception that unsolicited AMS input is considered an imposition on specialist territory and
328 clinical autonomy among some medical specialists who consider themselves 'experts in their
329 own fields' is a considerable barrier to AMS interventions[33].
330 One clinician highlighted that procalcitonin "*has been around for quite some time'* and
331 questioned it's relative advantage over other infection markers. However most participants
332 viewed the intervention positively which suggests that procalcitonin is a potentially effective
333 intervention as it combines clinician enablement, improved diagnostics to support AMS but
334 requires engagement with clinicians to optimise effectiveness. An intervention of this nature
335 would fulfil the recommendations of a recent study[34] to overcome barriers in AMS in
336 respiratory medicine. These findings align with a qualitative study of clinicians experience
337 with procalcitonin where the intervention was viewed positively as an AMS adjunct but it
338 could not replace other tests or clinical judgement[35].
339 The CFIR provided a framework to explore the two main contextual factors of AMS and the
340 hospital/organisational context into which the intervention was introduced. Contextual

341 factors influencing AMS interventions have been poorly explored in the past[6] and a lack of
342 understanding of the contextual factors contributing to a given problem can lead to sub-
343 optimal implementation[36].
344 The concepts of fear and risk-aversion were prominent themes in the AMS/AMR context. The
345 care of their patients and patient safety is the primary concern for clinicians[37]. Patients
346 admitted to hospital with a suspected infection are perceived to be more *"complex"* and
347 *"sick"* which heightens the fear of missing an infection and the potentially serious outcomes
348 for patients including death which heavily influences antimicrobial prescribing decisions. Fear
349 of adverse clinical outcomes especially in hospital patients has a powerful influence on
350 antimicrobial prescribing which can escalate the risk perception of clinicians[33]. Clinicians
351 were risk-averse even in situations where the risk of a bacterial infection is low *"I think a lot*
352 *of people will still cover with antibiotics".* Clinicians also cited concerns on a personnel level
353 perceiving a need for self-protection and a fear of litigation which results in the prescription
354 of antimicrobials "*just in case*". Justification of the fear of litigation may be due to the fact
355 that medical negligence suits filed in the Irish High court have increased by 136% from 2007
356 and 2018[38] and clinical negligence claims against the NHS in the UK have doubled over a
357 similar period[39]. In the ever-increasing litigious world we live in, this is a significant barrier
358 going forward.
359 The findings demonstrate that clinicians consider the short terms risks to patients and
360 themselves more heavily than the longer term consequences of AMR which "*aren't as*
361 *apparent"* when making antimicrobial prescribing decisions similar to the findings of a recent
362 systematic review[40]. Risk, real or perceived, is challenging to mitigate against. AMS
363 programmes must acknowledge the experiences of risk faced by clinicians when designing
364 AMS interventions. An intervention such as procalcitonin acting as an "*extra marker"* of the

infection process offers clinicians further information when making antimicrobial prescribing decisions potentially reducing the perceived risks for both patient and clinician.

The hospital context consisted of both barriers and facilitators to implementation. The hospital administrator highlighted the recognition of the problems associated with AMR having gained greater insight during the hospitals response to a carbapenemase producing *Enterobacteriaceae* outbreak and the significant costs associated with it. Unfortunately the realities of managing limited resources in a hospital environment where the short term demands of trying to *"push people through the system"* is difficult and limits the ability of hospitals to invest in new interventions or diagnostics to mitigate the long-term consequences of AMR. These findings are similar to the findings of another study investigating the perspective of hospital managers on optimising antimicrobial use[41]. A medical laboratory scientist expressed frustration with the economic constraints of the healthcare system where it appears that resources are allocated to *"he who shouts loudest".* In the current setting of a resource limited health service new interventions such as procalcitonin must be supported by "*a really strong business case"* and an economic evaluation of the intervention should be incorporated into a future trial particularly in the Irish hospital setting. Procalcitonin testing has been shown to be a cost-effective AMS intervention in the U.S. setting[42] but the overuse of procalcitonin testing has also been highlighted[43]. Long term investment in the health system is necessary to alter the realities of AMR. This is particularly important given our current population demographic in Ireland where the proportion of the population over 65 years is expected to increase to 1.6 million in the next 35 years[44].

