Application of Consolidated Framework for Implementation Research to Improve Clostridioides difficile Infection Management in South African District Hospitals

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Abstract

Background

Clostridioides difficile infection (CDI) is a global health threat. Measurable gaps exist in CDI quality of care and CDI knowledge in South Africa. This study describes the development of a CDI intervention informed by the local context within South African public district level hospitals, and analyzes the CDI intervention development, implementation process and adaptations to understand acceptance, uptake, successes, and failures of the CDI intervention.

Methods

A CDI checklist intervention was designed and implemented at three district level hospitals in the Western Cape, South Africa. The Consolidated Framework for Implementation Research (CFIR) was used as a framework to contextualize study findings, including a description of the implementation process and adaptations for each hospital. A mixed-methods approach was applied with quantitative outcomes data and qualitative interview and focus group data with frontline and administrative healthcare personnel. Transcripts were coded to *a priori* workflow steps as well as to aspects of the CDI checklist intervention and emerging themes. The CFIR framework was applied to results from the qualitative interviews, observations by research team members, and quantitative patient outcomes data in order to identify drivers and barriers to implementation and to understand differences in uptake at the three sites. Highly relevant and moderately relevant constructs for the Intervention, Inner Setting, and Implementation Process domains were identified.

Results

Each hospital adapted the implementation process based on available resources, while maintaining the intervention core elements. One hospital displayed high uptake of the intervention compared to the two other hospitals. Highly relevant CFIR constructs linked to intervention uptake included tension for change, strong peer intervention champions, champions in influential leadership positions, and intervention complexity, among others. Tension of change at the high uptake hospital was also supported by an academic partnership for antimicrobial stewardship.

Conclusion

We provide a straight-forward health systems strengthening intervention for CDI that is both needed and uncomplicated, in an understudied LMIC setting. Intervention uptake was highest in the hospital with tension for change, influential champions, and existing academic partnerships. Further research is
needed in reaching and involving understudied settings with fewer academic connections and to examine impact on patient outcomes.

**Contributions To The Literature**

- We describe a process for developing a simple evidence-based intervention informed by the local context, specifically the needs, gaps, and available resources in South Africa.

- Our methods and findings add to the field of Implementation Science by providing a practical application of the Consolidated Framework for Implementation Research for a common infection in an understudied and low-resource setting, South African public district level hospitals.

- This research contributes to the literature both unique and universal implementation challenges in South Africa that can be considered for both scaling this *Clostridium difficile* infection intervention and developing new interventions in similar low resource settings.

**Background**

Patients with *Clostridioides difficile* infection (CDI), can suffer from health outcomes that range from mild-to-severe diarrhoea to mortality, as well as experience costly hospitalizations and readmissions.\(^1\)\(^{-6}\) In addition to physical impacts, CDI impairs patients’ psychological, social, professional, and financial lives.\(^7\)\(^8\) CDI remains a global health threat.\(^4\)\(^5\) CDI hospital outbreaks may trigger changes in patient care protocols including closure of hospital wards to limit further transmission.\(^9\)\(^{-11}\) Quality CDI care requires timely identification, rehydration, antibiotic treatment, and use of infection prevention and control (IPC) measures to prevent devastating hospital outbreaks.\(^5\)\(^12\)\(^13\) We found measurable gaps in the delivery of these steps as well as CDI knowledge across healthcare providers in hospitals in the Western Cape, South Africa.\(^14\)\(^15\) CDI interventions developed and proven in high resource settings, where most CDI epidemiological and quality improvement studies are performed, may not apply directly to low resource settings.\(^16\)\(^17\) There is a gap in CDI literature from low resource settings, especially sub-Saharan Africa, particularly in adapting CDI interventions to low resource settings.\(^17\)\(^{-19}\) Authors of a recent meta-analysis of CDI in developing countries concluded CDI prevalence in patients with diarrhoea (15%) is likely an underestimate due to inconsistent diagnostics, surveillance, and low awareness.\(^18\) Thus, CDI interventions and the description for their implementation tailored to these local circumstances are urgently needed.

Implementation Science is a multidisciplinary research field and often aims to improve healthcare systems by optimizing the fit of evidence-based practices and interventions with implementation context.\(^20\)\(^21\) It also aims to increase intervention reproducibility and transferability, and reduce the lag time between evidence generation and practice.\(^20\)\(^{-23}\) The Consolidated Framework for Implementation Research (CFIR) is a highly cited and adaptable meta-theoretical framework that excels in examining the interplay of contextual factors surrounding an intervention.\(^24\) CFIR organizes theory and evidence-based
constructs into five domains with a total of 39 constructs. However, Implementation Science applications are lagging in low- and middle-income countries (LMICs). Limited CFIR applications have been done in sub-Saharan Africa, primarily via academic partnerships in Kenya, Mozambique, and South Africa. No prior work to our knowledge has leveraged implementation science to develop and explain a CDI intervention in South Africa.

The objectives of this study are first to develop a CDI intervention informed by the local context within South African public district level hospitals following implementation science principles. The second objective is to analyse the CDI intervention development, implementation process and adaptations to understand differences in acceptance, uptake, successes, and failures of the CDI intervention.

