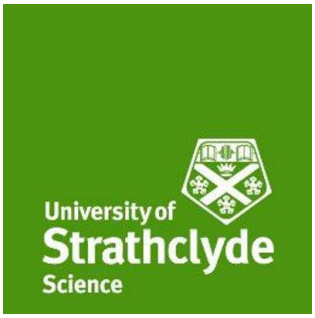
Development of a *Clostridioides difficile Infection* Risk Predictor for the Scottish health care system



Ansu Joseph Arumanatharayil

A thesis presented in fulfilment of the requirements for the degree of

Doctor of Philosophy

2025

Strathclyde Institute of Pharmacy and Biomedical Sciences

The University of Strathclyde, Glasgow

Copyright declaration

Signed:

Date: 28.01.2025

Trust in the LORD with all your heart and lean not on your own understanding; in all your ways submit to him, and he will make your paths straight. ***Proverbs 3:5-6***

Acknowledgements

I extend my heartfelt gratitude to God, who has given me the strength to persevere. I dedicate this thesis to Jesus Christ, my Savior, who encouraged me to take a leap of faith and embark on this PhD journey. His support lifted me when I felt like giving up, providing me with the courage to see it through to the end. The past few years have been a challenging roller coaster, but with the support of those around me, I have been able to complete this thesis. There were many moments when I doubted my ability to continue, but God taught me perseverance and trust, reassuring me that I am exactly where I am meant to be.

Several individuals played crucial roles throughout my PhD, and I would like to express my immense gratitude for their support. My supervisors, Dr. Amanj Kurdi and Prof. Marion Bennie, have been exceptional. They believed in me when I doubted myself and were patient during difficult times. I am truly blessed to have had such supportive supervisors, and I am forever thankful.

I would like to thank all the clinicians who participated in my studies. This thesis would not have been possible without their time and effort. Additionally, I am grateful to the Scottish Antimicrobial Prescribing Group and the Association of Scottish Antimicrobial Pharmacists for their support in recruiting clinicians for my research. To my colleagues in the Pharmacoepidemiology & Health Care Research Group, their support throughout various phases of this journey has been invaluable. When I started my PhD, I often felt lost and unsure of how to proceed, but my colleagues were always ready to offer advice and assistance. They have become great friends who significantly helped me navigate my PhD and the challenges of the COVID-19 lockdown.

Finally, I want to thank my family for their unwavering belief in me, especially my mum, whose prayers have supported me throughout this journey. To the love of my life, my husband Donel, thanking him for his constant encouragement and motivation. My daughter, Eleasha, was my inspiration during the final write-up. She motivated me to persevere through challenges, and this thesis is my way of showing her that hard times can be overcome. Although it has been a long journey, none of this could have been achieved without the incredible support of the people mentioned above.

Table of Contents

Table of figures

Table of tables

Abbreviation

AMT – Antimicrobial Management Team

CA-CDI – Community Acquired *Clostridioides difficile Infection*

CDI – *Clostridioides difficile Infection*

C.diff – *Clostridioides difficile*

CDS – Computerised Decision System

CFIR – Consolidated Framework for Implementation Research

CT – Computerised Tomography

DDD – Defined Daily Dose

EBP – Evidence Based Practice

EHR – Electronic Health Records

GP – General practitioner

GUIDES – The Guideline Implementation with Decision Support

HA-CDI – Healthcare Associated *Clostridioides difficile Infection*

HPS – Health Protection Scotland

H2 – Histamine-2 antagonist

ISD – Information Services Division

PIP – Proton pump inhibitor

PMC – Pseudomembranous colitis

SAPG – Scottish Antimicrobial Prescribing Group

TAM – Technology Acceptance Model

USA – United States of America

Glossary

Digital tools – Refers to all types of technology such software, apps, and websites.

The CDI risk predictor – Name of the tool developed in this thesis.

Low fidelity prototype – Paper based design of the tool.

Beta version – Test version of the tool.

Thesis abstract

Antibiotic use, particularly with 4C antibiotics (clindamycin, co-amoxiclav, ciprofloxacin, and cephalosporins), has been linked to *Clostridioides difficile* infection (CDI). Despite a reduction in CDI incidence in Scotland due to antibiotic stewardship, approximately 1,000 cases still occur annually. To assist clinicians with antibiotic prescribing, the University of Strathclyde developed a mathematical algorithm using Scottish CDI patient data from 2010 to 2013 to predict CDI risk within 12 months. This thesis aimed to create a digital tool for CDI incorporating this algorithm, developed in collaboration with primary and secondary care clinicians.

The tool's development was conducted across four stages using implementation frameworks and user-centred design principles:

Stage 1: Engaged three primary care GPs and a nurse through interviews, patient consultation observations, and a co-design workshop to understand their perspectives on CDI and assess the feasibility of implementing a digital tool.

Stage 2: Conducted face-to-face interviews with 10 clinicians from primary and secondary care to validate findings from Stage 1, understand the burden of CDI in secondary care, and explore the potential implementation of a low-fidelity prototype.

Stage 3: Collaborated with the digital solutions company SWARMonline to develop a beta version of the CDI tool, named the CDI Risk Predictor, which was web-accessible on various devices. Insights from Stages 1 and 2 informed this development.

Stage 4: Tested the CDI Risk Predictor with 17 clinicians from primary and secondary care through focus groups and one-on-one interviews. Participants provided feedback on layout, content, ease of use, and usefulness, which was supplemented by survey statements. Amendments were made to the CDI Risk Predictor based on participant feedback.

This comprehensive approach ensures the development of a user-informed digital tool to aid in CDI risk prediction and management in Scotland, potentially enhancing CDI prevention strategies.

Thesis summary

Background: *Clostridioides difficile* is a spore-forming anaerobic bacteria that can reside asymptomatic in the gastrointestinal tract. However, the bacteria transform into its activated form following the consumption of antibiotics especially 4C antibiotics (clindamycin, co-amoxiclav, ciprofloxacin and cephalosporins), colonializes the gut and start to produce toxins that cause diarrhoea, abdominal pain, colitis and in some cases death.