Positive findings from the hospital context included the recognition of developing a culture of quality improvement in the hospital. Additional resources and support are required to develop the *"scaffolding"* within the hospital but this is an important facilitator for the

development of new interventions. We know from previous work that organisations which have a patient centred culture are more likely to implement change effectively[45]. Communications within an organisation has been recognised as being important in intervention implementation. There was some variation in the assessment of it in the hospital context and both positive and negative aspects were identified. The small size of the hospital was noted as having a beneficial effect on communication in this study. Implementation has been described as a 'social process' which is intertwined with the context in which it takes place[46]. The importance of factors such as gaining "*consultant buy-in*" and using educational forums such as grand rounds to encourage engagement and discussion of interventions by senior clinicians are noted.

Strengths and limitations

The findings of this study and our earlier quantitative work[19] support the finding that procalcitonin is an effective intervention and thus support the recommendations to link the CFIR constructs to intervention outcomes[13]. We have outlined the justification for our choice of the CFIR[13]. The study included a broad range of participants not just those directly involved in the study implementation.

The study had several limitations. The study took place in a single hospital setting and contextual influences may differ in other hospitals and this may limit its transferability. However, as this is a feasibility study, this could not be mitigated for in this instance. Only one hospital administrator was interviewed which limits the insight from the administrative perspective on the hospital context. However due to the single study site it was only possible to interview one administrator who would have the knowledge to provide these details. The feasibility study and PE were conducted by the same researchers increasing the risk of positive reporting. There was also a risk of the hawthorn effect during the data collection process as

413 it is possible the interviewer could have influenced the way people behave or respond. Efforts
414 to avoid or minimise bias and the hawthorn effect included purposive sampling and inclusion
415 of a diverse sample of individuals.

Conclusion

This PE provides a detailed qualitative analysis of the implementation of procalcitonin testing as an AMS intervention. Positive elements of intervention implementation were highlighted along with modifications to improve the delivery of the intervention such as the prompt availability of procalcitonin levels at the point of care to allow the test to be "*more of a clinical influence"* on prescribing. Contextual factors which influence implementation were identified and explored including the concepts of fear, risk and the influence of respiratory clinicians on AMS interventions. We would recommend that the positive findings of this PE and feasibility study should be built upon and that a full randomised controlled trial and economic evaluation should be conducted in a variety of hospital settings to confirm the effectiveness of procalcitonin as an AMS intervention.

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Conflict of interest

There were no conflicts of interest to declare

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556 **Table 1.** Health professionals` role during the procalcitonin implementation

Health professional	**Role in implementation**
Hospital administrator	Hospital-wide managerial responsibilities and oversight of funding decisions
Respiratory clinicians	Involved in the procalcitonin intervention implementation and assessment
Clinicians	Provided insight into the contextual elements of implementation
Medical laboratory scientists	Laboratory processing of the procalcitonin tests

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558 **Table 2.** Consolidated framework for implementation research domains and constructs

559 associated with qualitative themes

Theme	**CFIR domains**	**CFIR constructs**
Procalcitonin intervention and implementation process	Intervention characteristics	Evidence strength and quality, Relative advantage, Adaptability, Trialability, Complexity, Design quality and packaging, Costs (opportunity)
	Process	Champions, Reflecting and evaluation
	Characteristics of the individual	Self-efficacy
Antimicrobial stewardship/antimicrobial resistance context	Outer setting	Patient needs and resources, Cosmopolitanism, External policy and incentives
	Inner setting	Culture, Tension for change, Relative priority Leadership engagement, Available resources,
Hospital/organisational context	Inner setting	Structural characteristics, Networks and communications, Culture, Leadership engagement
	Process	Champions, Available resources

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