**Methods**

A CDI checklist quality improvement intervention was designed and implemented as a ‘Diarrhoea Alert’ at three district level hospitals in the Western Cape, South Africa. The checklist design and its implementation were informed by baseline quantitative and qualitative results from pre-implementation interviews with healthcare providers. Post-intervention quantitative medical records data were also collected to assess the implementation and intervention effects. CFIR is the conceptual framework used to contextualize study findings, including a description of the implementation process and adaptations for each hospital.

This study received approval from the University of the Western Cape Department of Research Development, (Ethics Reference Number: HS/16/1/24), the National Health Laboratory Service, Western Cape Department of Health, and the participating hospitals. The four hospitals included in the baseline epidemiology study were invited to participate. All invited hospitals were public district level hospitals in the Cape Town metropole. Three hospitals accepted the implementation package, and one hospital declined to meet with the research team at the time of implementation.

The study utilized a mixed methods approach with quantitative outcomes data and qualitative interview and focus group data. Data on CDI provider perceptions and CDI care provided were collected both before and after intervention implementation. The source of the intervention, collection of baseline data, and development of the implementation package are outlined in four phases (Fig. 1). The phases mirror quality improvement principles and are an adapted version of the Plan, Do, Study, Act cycle. Details on intervention development and implementation strategies utilized are presented with corresponding Expert Recommendations for Implementing Change (ERIC) strategies in Table 1.
Table 1
ERIC implementation strategies used to develop the intervention and implementation

| Strategy | Actions taken |
|----------|---------------|
| **Develop stakeholder interrelationships** | Conducted a country-wide qualitative needs assessment of the South African health system via 1.) scoping review of policies and published literature to identify national priorities, and 2.) discussions with stakeholders and providers at policy, administrative, supervisory, operational, managerial, and patient care levels. Antimicrobial Stewardship was chosen as the intervention topic by those who conducted the needs assessment.  
Consulted with academic leaders at various universities across South Africa and in Cape Town.  
Narrowed needs assessment to the Western Cape province level.  
Consulted with stakeholders at policy level regarding needs in both public and private sectors (e.g. Pharmacy Services, Western Cape Department of Health).  
Consulted with both infectious disease leaders in public and private sectors (e.g. South African Department of Health, private sector heads of microbiology).  
Consulted with internationally recognized infectious disease researchers and clinicians in South Africa and the United States, including those leading work in Antimicrobial Stewardship and *Clostridioides difficile* infection (CDI).  
Presented chosen problem (CDI) to leaders previously engaged in needs assessment and departments of internal medicine to affirm chosen problem was important and determine if clinical innovation to address it was appropriate. |
| **Build a coalition** | High-level hospital chief executive officers and administrators were engaged for project approval with the intervention.  
Heads of departments and managers assisted with introductions to the “educationally influential” and local opinion leaders to recruit and cultivate relationships with partners in implementation effort. |
| **Conduct educational meetings & Inform local opinion leaders** | Conducted pre-intervention interviews and meetings with “educationally influential” hospital administrators, senior physicians, infection prevention and control nurses, nurse educators, and pharmacy managers to teach them about the intervention as well as local opinion leaders with hope that they would influence colleagues to adopt the intervention. |
| **Identify and prepare champions** | Identified and prepared champions at each hospital who would “dedicate themselves to supporting, marketing, and driving through an implementation, overcoming indifference or resistance that the intervention may provoke in an organization.” |
| Strategy                               | Actions taken                                                                                                                                                                                                 |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Develop academic partnerships          | Strengthened existing academic partnership between the University of Wisconsin-Madison and University of the Western Cape (UWC) Schools of Pharmacy. Engaged pharmacy students from both universities for shared training and skill-building with the research project, including partnership with the 1-year UWC longitudinal research program for final year pharmacy students (two groups of students over two years) and inclusion of UW-Madison independent study and Advanced Pharmacy Practice Experience (APPE) students. |
| Use evaluative and iterative strategies |                                                                                                                                                |
| Conduct local needs assessment         | Conducted baseline CDI management and patient outcomes retrospective review including in-hospital mortality and identification of gaps in treatment and infection control. |
| Assess for readiness and identify barriers and facilitators | Identified barriers and facilitators through qualitative interviews with healthcare providers and stakeholders. |
| Audit and provide feedback             | Visited hospital wards during implementation to audit use of the innovation and provide feedback to clinicians.                                                                                         |
| Train and Educate Stakeholders         |                                                                                                                                                |
| Develop educational materials          | Developed training handouts and reference/reminder.                                                                                             |
|                                        | Developed educational reminder/recognition wearable buttons.                                                                                      |
| Distribute educational materials       | Delivered educational materials in person during training and education sessions.                                                               |
| Make training dynamic                  | Tailored training to each healthcare profession (nurses, pharmacists, physicians).                                                              |
|                                        | Included dynamic interactive learning delivery with open-ended questions and patient examples in training.                                        |
|                                        | Included examples to show when to apply the intervention that encouraged participant engagement in each stage of infection identification, diagnosis, treatment, and prevention. |
|                                        | Provided in-person reinforcement follow-up training in the ward and asked about current patient needs (patients with diarrhoea).                        |
|                                        | Provided training individually to any providers who missed initial group training sessions.                                                      |
| Support Clinicians                     |                                                                                                                                                |
| Remind clinicians                      | Developed reminder posters for the intervention that were posted in the wards to prompt clinicians to use the intervention for applicable patients. |
| Strategy | Actions taken |
|----------|---------------|
| a. Powell et al. *Implementation Science* 2015 |
| b. Legenza et al. *BMJ Global Health* 2018 |
| c. Legenza et al. *Antimicrobial Resistance and Infection Control* 2018 |