In order to reduce the incidence of the infection it is important to reduce unnecessary antibiotic prescribing. As a result of the nationally coordinated and funded antimicrobial stewardship programme, the incidence of CDI has been reduced from its peak of 6,516 cases in 2008; nevertheless, there are around 1000 incidences of CDI annually. In order to support clinicians during antibiotic prescribing and to further reduce the incidence of CDI, a mathematical algorithm has been created by University of Strathclyde using Scottish patient data from 2010 to 2013, with the aim of calculating a patient's risk to develop CDI within 12 months. Therefore, the overall aim of this thesis was to use the mathematical algorithm to develop a digital solution for CDI to support clinicians during antibiotic prescribing.

Methods: The development of the digital tool for CDI took place in four stages which were informed through the Consolidated Framework for Implementation Research (CFIR), the Guideline Implementation with Decision Support (GUIDES) checklist and the Technology Acceptance Model (TAM). Stage 1 involved face to face interviews with primary care GPs to understand their perception on CDI, investigate their perception of using technology during consultation with patients, understand their preferred layout and format for a digital tool for CDI. The interviews were then followed by observation of patient consultation with the clinicians that allowed investigation of what stage of the consultation the CDI tool could potentially be used. Finally, the last activity in stage 1 was conducting a co-design workshop with GPs to create a low fidelity prototype of the CDI tool. Stage 1 began in February 2018 and concluded in October 2018. Stage 2 involved face to face interviews with clinicians from primary and secondary care between April and May 2019. The aim of the study

was to understand clinician's perception of CDI in secondary care, their use of technology during consultation, obtain feedback on the low fidelity prototype developed in stage 1 and investigate its implementation in secondary care. Stage 3 involved developing a beta version (a version that is made available for testing) of the CDI tool using the findings from the previous stages. Finally, stage 4 utilised mixed methods to test the beta version created in stage 3 (November - December 2019). Firstly, clinicians were asked to access the beta version for CDI through their web browser on their phone and provide feedback on the tool's layout and content. Secondly, survey statements were disseminated for participants to complete to gather their perception on ease and usefulness of the tool. The study concluded by making amendments to the beta version for CDI using the feedback gathered in stage 4.

Results: The first section of stage 1 involved interviews with three GPs, who questioned the need for a digital tool for CDI, as the incidence of CDI in community is very low. Setting aside their reservations for the tool, they proposed that having a digital tool integrated into their prescribing system, that would alert them of the patient's risk to develop CDI when a 4C antibiotic were to be prescribed, as useful. Furthermore, during the observations that took place with two clinicians, a GP and a prescribing nurse, it was noted that clinicians use digital tools or prescribing guidelines while deciding the treatment choice. Similarly, the digital tool could be used while deciding the treatment to prescribe and / or to support their decision to not prescribe an antibiotic. The second section of stage 1 involved using the themes emerged in the first section to inform the co-design workshop with a GP. The workshop resulted in developing a low fidelity prototype for CDI that would be implemented into the clinician's prescribing system.

Stage 2 involved face to face interviews with 10 clinicians from primary and secondary care. The findings demonstrated that although the incidence of CDI has been reduced through the efforts put in place by antimicrobial stewardship, CDI is still perceived as a threat in secondary care. Therefore, clinicians expressed desire for a digital tool for CDI that would support their decision making. Differently from the findings in stage

1, a digital tool for CDI could not be integrated into clinician's prescribing system, due to insufficient electronic patient data. Nevertheless, clinicians were inclined to using the digital tool for CDI through an app or a website. As part of the interviews, clinicians were shown two possible risk formats for CDI if an app or website were to be developed. The first format was a bar chart that showed the patient's current risk of CDI (without being prescribed any antibiotic), the risk if a non-4C antibiotics were to be prescribed and if a 4C antibiotic were to be prescribed. The same information was also shown in a population diagram format. Despite the fact that a population diagram was easier to understand and therefore to be used during shared decision making with patients, clinician expressed usefulness in having both formats integrated into the tool.

Stage 3 involved developing a beta version, (a version that can be used for testing), with a digital solution company named SWARMonline. A procurement document was developed and shared with the company that outlined the format, layout, and content for the digital tool for CDI. The procurement document was developed using the findings that emerged from the previous stages. The beta version named The CDI Risk Predictor was developed into a website as it was easier to access through the web browser of any mobile phone, PC, laptops, or tablets compared to an app. In addition, both result formats (bar chart and population diagram) were incorporated in the digital tool for CDI.

Stage 4 aimed at testing the beta version that was created in stage 3 with clinicians from primary and secondary care. The testing of the tool was conducted in two focus groups and two one to one interviews comprising a total of 17 clinicians in the study. Clinicians used the beta version of their phones and provided feedback verbally and through completing the survey statements on the layout, content, ease of use and usefulness. Suggestions such as changing the content in the information boxes, name of the variables, and making the font size more eligible were shared. Similarly to Stage 2, in this study clinicians shared preference towards the population diagram due to its ease to understand, however they were in concordance that both formats should be kept in the tool to allow clinicians to choose whichever format they like while using

the tool. In the survey statements when asked whether the tool is relevant, out of 11 participants who completed the survey, 9 (82%) respondents stated they agree with the statement. When asked whether the tool is easy to use 8 (72%) respondents stated they agree / totally agree with the statement. Lastly, when asked whether they would use the tool, 10 (90%) respondents stated they agree / totally agree with the statement. The feedback on the layout and content were used to amend and finalise version 3 of the digital tool for CDI (The CDI Risk Predictor).

Conclusion: The four stages in this thesis informed the development of Version 3 of the digital tool for CDI (The CDI Risk Predictor). Notably, clinicians in secondary care from stage 2 showed a greater inclination towards using a digital tool for CDI compared to clinicians in stage 1. It is important to note that stage 2 had more participants (n=10) than stage 1, which had only three GPs. The preference for digital tools among secondary care clinicians could be attributed to several factors: longer appointment times, the absence of other digital tools to support their decision-making, and the majority of participants being non-medical prescribers. Although a website for the CDI digital tool was created at the end of stage 4, a future direction would involve developing a beta version of the low-fidelity prototype created in stage 1 and testing it. This approach is particularly relevant given the increasing number of non-medical prescribers conducting consultations in primary care, driven by increased demand and a shortage of GPs.

The Clostridium Difficile Infection (CDI) Risk Predictor – test Version can be accessed using the following link:

https://outreach.mathstat.strath.ac.uk/outreach/cdi/

*Currently the tool is named "The Clostridium Difficile Infection (CDI) Risk Predictor" however the nomenclature of "*Clostridium difficile*" has been changed to "*Clostridiodes difficile*". In future amendments of the tool the new nomenclature will be used.