**Study Setting**

South Africa has the greatest income inequality in the world, and the urban area surrounding Cape Town is still marked by a deep history of racial segregation. The South African Department of Health, the national health system, serves 84% of the population. Meanwhile the private sector serves those who can afford it, approximately 16% of the population. The cost to use the public health system is adjusted based on income, embodying a right to healthcare approach. District level hospitals, also known as secondary level hospitals, often provide care for complex patients suffering from Human immunodeficiency virus (HIV) and Tuberculosis (TB), and patients of all ages, including the elderly with chronic conditions. The hospitals included in our research averaged 265 inpatient beds and had similar but limited government funded resources (e.g. paper health records). The South African Department of Health's organizational structure is similar to many public sector national health systems globally. Overall, the health system experiences many of the same challenges as other LMICs in Africa and globally, such as staffing shortages and overcrowding. The tangible resources needed for CDI treatment (e.g. gloves, gowns, antibiotics, soap) are usually available within the hospitals. However, they are not always utilized, potentially due to knowledge gaps and/or a lack of awareness of the infection.

**Phase I: Identify And Analyze Problem**

**STEP 1. Stakeholder engagement and identification of CDI need in South Africa**

We defined and detailed the steps taken to develop stakeholder interrelationships with ERIC strategies in Table 1. CDI was chosen through a local needs assessment of healthcare providers, stakeholders, and infectious disease leaders. The innovation area was selected by internal South African leaders and healthcare providers. Through visits with stakeholders, including Department of Health administrators, the topic area of Antimicrobial Stewardship (AMS) was selected. Subsequently a ‘Strengths, Weaknesses, Opportunities, and Threats’ or SWOT analysis of AMS projects and innovation areas was conducted, and
CDI was selected as the specific project due to the scarcity of available data on CDI at the district level in the Western Cape province.

**STEP 2. Pre-intervention retrospective review of CDI patient care and outcomes**

The first CDI epidemiology and outcomes study was designed to serve as baseline data for the intervention and provide data on the magnitude of CDI in public district hospitals in this LMIC. The published results of the CDI epidemiology and outcomes study in South Africa pre-implementation are available. The identified opportunities to improve patient care are also included in the outcomes study.

**STEP 3. Stakeholder engagement on CDI treatment in South Africa and intervention**

Identification of facilitators and barriers commenced in August 2016 with pre-intervention qualitative interviews. Twenty-eight qualitative interviews and focus groups were conducted with frontline and administrative healthcare providers including nurses, pharmacists, and physicians at the participating hospitals. Engagement included physicians with varying experience: interns (1–2 years post qualification), medical officers (often ~ 3–4 years post qualification), specialist registrars (~ 4–8 years post qualification) and consultants (~ >8 years post qualification). Semi-structured interviews were conducted in-person at a location convenient for the interviewee, such as in hospital ward offices, administrative offices, or the pharmacy. The qualitative interview methodology and results mapping pre-intervention CDI workflow with workflow facilitators and barriers are previously published. Additionally, pre-implementation interviews and focus groups gleaned information about what resources already existed and what elements of a CDI intervention would be both possible and helpful.

**Phase II: Develop Implementation Package**

**STEP 4. Consideration of local context and synthesis of data to develop implementation package**

The implementation package was informed by stakeholder engagement, baseline epidemiology and outcomes data, and local context. We considered the CDI workflow steps to identify, diagnose, treat, and prevent CDI revealed by qualitative interviews and observations. We also considered the barriers and facilitators to these steps in the design of the checklist intervention and implementation package. Finally, we took into consideration elements of interventions already successful in the hospitals and feedback from both local stakeholders and infectious diseases leaders. We conducted a literature review of existing checklists and bundle interventions globally for CDI; CDI bundle interventions have proved to be highly effective in high-resource countries. We considered what resources were available in the hospitals when deciding which elements of CDI care should be emphasized in education and on the checklist. The synthesis of these results and the facilitators and barriers present in the local context of the Western Cape, South Africa, led to the development of the 'Diarrhoea Alert,' or CDI checklist.
Phase III: Implement

STEP 5: Put into practice and adapt implementation package

We continued to adapt the implementation package created in Step 4 to meet the local environment at each hospital based on feedback from local healthcare providers at each hospital. Implementation at Hospitals 1 and 2 began with a trial of the training session at Hospital 1 delivered by the lead researcher, continued with adapted training across hospital wards and departments, and concluded with local champions, or individuals who dedicated themselves to the intervention and conducted follow-up. A more independent implementation model was utilized at Hospital 3 in order to see the effect of a train-the-trainer model for the project. The lead researcher trained a local champion to lead intervention implementation. Finally, implementation at Hospital 4 did not occur until after results from Hospital 2 were presented to Hospital 4 leadership.

Phase IV: Collect And Examine Results

STEP 6: Post-implementation engagement and interviews

Post-intervention interview participants were recruited with purposive sampling of both providers who were previously engaged with intervention implementation and providers unfamiliar to the research team; twenty post-implementation interviews and focus groups were conducted. Interview audio files were transcribed verbatim, and transcripts were coded *a priori* to workflow steps, aspects of the CDI checklist intervention, and emerging themes. Post-intervention interviews were conducted to gather qualitative data about the efficacy of the intervention and feedback for future adaptations. Post-intervention interviews were processed following the same previously published methods as pre-intervention interviews. Briefly, two researchers coded verbatim interview transcripts from both before and after the intervention to CDI workflow steps and feedback on the intervention as well as the implementation process post-implementation. The qualitative data analysis software NVIVO (Version 11, QSR International) was used for coding. Discrepancies in coding were discussed and resolved as previously described in our qualitative study.

Step 7: Preparation Of Results And CfIr Framework Application

Post-implementation patient characteristics, CDI management, and patient quantitative outcomes were reviewed. Patient test results from laboratory orders for *C. difficile* tests were collected from the National Health Laboratory Services. Medical records for patients hospitalized with positive test results during the 90 days following the initial implementation and training week were reviewed. Outpatient test results were collected from the National Health Laboratory Services.
excluded. We summarized collected data on the steps of CDI care provided and patient outcomes, which was later presented to each participating hospital through formal presentations and individual meetings as interest and schedules allowed.

We pragmatically applied the CFIR framework to results from the qualitative interviews, observations by research team members, and quantitative patient outcomes data in order to identify drivers and barriers to implementation and to understand differences in uptake at the three sites.\textsuperscript{43} We chose a qualitative approach to the CFIR analysis to produce translational results and a reproducible description of the intervention, while continuing to strengthen collaborative partnerships with community stakeholders.\textsuperscript{44} Producing robust numeric ratings was not a priority of this project and thus not performed. The relevance of the CFIR constructs was determined following a multi-step filtering and assignment process.

First, LL reviewed all 39 CFIR constructs, including the “Detailed Description” and “Codebook Guidelines” as available at the https://cfirguide.org/constructs/ website and then described in narrative and outline form the relevance of each applicable construct. Constructs that were non-applicable were excluded. Additionally, two CFIR domains were excluded: 1) the Outer Setting was excluded because all hospitals were affected by the same complex socio-cultural history, national politics, and Department of Health provincial- and national-level policies; and 2) the Individuals Involved domain was excluded as the project was a system-level intervention. Finally, LL and RC discussed these methods and construct results.

In the second step, constructs from the CFIR domains Intervention, Inner Setting, and Implementation Process were assigned to high or moderate relevance categories. Moderate constructs with overlapping findings were consolidated to the most pertinent construct. Constructs with low relevance were excluded. TE provided feedback on this construct list, relevance assignments, and drafted descriptions, emphasizing aspects of construct details. The ‘Planning’ construct was then excluded as the key aspects were described in other more substantiated constructs.

Third, adjustments in the relevance assignments were made. Specifically, during subsequent iterative drafts of the manuscript, the following construct changes were made:

- Intervention: Complexity was moved to highly relevant and Evidence Strength and Quality was moved to moderately relevant;
- Inner Setting: Leadership Engagement was added;
- Implementation Process: Reflection and Evaluation construct, originally unassigned, was designated as highly relevant to complete the description of the implementation.

In this way, constructs that were unique to this intervention and those that described the intervention’s level of uptake between hospitals remained in the highly relevant category. No other changes were made to the relevance distinctions.

For the sake of focus and brevity, moderately relevant constructs were presented in the results table with further details explained in the Appendix, as they are here. Ultimately, findings were reviewed by all co-
authors, including local healthcare providers from the participating hospitals. A Revised Standards for QUality Improvement Reporting Excellence (SQUIRE 2.0) checklist was completed as a reporting guideline (Supplement 1). Here we present the relevant pre- and post-implementation feedback and post-intervention findings within the CFIR framework to frame the intervention development and explain the implementation process.

Results

Here we use the CFIR framework’s replicable language to describe the intervention and results as well as to understand instances of high uptake and acceptance juxtaposed with resistance at hospital and individual levels. Highly relevant and moderately relevant constructs for the Intervention, Inner Setting, and Implementation Process are presented in Table 2 and summarized in Table 3. Moderately relevant constructs and additional details on select highly relevant constructs are provided in Appendix A.
Table 2