CHAPTER 1: Introduction

1. History of *Clostridioides difficile*

Clostridioides difficile (formerly known as *Clostridium*) is a gram-positive spore-forming anaerobic bacterium, first described by Hall and O'Toole in 1935 that produces lethal toxins (Bartlett, 2008). Symptoms of *Clostridioides difficile infection* (*C.diff*) include diarrhoea, abdominal pain, inflammation, and fever. Complication can lead to pseudomembranous colitis, sepsis, and death. The bacterium was initially named *Bacillus difficilis* due to its challenging isolation properties and slow growth, it was renamed *Clostridium difficile* in the 1970s (Kuipers and Surawicz, 2008; Goudarzi *et al.*, 2014). However, since 2016 the new nomenclature of the bacterium is *Clostridioides difficile* (Oren and Rupnik, 2018). Currently it is well known that there is a direct link between pseudomembranous colitis (PMC), antibiotics, and *C.diff,* however, this was not the case until 1978 when scientists recognised the risk of *C.diff* associated with antibiotic consumption. This thesis will begin by examining the history that has contributed to the current understanding of *C.diff*, followed by an exploration of its clinical presentation.

The first observation of PMC was described in 1893 as a diphtheritic membrane in the small bowel of a 22-year-old woman who died after surgery for a gastrointestinal tumour (Bartlett, 1994). PMC involves inflammation of the inner lining of the large intestine, leading to yellow and white plaques forming pseudomembranous on the mucosa of the colon. Symptoms include diarrhoea, abdominal pain, and fever (Farooq *et al.*, 2015). The cause of PMC was unknown and notably rare until the 1950s, when the use of antibiotics increased and PMC began to merge (Depestel and Aronoff, 2013). Initial studies linked PMC to antibiotics but presumed *Staphylococcus aureus (S. aureus)* as the cause. In 1974, Tedesco et al. discovered that clindamycin, introduced a few years earlier, was a primary cause of PMC (Tedesco, Barton and Alpers, 1974). In Tedesco's study of 200 patients treated with clindamycin, 21% developed diarrhoea, and 10% had PMC. Tedesco also examined the stool of patients treated with clindamycin for the presence of *S.aureus* as previously presumed to cause PMC. Noteworthy, the stool of patients treated with clindamycin lacked the

presence of *S.aureus.* The PMC-causing bacterium remained unidentified until Larson et al. observed toxins in the stool of PMC patients in 1977 (Larson *et al.*, 1977). In fact *C.diff* has a particular characteristic of producing toxins that lead to PMC (Voth and Ballard, 2005). Larson's discovery was a significant milestone in the research around *C.diff* and probably the closest in understanding the association of *C.diff* and antibiotic-induced PMC as presently known. The same year, a study conducted by Bartlett et al. around the hamster model, found that *Clostridioides* strains were causing similar colitis that were previously reported in humans (Bartlett *et al.*, 1977). When the results from the hamster model were compared with samples of a patient with PMC, the same toxins were found in both studies, discovering *C.diff* as the bacterium producing the toxins and causing PMC in humans (Chang *et al.*, 1978)(Bartlett, Chang and Onderdonk, 1978).

There are several other studies that contributed to the comprehension of the mechanism of action of *C.diff.* However, the above mentioned studies are the key studies that led to the discovery of *C.diff* and its association to antibiotic induced PMC.

2. Pathogenesis

It took around 85 years, from the first report of PMC to the complete comprehension of the mechanism of action of *Clostridioides difficile*. History of *Clostridioides difficile* discussed the link between PMC, antibiotics, and *C.diff* bacteria, however, the pathogenesis of *C.diff is* more complex.

Bacterial species frequently colonise all surfaces of the human body with greater agglomeration in the gastrointestinal track known as microflora or microbiota. An adult's gut can contain more than 500 - 1000 different species, which differs with every individual with their age, genetics, health, and diet (Ciarán P. Kelly MD and J. Thomas LaMont, 2005). These microorganisms play a crucial role in the digestion of food, production of vitamins, and regulation of the immune system such as

prevention of pathogenic bacterial growth including *C.diff* (Ciaran P. Kelly M.B. and J. Thomas LaMont, 1991).

Following the ingestion of *C.diff* spores through the faecal-oral route, frequently found in hospital and care home surfaces, *C.diff* spores germinate and evolve into a vegetative state in the gut (Rineh *et al.*, 2014). *C. diff* bacteria and spores can reside asymptomatically in the gut due to the presence of a healthy microbiota that inhibits pathogenic growth. However, in elderly and immunosuppressed individuals, the consumption of antibiotics, especially broad-spectrum antibiotics, can lead to a phenomenon called dysbiosis. Dysbiosis is the disruption of the gut microbiota, which normally restrains *C. diff* in its vegetative state (Yoon and Yoon, 2018). This results in the outgrowth of *C.diff* which begins to produce toxins, as illustrated in Figure 1. These toxins, classified as A and B, are the main cause of intestinal inflammation, leading to abdominal pain, diarrhoea, fever, and subsequently, pseudomembranous colitis (PMC).