| CFIR Domain          | Intervention                                                                 | Inner Setting                                                                 |
|----------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| **Intervention**     |                                                                              |                                                                              |
| Relevance            | Construct Theme                                                              | Source (High*)                                                               |
| High                 | Adaptability                                                                 | Internal South African leaders and local healthcare providers selected the innovation area via a participatory process. |
|                      | Theme: We adapted existing evidence-based CDI interventions and checklists to fit the local healthcare setting and resources available. Intervention training was also adapted at each hospital. |                                                                              |
| High                 | Complexity                                                                   |                                                                              |
|                      | Theme: The simple intervention avoided altering standard work processes, and instead simply triggered reminders to identify patients with diarrhoea, provide quality of care measures, test patients at risk for CDI, treat patients with CDI, and apply IPC procedures. Physically applying the checklist sticker to the blue boards of patients with diarrhoea was the most complex step. |                                                                              |
| High                 | Source                                                                       |                                                                              |
|                      | Theme: Internal South African leaders and local healthcare providers selected the innovation area via a participatory process. |                                                                              |
| Moderate             | Evidence Strength and Quality                                                 |                                                                              |
|                      | Theme: Awareness and perceptions of evidence-based CDI interventions and other bundle approaches varied among healthcare providers. |                                                                              |
| **Inner Setting**    |                                                                              |                                                                              |
| High*                | Leadership Engagement                                                        | All three sites required engagement of the hospital Chief Executive Officer or another executive-level representative before implementing the project. Hospital 2 leadership showed the strongest commitment. The Hospital 1 executive leadership welcomed the intervention and appreciated its value but expressed some skepticism on the long-term sustainability. At Hospital 3, attempts to meet with consultant level physicians were sometimes unsuccessful; meeting requests were declined, ignored, and/or canceled at the scheduled time of meeting. |
| High                 | Tension for Change                                                           | Hospital 2 leaders uniquely recognized the need to improve CDI identification and treatment. |
|                      | Theme: Providers prioritized TB and HIV above CDI. Concurrent IPC programs, such as hand hygiene trainings, lacked organization wide support. |                                                                              |
| Moderate*            | Structural Characteristics                                                    | The social structure of the district hospitals included is similar to other public district level hospitals across Africa and other low resource healthcare settings. Uniquely, a weekly Antimicrobial Stewardship (AMS) ward round occurs at Hospital 2 and includes pharmacy and medicine presence along with trainees. The AMS ward round is often led by an infectious diseases expert from the tertiary teaching hospital/university. |
### CFIR Domain

| CFIR Domain                  |     | Details                                                                                                                                 |
|-----------------------------|-----|------------------------------------------------------------------------------------------------------------------------------------------|
| **Moderate**                |     | **Networks and Communication** The Department of Internal Medicine at Hospital 2 uniquely had a WhatsApp communication system for laboratory results, patient needs, and program reminders, including reminders about the CDI intervention. |
| **Moderate**                |     | **Available Resources** Time and the personnel involved with the project were resources that varied for the implementation at each hospital. Tangible resources available, such as medications, IPC supplies (gloves, gowns, soap, etc.), and other supplies were similar at all publicly funded district hospitals. |
| **Moderate**                |     | **Access to Knowledge and Information** The barriers and facilitators study identified limited CDI knowledge as a major barrier to CDI treatment. The implementation process included CDI education and training materials in a digestible format. These materials, handouts, reminder posters, and the in-person training sessions on the ward or other convenient locations were similar across sites. |

### Implementation Process

| Level | Engaging: | Description                                                                                                                                 |
|-------|-----------|---------------------------------------------------------------------------------------------------------------------------------------------|
| **High** | Stakeholders | The stakeholder engagement process was most similar between Hospitals 1 and 2. At Hospital 3, the external researcher started stakeholder engagements (interviews) and trained a pharmacy intern to continue engagements (training). |
| **High** | Opinion Leaders and Champions | Opinion leading Hospital 2 physicians uniquely influenced the intervention uptake. |
| **High** | Reflecting and Evaluating | An increase in CDI testing and awareness observed in post interviews indicates that there was an increase in CDI knowledge due to the implementation package. The lead researcher presented results at Hospitals 1 and 2 in person via formal individual and group discussions and presentations. Results at Hospital 3 were presented to the Western Cape Department of Health as part of the internship program. Results from Hospital 2 were also presented to the Department of Health and Hospital 4 during an invited presentation to hospital leadership. |

* Uniquely distinguishes the hospital with high intervention uptake (Hospital 2) and differences between the three hospitals.
As stated in the methods, we present the CFIR constructs most relevant and differentiating to the intervention and implementation. Highly relevant constructs are detailed here.

### I. Intervention/innovation

**Adaptability, Complexity, and Source**

The specific checklist implemented in this study was informed by existing CDI checklists and input from internal stakeholders, including local healthcare providers, hospital administrators, and local students.\(^40\) We designed the intervention to fit the local healthcare setting and resources available, and address the gaps in CDI management described elsewhere.\(^14\)^15 An intervention sticker for TB was already in use and appeared to work well in the public hospitals. The CDI intervention was adapted to be applied to the medical chart orders page, or ‘blue board,’ of all patients with diarrhoea. While initially designed as the ‘CDI Checklist,’ we later changed the name to ‘Diarrhoea Alert’ to prompt a screening of all patients with diarrhoea. The checklist served as an alert and simple job aid for the elements of quality CDI care (Fig. 2; see Intervention constructs in Table 2 and further construct details in Appendix A). The CDI antibiotic treatment recommendations were based on the 2015 South African Standard Treatment Guidelines in place at the time of development.\(^45\) The revised guidelines released in 2020, recommend metronidazole for mild-moderate CDI and vancomycin for severe CDI.\(^12\) The intervention source and development are detailed in the methods and appear with ERIC implementation strategies in Table 1.
The intervention implementation was adapted to three district level hospitals but invariably maintained two core elements: the checklist and items on the checklist. Training sessions were led by the lead champion and adapted to resources at each hospital. Training at Hospitals 1 and 2 was performed by the external project lead. At Hospital 2, a medical registrar (medical resident) and medical student took roles of local peer champions. The adaptation to include a registrar proved to be the most effective and key differentiating factor.

For implementation at Hospital 3, the lead researcher trained a local champion to lead intervention implementation and provide the training sessions. The lead researcher and this local champion conducted the first education and intervention training at one of the hospital wards together. The local champion completed the intervention implementation at Hospital 3 as a project for a 1-year pharmacy internship through the Department of Health with guidance from the research team. However, gaining internal physician support was challenging.