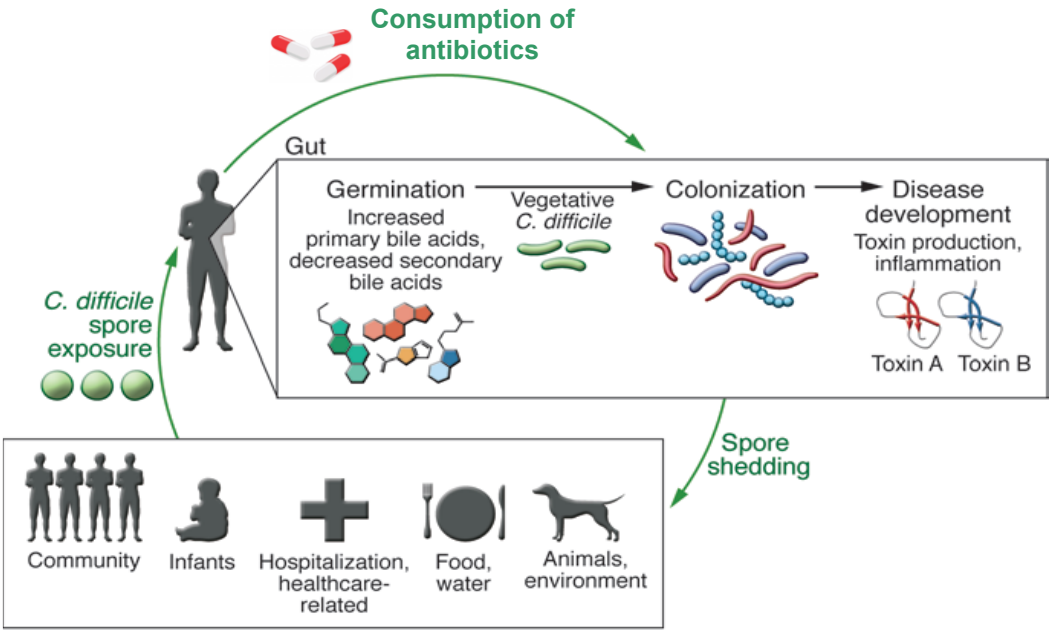


Figure 1. Mechanism of action of Clostridioides difficile infection, from first exposure to C.diff spores to the disease development and spore shedding (Seekatz and Young, 2014).

3. *Clostridioides difficile* toxins

Clostridioides difficile is a gram-positive anaerobic bacterium that has the ability to form spores (Rineh *et al.*, 2014). It is known as being the causative agent of antibiotic associated diarrhoea by its enterotoxic and cytotoxic activity through Toxin A and Toxin B. The *C.diff* spores are metabolically dormant and have the ability to survive in high temperature and to physical and chemical treatments (Voth and Ballard, 2005; Karen C. and John G., 2011; Rineh *et al.*, 2014).

Toxin A and Toxin B have the capability to disrupt and impair the actin cytoskeleton and tight junctions of epithelial cells in the intestine by binding to the *C.diff* toxin receptors (Schäffler and Breitrück, 2018), resulting with damage to the large intestine (Carter, Rood and Lyras, 2010). Initially, Toxin A was assumed to be the dominant toxin associated with CDI and necessary for virulence, however, it has been reported that actually Toxin B could be more potent, causing between 100 – 1000-fold more damage (Loo *et al.*, 2011). A study with hamsters demonstrated that the animal had greater chance to survive with the presence of Toxin A and without Toxin B, as the latter caused higher damage and highlighted its role of virulence compared to Toxin A (Karen C. and John G., 2011).

Another prominent toxin found in some strains, is the *C. difficile* Transferase or binary toxin that causes disruption of the cell's cytoskeleton that leads to fluid loss, cell rounding, and then apoptosis. It is also associated with higher mortality (Karen C. and John G., 2011)(Schäffler and Breitrück, 2018). The damages caused by toxins in PMC, have been shown to be different among people, however the lesion in the same person seems to be uniform throughout the whole infected area. Mild to moderate cases of PMC exhibited necrosis and inflammation on the infected areas, while severe cases showed complete structural necrosis with damages in the lamina propria overlaid the pseudomembranous. The PMC lesions can be detected through colonoscopy in 20-30% of the cases while characteristics lesions can be seen through computerised tomography (CT) scan (Bartlett, 2008).

4. Symptoms

CDI can be clinically presented with a wide range of symptoms, ranging from asymptomatic carriers that don't demonstrate any sign of the infection to toxic megacolon (this occurs when swelling and inflammation spread to deeper layers of the colon) (Sayedy, Kothari and Richards, 2010). Symptomatic patients can initially start with a mild to moderate CDI accompanied by a watery diarrhoea and abdominal cramping that can be resolved with medical treatment within three-four days. However, some patients can progress from mild CDI to more severe CDI that leads to inflammation, lesions, and necrosis, leading to the accumulation of neutrophils that forms the pseudomembrane in the colon (Farooq *et al.*, 2015). Individuals with severe CDI, including prolonged watery diarrhoea and abdominal pain, can exhibit symptoms such as discharge of blood and pus in the stool, dehydration, fever, kidney failure, nausea, leucocytosis, hypotension, increased lactate levels, and higher toxicity levels (Heinlen and Ballard, 2010). Severe colitis can also require colectomy procedures with some patients; however, mortality can still remain high up to 57% (Seltman, 2012).

It is still unknown why certain patients progress from mild to severe CDI, although factors such as age, and the immune vulnerability of the host are considered to be the reason of severe and persistent manifestation of CDI.

5. Risk factors

CDI is induced following the phenomenon called dysbiosis, the imbalance of the organisms in the gut (as seen in Pathogenesis). Dysbiosis can be caused by many diseases such as inflammatory bowel disease, gastrointestinal disorder and other diseases. However, studies have shown that broad-spectrum antibiotics, along with the targeted infection, affect and disrupt the protective microbiota. The state of dysbiosis leads the patient to be more susceptible to infections including CDI. Studies have shown that the colonisation and the presence of *C. diff* in the gut differs within

age groups. The highest rate of the bacteria is found in new-born babies until the age of one, subsequently decreasing with age. Although the rate of toxins in babies' stools are higher, the incidence of colitis or diarrhoea is uncommon. A theory that explains this factor is the lack of toxin receptors that binds the *C.diff* toxin A in infants (Ciaran P. Kelly M.B. and J. Thomas LaMont, 1991; Shim, 2014; Lees *et al.*, 2016). Other studies have examined the role of breast milk immunoglobin that prevents the binding of toxin A to the receptor (Shim, 2014; Lees *et al.*, 2016). Another possible cause is the immature gut microbiota in children, which compared to adults. As children's gut flora is developing, it may be more resistant to overgrowth of bacteria like *C.diff* and inhibiting its expression of toxins, and allowing for asymptomatic carriage (Vasilescu *et al.*, 2021).

Differently from children, only 3% of healthy adults are carriers of *C.diff* strains, while in elderly or immunosuppressed people the bacteria is found to be more prominent (Levinson, 2012). Although CDI causes severe cases of hospitalisation and recurrence, there are characteristics that make a person at higher risk to contract CDI than others. One of the main risks is age, with patients aged over 65 years having a greater risk than someone younger. In fact, elderly people have demonstrated to be more susceptible to *C.diff* since the changes to the immune system are a consequence of age advancement (Asempa and Nicolau, 2017). Additionally, consumption of antibiotics, use of proton pump inhibitors (PPI), Histamine-2 (H2) antagonist, and comorbidities such as cancer chronic kidney disease and inflammatory bowel disease have been reported to increase the overall risk to contract CDI (Weiss *et al.*, 2015; Berenson *et al.*, 2023).

A further risk factor is previous hospitalisation, as studies have shown that the bacteria can be transmitted through the faecal-oral route from hospital surfaces and caregivers. Exposure to healthcare settings places patients at a higher risk of infection and other complications compared to the general population due to increased pathogen exposure, frequent procedures, and close contact with others(Liubakka and Vaughn, 2016; Miller *et al.*, 2020).

Other risk factors for CDI include the use of non-steroidal anti-inflammatory drugs (Permpalung *et al.*, 2016), the host's genetics composition which can protect or increase the risk of contracting CDI (Ananthakrishnan *et al.*, 2013), deficiency of Vitamin D (Furuya-Kanamori *et al.*, 2017), and obesity (Leung *et al.*, 2013).

5.1. Pharmacological agents

Antibiotics are widely used for the treatment of infectious disease and as prophylaxis. There are many benefits of the use of antibiotics, however, there are also reports of their side effects including CDI.

The use of antibiotics was associated with colitis from the 1950s as noted in the History of *Clostridioides difficile*. Patients using antibiotics increase the risk of CDI by sixfold compared to those who are not consuming antibiotics (Deshpande *et al.*, 2013; Eze *et al.*, 2017) as it is thought to be correlated with dysbiosis that leads to the colonisation of CDI and display of symptoms. Most antibiotics increase the risk of CDI however the 4C antibiotics (clindamycin, cephalosporins, co-amoxiclav and ciprofloxacin) have demonstrated to increase the risk of CDI greatly compared to other antibiotics (Castro *et al.*, 2019). Hence antibiotic stewardship targeting the reduction of CDI has been highly recommended, targeting the reduction of the 4C antibiotics (Eze *et al.*, 2017). Although most antibiotics increases the risk of CDI (Ticinesi *et al.*, 2015), there has been reports suggesting that certain antibiotics such as fluroquinolones have greater interactions with the CDI NAP1/B1/027 strain (Wilcox *et al.*, 2017).

Furthermore, a 2023 case-control study that aimed at evaluating which antibiotic types are greatly linked with community-associated CDI, found that clindamycin and cephalosporins were associated with the highest levels of risk while tetracyclines such as minocycline and doxycycline were associated with the lowest levels (Miller *et al.*, 2023).

Another factor that makes some antibiotics more susceptible to causing CDI is the host's characteristics such as their age, gender, and/or comorbidities. Therefore, although the 4C antibiotics may significantly increase the risk to contract CDI, other antibiotics cannot be excluded as potential risk factors.

Despite the known risk of antibiotics for CDI, a nested case-control study in Quebec demonstrated that among 836 patients with CDI, 442 had no antibiotic exposure in the previous 45 days, and 382 had no antimicrobial exposure in the previous 90 days

before contracting CDI, questioning the strength of the link between antibiotics and CDI (Dial *et al.*, 2008). While antibiotics significantly impact the incidence of CDI, other risk factors, such as the use of gastric acid suppressors, also contribute to the development of CDI.

Gastric acid suppressors are used to treat gastrointestinal disorders such as dyspepsia, gastro-oesophageal reflux disorders and, peptic ulceration. The commonly used gastric acid suppressor PPI and H2 antagonists, are also commonly associated to increase the risk of CDI. Exposure to PPI and H2 has been associated to cause imbalance in the microbiota of the digestive track, allowing pathogenic microbes such as *C.diff* to proliferate (Weiss *et al.*, 2015). A systematic review conducted by Leonard et al in 2007 on the risk of enteric infections caused by acid suppressors reported a greater association of CDI with the use of PPI compared to H2 antagonist.

This effect could be due to PPIs being highly potent acid suppressors that elevate the pH level within the stomach. By inhibiting the enzyme system responsible for secreting gastric acid, PPIs reduce overall acid production, leading to increased intragastric pH in the digestive tract. This less acidic environment can affect various digestive functions, potentially impacting the balance of gut microbiota and absorption of certain nutrients, as well as the efficacy of drugs that depend on acidic conditions for optimal absorption. (Leonard, Marshall and Moayyedi, 2007; Tian *et al.*, 2023). A meta-analysis found similar findings on the impact of PPI on CDI compared to H2 antagonist. Additionally, the meta-analysis also highlighted the risk of combining PPI with antibiotics which was observed to be greater than the two treatments alone (Kwok *et al.*, 2012).

5.2. Patient demographics

A risk factor for CDI is the patient's age, where many studies have observed that patients older than 65 years are at a greater risk of contracting CDI compared to the younger population (Bignardi, 1998; Beaulieu *et al.*, 2007; Eze *et al.*, 2017). This is due to immuosenescence caused by the deterioration of the immune system due to

ageing as it is a factor for the decrease in the cell function and reduction of B-cells and T-cells that play crucial roles for microbial suppression within the body (Asempa and Nicolau, 2017).

In the United States of America (USA), 93% of deaths in 2008 due to CDI occurred in patients older than 65 years (Depestel and Aronoff, 2013). In 2011, individuals over 65 years had a fourfold increased risk of CDI compared to those aged 44 and 65 years, and thirteenfold higher risk compared to those aged 18 and 44 years (Eze *et al.*, 2017; Olsen *et al.*, 2018).

However, the USA Emerging Infection Program reported that in 2011, only 57% of CDI cases were in the elderly population, suggesting that younger individuals are also at a higher risk of CDI than previously assumed (Olsen *et al.*, 2018). In fact, a Canadian study reported that every year after the age of 18 years the risk to contract CDI increases by 2% (Loo *et al.*, 2011). This is due to the body ageing and causing physiological alteration such as the reduction of intestinal microbiological diversity and the impairment in bladder function that can make an individual more susceptible to infections and illnesses. Olsen et al, conducted a study to observe the impact of age on CDI, where the findings suggest that age is not a direct contributor to CDI, whereas the physiological conditions of the individual are the contributing factors to CDI (Olsen *et al.*, 2018). This suggests that younger individuals with deteriorative medical conditions may be at a greater risk of CDI than healthy older individuals.

Gender has also been recognised as a risk factor towards CDI (Beaulieu *et al.*, 2007). Females have been shown to be at a greater risk compared to males (Lessa *et al.*, 2014). The risk of CDI is greater in women due to the differences in the microbiota caused by hormone levels (Natarajan *et al.*, 2015). Although the stereotype around gender roles has changed, there is an assumption that women are more prone to CDI than men due to their role of being care giver. This includes working in health care facilities and caring for elderly and children, which increases the likelihood of being in contact with *C.diff* spores and develop asymptomatic or symptomatic CDI.