Hospital 4 was not yet ready for the intervention during the implementation phase at Hospitals 1–3. Requests to introduce the project and gain necessary approvals were unsuccessful. However, the research team was able to present the project to Hospital 4 with the intervention results and changes in quality of care observed at Hospital 2 one year later. Hospital 4 then added a ‘Diarrhoea Alert’ block checklist permanently printed on the bottom right corner of the inside page of the blue board for all patients. This adaptation reduced the size of the checklist and avoided disruption to the front nursing orders page.

II. Inner Setting

Leadership Engagement, Tension for Change, and Relative Priority

All hospital sites required engagement of the hospital Chief Executive Officer or another executive-level representative before implementing the project. However, Hospital 2 leadership, executive leaders and front-line consultants (attending physicians), more widely communicated their support, increasing the tension for change and CDI intervention’s priority. For example, influential senior consultant physicians invited the intervention for presentation at the weekly department of medicine meeting including consultant and physician trainees. Pre-implementation, the research team gathered feedback for adaptation, and then post-implementation presented the results at these department meetings.

Overall, the epidemiology and outcome results proved current quality of care was an intolerable status quo, with mortality at 30% and treatment inconsistent with global guidelines or not provided at all. At the time of implementation, these epidemiology results were not yet published. Understandably, healthcare providers perceived TB and HIV as higher priority infectious diseases; South Africa has the greatest number of people living with HIV in the world and TB is a leading cause of death in people with HIV. Nevertheless, Hospital 2 recognized the potential for the intervention to facilitate needed change and improve quality of care with evidence-based interventions. Key opinion leaders at Hospital 1 did not perceive the need for change; some providers did not see CDI as a problem.
III. Implementation Process

Engaging & Reflecting and Evaluating

Engaging: Stakeholders

Overall, we engaged stakeholders, opinion leaders, peers, and experts similarly across the included hospitals as described in the methods, Table 1, and the Leadership Engagement construct in the Inner Setting domain (Table 2). Healthcare providers who were to use the new checklist were also engaged in the project with interviews and focus group discussions before and after implementation as described in the methods. Front-line provider stakeholders were also engaged with the CDI education and intervention training sessions. These sessions included a socially engaging component with the distribution of “CDI Trained” buttons/badges to staff who completed the sessions. The buttons served to remind staff of the intervention, engaging those who may have missed the training, and create a community around the implementation process. The number of providers who became strong project champions varied substantially between sites.

Engaging: Opinion Leaders and Champions

Support from opinion leaders for the intervention was a major distinguishing construct between hospitals. Some of these opinion leaders were also champions for the intervention. Initial contact with opinion leaders was made by the external project lead except when one of those opinion leaders introduced the project to their senior administrators (e.g. the head of a department contacting a hospital administrator).

Project implementation leads were appointed for the project based on available resources and interest (external lead at Hospital 1, registrar and student at Hospital 2, pharmacy intern at Hospital 3). At Hospital 2, one of the project leads was an opinion-leading registrar. The registrar was a respected peer physician role model and informal leader; his opinion was valued by both senior and junior staff across the hospital. Together with the Department of Internal Medicine opinion leaders, the project leads were able to increase uptake at Hospital 2.

At Hospitals 1–3, nurse managers and administrators, including IPC and nurse educators, were engaged in the project. They accepted the project, recognized the need for the intervention, and affirmed its potential; however, they did not champion the project. Similarly, IPC nurses and nurse educators were engaged and supported the project but did not have as much influence as the consultant physicians. However, training sessions were introduced by the senior nurse administrators, nurse educators, and/or IPC nurses. These introductions were instrumental for building trust with the frontline staff. The training sessions were essential for creating awareness about CDI and its complications, as many of the nurses had limited awareness/knowledge preceding the sessions.14 While nurses supported the intervention, they did not take ownership or see the intervention as part of their daily tasks. Nurses across the hospitals did not advocate for the intervention at the level the physicians championed at Hospital 2.
Furthermore, departments peripheral to internal medicine, such as surgery and emergency medicine, were also engaged and provided support for the intervention at both Hospital 1 and Hospital 2. Emergency medicine physicians were more supportive at Hospital 2 than Hospital 1. While Hospital 1 leaders were supportive, they did not have the same level of influence that consultants at Hospital 2’s Department of Medicine had on other providers. The Hospital 2 consultants were then able to facilitate successful recruitment of staff, nurses, and junior physicians to participate in the intervention. As a result, the strong opinion leaders, including the senior level physicians, who championed the intervention at Hospital 2 were able to overcome indifference toward the intervention.

Reflecting and Evaluating

Preliminary assessment of progress and impact of the implementation pilot included the quantitative data from patients with CDI test results, observations, and qualitative interview data. Despite perceived challenges and low use at Hospital 1, the increase in CDI testing and awareness observed in post interviews indicates that there was an increase in CDI knowledge due to the implementation package. The centralization of printing checklists for Hospitals 1 and 2 suggests that the implementation package initiated became a sustained change in organizational structure.