5.3. Comorbidities

It is also important to consider the impact of comorbidities on CDI. An individual with inflammatory bowel disease, cancer, chronic pulmonary disease, renal disease, and / or congestive heart disease has been linked with a greater risk to contract CDI (Boven *et al.*, 2023). This is due to physical changes the patient experiences due to the comorbidity and the effects that may be caused by the consumption of antibiotics or gastric acid suppressant as a treatment (Boven *et al.*, 2023).

In 2015, a systematic review and meta-analysis conducted in the USA on community acquired CDI (CA-CDI), with the aim of understanding the association of commonly prescribed medications and comorbidities with CA-CDI identified that individuals with inflammatory bowel disease had the highest risk of contracting CDI compared to other comorbidities, followed by renal disease and cancer (Furuya-Kanamori *et al.*, 2015).

6. Transmission of *Clostridioides difficile* infection

Clostridioides difficile is transmitted via faecal-oral route among individuals. Transmission within healthcare setting is common with CDI patients and healthcare workers (Weber *et al.*, 2013). Hospitalised patients with CDI transmit *C.diff* spores 15 times more than asymptomatic carriers (Durham *et al.*, 2016). Patients with CDI shed a high concentration of CDI spores, which can reside in the skin, bedding, equipment, and hospital surfaces (Donskey, 2010). Studies have shown that healthcare worker's hands distribute the infection around the hospital because of poor coherence to hand wash guidelines. Airborne dispersal has also been demonstrated to be another approach for spore diffusion around health care settings. Patients residing in the same room of previously admitted CDI patient have greater chances to develop CDI compared to those who reside in other rooms. Highlighting that there is a poor adherence to disinfection protocols of previously admitted CDI patients (Donskey, 2010). In a study conducted by Durham et al, in the USA, uninfected patients in

hospital have the probability to contract CDI on a daily basis of 2.3%, while in nursing home the probability of 0.37% and in community of 0.12% (Durham *et al.*, 2016).

Differently within the community, CDI is commonly transmitted through the environment including parks, chain stores, restaurants, and commercial stores (Alam *et al.*, 2017). There has been reports that *C.diff* strains were found in domestic animals and livestock farms including retail meat and animal food across Europe. A study on ready to eat meals demonstrated 47.8% meals were contaminated with *C.diff* strains (Durovic, Widmer and Tschudin-Sutter, 2018). In a study conducted in South Wales, *C.diff* was isolated from 21% of the soil and 2.4% of unwashed vegetables (Al Saif and Brazier, 1996).

As *C.diff* spores have the ability to survive long periods in water, there has been reports of *C.diff* spores found in water in different parts of the world. In 2007 Finland experienced contamination with sewage effluent from a municipal wastewater treatment plan that caused around 8,000 people to become ill, of which 1,000 experienced symptoms of gastroenteritis as experienced with CDI (Kotila *et al.*, 2013). In the UK, *C.diff* has also been isolated in sea water, rivers, lakes, and chlorinated water (Al Saif and Brazier, 1996). The water contamination is highly assumed due to the presence of sewage treatment plants in rivers. An explanation to swimming pool contamination could be due to children being carriers of asymptomatic CDI (Shim, 2014). A study in Zimbabwe has shown the presence of *C.diff* in well water and household stored water. The author explained that water contamination could be the result of free range domestic animal, as their faeces were commonly contaminated with *C.diff* (Simango, 2006).

6.1. Epidemiology

Outbreaks of CDI reported in the USA and Europe have been attributed to the emergence of the *C.diff* strain PCR-ribotype 027, also known as North American pulsed field gel electrophoresis type 1 (NAP1) or restriction endonuclease analysis group BI (BI/NAP1/027) (Oka *et al.*, 2012; Sartelli *et al.*, 2019). Different strains are

currently causing CDI around the world however the BI/NAP1/027 strain has been associated as the most potent with greater damage to the patient's intestine and with increased chances of relapse compared to other strains (Kaltsas *et al.*, 2012). Other studies have shown that the strain is also associated with a greater incidence in North America and in Europe (Depestel and Aronoff, 2013; Spigaglia, 2016; Sartelli *et al.*, 2019).

Clostridioides difficile infection is classified as healthcare associated (HA) if the patient contracts CDI within 48 hours after hospitalisation or inpatient in a hospital facility 12 weeks prior to the occurrence of the infection. Initially CDI was presumed to be only healthcare associated, however community acquired (CA)-CDI has been rising more in recent years. Several studies have been reporting cases of CA-CDI among young and healthy individuals. Patients are classified as CA-CDI when no prior hospitalisation in the previous 12 weeks has occurred.

The cost of CDI to health care systems is increasing. A study in Ottawa estimated the median length of hospitalisation for patients who were diagnosed with CDI was 34 days compared to patients without CDI that was 8 days (Forster *et al.*, 2012). The US Healthcare Cost and Utilisation Project estimated the cost of all CDI cases for 2009 to be around $8.2 billion while the average cost for the treatment of a single CDI case was $24,400 (Depestel and Aronoff, 2013). A 2020 retrospective cohort study in Scotland that aimed at investigating the cost of CDI for health care services, found that the median initial cost for each CDI case was £1713, which increased to £5126 after 6 months (Robertson *et al.*, 2020).

6.2. Epidemiology of *Clostridioides difficile* globally

Clostridioides difficile has become a major healthcare burden from the beginning of the 2000s, leading to an increase in hospital costs, length of hospitalisation, and mortality. In the United States, the rate of CDI is escalated and doubled between 1996 and 2003 with an incidence rate of 61 per 100,000 population. Differently in Quebec, Canada the rate of CDI doubled between 1991 and 2003 from 65.6 to 156.3 per

100,000 population with an increased complication rate from 7.1 to 18.2% and a 30 day mortality increase from 4.7 to 13.8% (Depestel and Aronoff, 2013). Between 1999 and 2004, 20,642 deaths in the USA and 3,393 deaths in the United Kingdom were reported to be caused by CDI (Martinez, 2012).

Although CDI was initially assumed to be exclusively healthcare associated (HA)-CDI, there have been reports of an increasing percentage of CA-CDI occurring in the US and in the UK. A study conducted in Minnesota comparing the incidence of CA-CDI between 1991 and 2005 showed a 5.3-fold increase, from 2.8 per 100,000 person-years in 1991-93 to 14.9 per 100,000 person-years in 2003-05. The study also compared the incidence of HA-CDI, which increased by 19.3-fold, from 2 per 100,000 person-years in 1991-93 to 40.2 per 100,000 person-years in 2003-05 (Khanna *et al.*, 2012). Additionally, there have been reports that patients who experienced CA-CDI, seem to be generally female, younger in age and with less comorbidities compared to those experiencing HA-CDI (Fellmeth, Yarlagadda and Iyer, 2010). The reason why women are more frequently affected by CDI is not completely clear. However, one hypothesis suggests that hormonal differences between men and women may play a role. Additionally, women tend to have higher rates of urinary tract infections (UTIs), which often lead to increased antibiotic use, potentially contributing to a higher risk of CDI (King *et al.*, 2017).

A study conducted by King et al. compared the incidence of CDI in North America and England, finding similar rates in 2007 at approximately 108 per 100,000 population. Subsequently, in England, the implementation of strict patient isolation and antibiotic stewardship led to a 30% reduction in CDI by the end of 2010. By March 2015, the CDI rate in England had further decreased to 26.3 per 100,000 population, and deaths due to CDI had decreased by 70% between 2007 and 2010 (King *et al.*, 2017).

In contrast to the extensive reports discussing the epidemiology of CDI in North America and Europe, there is limited information about the incidence of CDI in regions such as Asia, South America, and Africa (Balassiano *et al.*, 2012; Legenza *et al.*, 2018). The reported incidence in these regions is lower compared to the US and UK, which may be attributed to a poor understanding of CDI and limited availability

of CDI testing equipment (Borren *et al.*, 2017). A systematic review measuring the incidence rate in Asia found it to be 5.3 per 100,000 patient days. Additionally, the prevalence of the ribotype BI/NAP1/027 strain in Asia was only 0.7%, significantly lower than the 20% prevalence found in England (Borren *et al.*, 2017).

6.3. Epidemiology of *Clostridioides difficile* in Scotland

Scotland has had outbreaks of CDI cases similar to other European countries. Although initially, ribotype BI/NAP1/027 was not frequently seen in Scotland, due to outbreaks in North America and in other European countries, it has been reported to be causing CDI since 2008 in Scotland (Wiuff *et al.*, 2011). In 2008, the Scottish Government established the Scottish Antimicrobial Prescribing Group (SAPG) to lead a national antimicrobial stewardship programme, primarily in response to rising deaths caused by CDI in hospitals. These infections raised significant public concern and led to a formal public inquiry. The findings of this inquiry were published in 2014 in the Vale of Leven Hospital Inquiry Report (Nathwani *et al.*, 2012; MacLean and Chairman, 2014). One of the strategies undertaken to reduce the incidence of CDI was minimising the utilisation of 4C antibiotics. Figure 2 illustrates the decrease of 4C antibiotic prescribing in Scottish primary and secondary care settings across the health care system in Scotland; there has been an almost 50% decrease of antibiotic prescribing in primary care since 2009. However little change in secondary care was observed. These factors have likely contributed to the 77% reduction in CDI among patients older than 65 years between 2007 and 2013, and the 54% decrease among patients aged 15 to 64 years between 2009 and 2013 (Health Protection of Scotland, 2013).

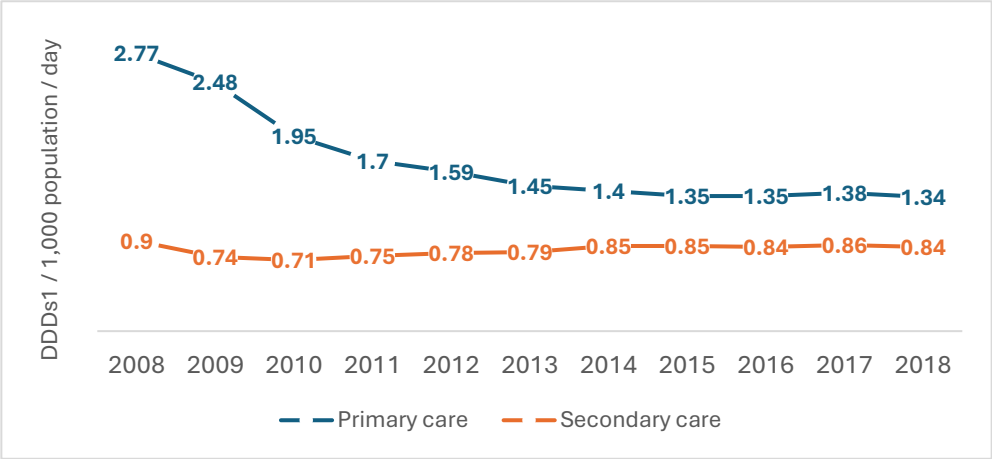


Figure 2. Total use of 4C antibiotics (clindamycin, cephalosporins, co-amoxiclav and ciprofloxacin) from 2008 to 2018 in Scottish primary and secondary care across NHS Scotland. The indicator DDD[1] per 1,000 population per day suggests what portion of a population are regularly using 4C antibiotics. (The data in this graph was shared through personal communication from a member of the staff of Health Protection of Scotland in 2019).

Initially, surveillance on CA-CDI was not reported in Scotland, however since 2013 there has been reports of CA-CDI cases, equating to around 26% of all CDI cases (Banks *et al.*, 2016). Table 1 summarises the incidence of CDI reported in Scotland by the Health Protection Scotland (now known as National Services Scotland) for the period 2014 - 2022.

Table 1. Incidence of CDI in Scotland between 2014 and 2022 reported as HA-CDI and CA-CDI cases (Data extracted by the annual reports from Health Protection of Scotland now known as National Services Scotland)

Year	Health care acquired CDI	Community acquired CDI
2014	1235	475
2015	1133	543
2016	1235	475
2017	970	399
2018	932	381
2019	806	253
2020	813	275
2021	859	276
2022	818	235
2023	917	292

Despite the fact that CDI cases are decreasing and 4C antibiotics have reduced (mainly in primary care) the prescription of all antibiotics in the Scottish primary care setting has remained relatively static: 20.06 DDDs / 1,000 population / day in 2008 and 20.49 DDDs / 1,000 population / day in 2018 (The data was shared through

[1] Defined Daily Dose

personal communication from a member of the staff of Health Protection of Scotland in 2019). As seen in pharmacological agents all antibiotics can increase the risk of CDI and consequently there is a continued need to develop tools and interventions that can support antimicrobial stewardship in the goal to reduce CDI and antimicrobial resistance more broadly. The next section of this chapter will discuss the development of a mathematical algorithm for CDI and computerised decision systems in general.