Comparison of our baseline data from four area hospitals (including Hospital 2) and Hospital 2 baseline results alone to post-intervention results signal improvements in CDI management and patient outcomes (Appendix: Reflecting and Evaluating). The results were not statistically significant nor was the study designed to detect statistically significant differences due to the short follow-up period. Measurable progress in improving quality of care and implementation uptake was greatest at Hospital 2.

Overall, the implementation of the intervention was associated with a self reported heightened awareness and increased use of evidence-based CDI practices at the participating South African hospitals. Furthermore, the intervention demonstrates the capacity and potential of the “Diarrhoea Alert” to improve the quality of CDI care in South Africa when appropriate champions are engaged in the implementation effort.

*Treatment follows the 2015 South African Standard Treatment Guidelines in place at the time the checklist was developed. The 2019 guidelines now specify metronidazole for treatment of mild to moderate Clostridioides difficile infection and vancomycin for severe infection.

Discussion

We achieved our objective of developing a context specific intervention for CDI and identified key constructs for intervention uptake in South African public sector district level hospitals. We identified key implementation science constructs that uniquely distinguish high intervention uptake at one hospital compared to two other South African district level hospitals with similar available resources and organizational structure. First, tension for change was one of the most relevant constructs to distinguish uptake between the hospitals. The tension for change and prioritization communicated from leadership
at Hospital 2 supported high intervention uptake. An academic partnership with the tertiary hospital, specifically the AMS ward rounds (Structural Characteristics), uniquely supported this tension for change at Hospital 2. Second, the individuals who championed the intervention at the hospital with a greater tension for change uniquely supported the intervention and contributed to its success. A position of influence and investment appeared to be a required characteristic of the champions to support intervention uptake. Additional CFIR constructs that proved to be highly relevant were intervention complexity and stakeholder engagement. The results imply strategies to engage low resource hospital settings without strong academic partnerships must adapt. The relevance of this work is that it unveils unique and universal challenges in South Africa that can be considered for how this applies to other low resource settings. Ultimately this study strives to promote the use of evidence-based practices for identifying, treating, and preventing CDI in low resource settings, and adds to the growing application of implementation science theories and frameworks in LMICs.

A recurring theme in South Africa was the importance not only of champions’ influence or seniority but also their level of investment in the project. At Hospital 2, the senior registrar (i.e. resident) and medical intern who championed the project had strong investment and the support of seniority to influence uptake. In contrast, the pharmacy intern at Hospital 3 was highly invested in the project but lacked seniority to influence uptake and spread change. Culture within professions and hierarchy among groups contribute to the challenges of interprofessional teamwork, meanwhile interprofessional communication is essential for patient safety.\(^48\)\(^49\) Broadly, South Africa can be categorized as having a moderate power distance where hierarchy is accepted and followed.\(^50\) Healthcare providers lower in the social hierarchy may not speak up to issues they perceive, threatening patient safety.\(^49\)\(^51\) The results of this study, specifically the key differences in uptake associated with the profession leading the intervention, is consistent with prior work in South Africa that a healthcare hierarchy seems predominant and negatively affects interprofessional communication.\(^52\) These cultural factors in South Africa may have also influenced the observed reluctance from nursing staff to take ownership of the intervention across the three hospitals. Thus, there is a crucial need to address inner setting factors such as readiness for change and psychological safety to support interprofessional interventions in the context of low resource settings.\(^24\)\(^53\)–\(^56\)

Strong academic partnerships and a culture of supporting new initiatives also distinguish Hospital 2 from the hospitals with low uptake. Broadly, community academic partnerships are described in implementation science research as a critical component to implementing evidence-based practices and a cornerstone of many academic programs.\(^57\) To various extents, our project utilized recognized strategies, specifically: identifying barriers and facilitators to implementation, facilitating interactive problem solving, tailoring strategies, promoting adaptability, and auditing and providing feedback during the implementation phase. While we engaged healthcare stakeholders throughout this research, a community advisory board, a strategy not deployed, could strengthen this intervention, uptake, and systematic evaluation of these strategies.\(^57\)
Finally, our straightforward intervention enabled its success at Hospital 2, and it could support sustained and scaled intervention. Simple interventions are more likely to be effective, and thus evermore crucial in overburdened public hospitals. The checklist can now be printed for the Western Cape hospitals on ‘tender’, a centralized procurement process all government facilities follow. The checklist can operate without intervention from the research team, should healthcare personnel continue to use the checklist and the administration sets this expectation. The adaptation of the checklist being printing directly onto the prescription chart Hospital 4 is a sustainable and scalable iteration. Training, monitoring and providing feedback on the checklist’s use could be provided through mechanisms for IPC monitoring already in place as well as be included in IPC training already routinely provided. Scalability is likely because the personnel, physical structure, and resources available within district level hospitals are very similar across the Western Cape. However, micro- and socio-cultural differences exist within each hospital, such as those that emerged in this study. Across South Africa, variations may exist in provincial level priorities, administrative structure, and funding. The National Department of Health could scale intervention dissemination in the Western Cape and across South Africa. Adaptation is likely needed to fit province level differences in supplies, such as the prescription chart and order forms. Globally, the intervention may also be relevant to other governmental health systems. A fidelity assessment of both the sticker and the embedded prescription chart checklist form is needed to guide continued improvement.

Limitations

Our study is a relatively small-scale study in a broadly understudied setting. However, the research identified compelling themes between the hospitals. The results may be generalizable to healthcare settings outside of the Western Cape, South Africa with similar resources, challenges, and education systems. Researchers have adapted and applied the CFIR framework with and without numeric valence ratings assigned to constructs, both prospectively and retrospectively. Earlier integration of the CFIR framework in our research could have strengthened our analysis and is recommended. Yet, we were able to detail facilitators and barriers to CDI care in our prior qualitative study, and apply the implementation science principles described in our methods. A limitation of our analysis is that the CFIR dimensions are not quantified, but nevertheless they identify the constructs that are strongly associated with uptake through a process of author consensus. Additionally, such investigator bias, including those leading the project and key collaborators from South Africa and the United States cannot be extracted. To reduce this bias, qualitative interview data was coded by two additional researchers less directly invested in the study results. Some authors were involved in all or select phases of the intervention development, implementation, data analysis, and reflective analysis. The CFIR conceptual framework also aided in structuring a systematic evaluation of the intervention and implementation. Accordingly, our participatory approach is both a strength of our research process and a limitation of the results.

Conclusions
We provide a health systems strengthening intervention for CDI that is both needed and uncomplicated, in an understudied LMIC setting, and an analysis of the intervention uptake with the CFIR framework. Our research provides a breakdown of the intervention development, implementation, and outcomes at three secondary level hospitals in Cape Town, South Africa. Our results show uptake was highest in the hospital with tension for change, influential champions, and existing academic partnerships. Future implementation research is needed in reaching and involving understudied settings with fewer academic connections and to examine impact on patient outcomes.

**Abbreviations**

AMS  
Antimicrobial Stewardship

CDI  
*Clostridioides difficile* infection

CFIR  
Consolidated Framework for Implementation Research

ERIC  
Expert Recommendations for Implementing Change

IPC  
Infection, Prevention, and Control

LMIC  
low- and middle-income countries

HIV  
Human Immunodeficiency Virus

TB  
tuberculosis

**Declarations**

**Ethics approval and consent to participate**

The study was approved by the Humanities and Social Science Research Ethics Committee, Department of Research Development of the University of the Western Cape (Ethics Reference Number: HS/16/1/24). The South African National Department of Health, Western Cape, and the National Health Laboratory Service (NHLS) also approved this study.

**Consent for publication**

Not applicable.

**Availability of data and materials**
The datasets generated and/or analysed during the current study are not available due to participant privacy but may be available from the corresponding author on reasonable request.

**Competing interests**

WR has received grant funding from Paratek and Merck, and consulting fees from Paratek.

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**Author's Contributions**

LL designed the study, led the intervention development and implementation, collected post-intervention data, conducted post-intervention qualitative interviews, led qualitative and CFIR analysis, interpreted the findings, and drafted and revised the manuscript. SB, RC, WR, and NS provided guidance and contributed to the intervention conceptualization and design. LL, RC, TE, KC, MM identified factors contributing to the intervention uptake and intervention implications. KC, MM contributed to the intervention implementation and audited the use of the intervention. LL, RC, TE contributed to the CFIR analysis and construct relevancy determinations. RC facilitated the collaborative project between the University of the Western Cape and the University of Wisconsin. All authors revised the manuscript. All authors read and approved the final manuscript.

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Figures

| PHASE I                      | PHASE II                      | PHASE III | PHASE IV                      |
|-----------------------------|-------------------------------|-----------|-------------------------------|
| Identify and analyze problem| Develop implementation package| Implement | Collect and examine results   |
| Time duration: < 1 year\(^a\) | < 3 months\(^b\)              | < 6 months\(^c\) |

Figure 1

Study design in four project phases. a. Estimated total time includes time to develop protocol and obtain research ethics approval. b. Estimated total time on site at hospitals preparing and implementing intervention. c. Estimated total time collecting and analyzing 90-day post-implementation results; does not include preparation of publication.
## Diarrhoea alert

For identification and treatment of Clostridium difficile infection (CDI)
Apply to the blue board for ALL patients with diarrhoea

Date: ____________

| Patient with acute diarrhoea? |
|-------------------------------|
| ☐ Yes                         |
| ☐ Oral rehydration ordered    |
| ☐ IV rehydration ordered if NPO |

| Risk factors for CDI? ex. antibiotic use, healthcare exposure |
|---------------------------------------------------------------|
| ☐ Yes                                                         |
| ☐ No → CDI Checklist end.                                     |

| CDI laboratory test ordered?        |
|-------------------------------------|
| ☐ Yes                               |

| All precipitating antibiotics are stopped if possible? |
|------------------------------------------------------|
| ☐ Yes                                                 |

| Positive CDI result: |
|----------------------|
| ☐ STOP loperamide if ordered |
| ☐ CDI antibiotic treatment initiated |
| ☐ Metronidazole, oral, 400 mg 8 hourly for 10 days |
| - Or – |
| ☐ Vancomycin, oral, 125 mg 6 hourly for 10 days* |

| Negative CDI result: |
|----------------------|
| → CDI Checklist end. |

*Severe disease or CDI not responsive to metronidazole after 5 days. Parenteral formulation given orally.

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### Figure 2

a) CDI intervention checklist* b) CDI checklist applied to medical record order form

### Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [LegenzaAppendixSupplementalDetailCFIRConstructs.docx](#)
- [LegenzaCFIRSQUIRE2.0ChecklistFINAL.docx](#)