7. Development of a mathematical algorithm for the CDI Risk Predictor

The development of the mathematical algorithm for the CDI Risk Predictor was outside the scope of this PhD and is therefore not the primary focus of this thesis. However, a brief description of the algorithm's creation is provided below.

A team of statisticians from the Health Statistics and Modelling group, at the University of Strathclyde developed the mathematical algorithm for the CDI Risk Predictor, which development will be seen in this thesis. The algorithm for the CDI Risk Predictor was derived using Scottish CA-CDI cases from August 2010 to July 2013 extracted from three NHS patient-level datasets: the Electronic communication of surveillance in Scotland (ECOSS), Prescribing Information System (PIS) and General/Acute and Inpatient Day Case dataset (SMR01).

From the collected data, there were a total of 1,446 of CA-CDI with 7,964 matched controls based on age, gender, and location (Kavanagh *et al.*, 2016). ECOSS records all positive *C.diff* tests from NHS laboratories in Scotland through mandatory reporting; SMR01 records episode-level data of inpatients and discharges from Scottish hospitals; and the PIS records all the prescriptions dispensed in the Scottish primary care setting. The mathematical algorithm was built using conditional logistic regression accounting for the matched case/control design. Additionally, ICD-10 codes were used to categorise the comorbidities used to develop the mathematical model for CDI (Kavanagh *et al.*, 2016).

The population-wide study to create the algorithm examined validated cases of CDI to assess the risk of CA-CDI linked to antibiotic prescriptions in the community. Antibiotic exposure within the previous six months was associated with an elevated risk of CDI, with this heightened risk persisting for up to three months post-exposure. Nearly 60% of CA-CDI cases had been prescribed antibiotics within the preceding six months, though clindamycin was rarely used. Notably, almost 30% of CA-CDI cases had received 29 or more DDDs of antibiotics in the six months prior to CDI onset, involving various antibiotics such as ciprofloxacin, co-amoxiclav, amoxicillin, flucloxacillin, doxycycline, nitrofurantoin, and trimethoprim (Kavanagh *et al.*, 2016).The algorithm was developed to support the development of a Computerised Decision System (CDS) in the form of an application (app) to predict a patient's risk of contracting CDI in the next twelve months, specifically at the point of antibiotic prescription in primary caree. The algorithm predicts the risk of CDI for three scenarios: no antibiotic prescription, non-4C antibiotics prescribed (all antibiotic not marked as high risk for CDI), and 4C antibiotics prescribed (high risk antibiotics for CDI). To predict the risk score for CDI, several variables including patient demographics, medication and comorbidities need to be entered.

While the algorithm was initially developed using patient data from 2010 to 2013, its applicability remains strong due to the stable incidence rates of CDI observed over the past decade. As shown in Table 1, the incidence of CDI has remained relatively consistent since 2014, highlighting the algorithm's continued relevance for predicting CDI risk in 2024. This stability in incidence rates suggests that the factors influencing CDI risk, as captured by the original algorithm, have not significantly shifted and therefore using a CDI tool with the current algorithm would be still beneficial in calculating a patient's risk to develop CDI.The statistical team initially created a list of potential predictors/variables (Table 2) for the CDS tool. After assessment through conditional logistic regression, a final list of variables was created to derive a risk score (Kavanagh *et al.*, 2016). The final list of predictors are fewer as the study to develop the algorithm found the final list to be more impactful towards CDI compared to the initial list. A website version of the tool was also created by the statistical team

to facilitate early testing of the algorithm and to explore the design of the CDS tool. Figure 3 represents the website version, which, for the purpose of this thesis, will be named Prototype 1.

Table 2. Initial and final list of risk predictors for the mathematical algorithm for CDI developed by the statistical team at the University of Strathclyde. All the words in blue are changes made in the final list. (List provided by a member of the team)

Variables	Initial list of potential predictors	Final list of predictors
Demographic variables	- SIMD (socioeconomic quintile) - Age, gender, location matched - Resident in care home	- Age, gender - Resident in care home
Health care variables	- Number of hospital admission in the previous year - Number of emergency hospital admission in the previous year - Days of hospital stay in the previous year - Total number of dispensed items last year - Total number of different dispensed items last year - PPI in the community in the last 6 months - H2 antagonist in the community in the last 6 months	- PPI in the community in the last **3** months - H2 antagonist in the community in the last **3** months
Antimicrobial exposure	- DDDs of any antimicrobial exposure in the community in the last 6 months - DDDs of 4C exposure in the community in the last 6 months - DDDs of non-4C antimicrobial exposure in the community in the last 6 months - Days since most recent exposure to any antimicrobial in the community in the last 6 months - Days since most recent exposure to 4C in the	- **Number of (different) antimicrobial** in the community in the last **3** months - **Number of (different) 4C** in the community in the last **3** months - **Number of (different) non-4C** in the community in the last **3** months - Days since most recent **dispense** to any antimicrobial in the community in the last **3** months - Days since most recent **dispense** to 4C in the

	community in the last 6 months - Days since most recent exposure to non-4C in the community in the last 6 months	community in the last **3** months - Days since most recent **dispense** to non-4C in the community in the last **3** months
Comorbidities	- Congestive heart failure, cardiomyopathy - Atherosclerosis, aortic aneurysm, vascular disease - Stroke - Dementia - Bronchitis, pneumoconiosis - Gout, lupus, rheumatoid arthritis - Gastro ulcers - Liver problems - Diabetes - Diabetes with complications - Hemiplegia, paraplegia - Renal problems - Cancer - Alcohol-related liver failure - Metastatic cancer - Inflammatory bowel disease	- Congestive heart failure, cardiomyopathy - Atherosclerosis, aortic aneurysm, vascular disease - Stroke - Dementia - Bronchitis, pneumoconiosis - Gout, lupus, rheumatoid arthritis - Gastro ulcers - Liver problems - Diabetes - Diabetes with complications - Hemiplegia, paraplegia - Renal problems - Cancer - Alcohol-related liver failure - Metastatic cancer - Inflammatory bowel disease

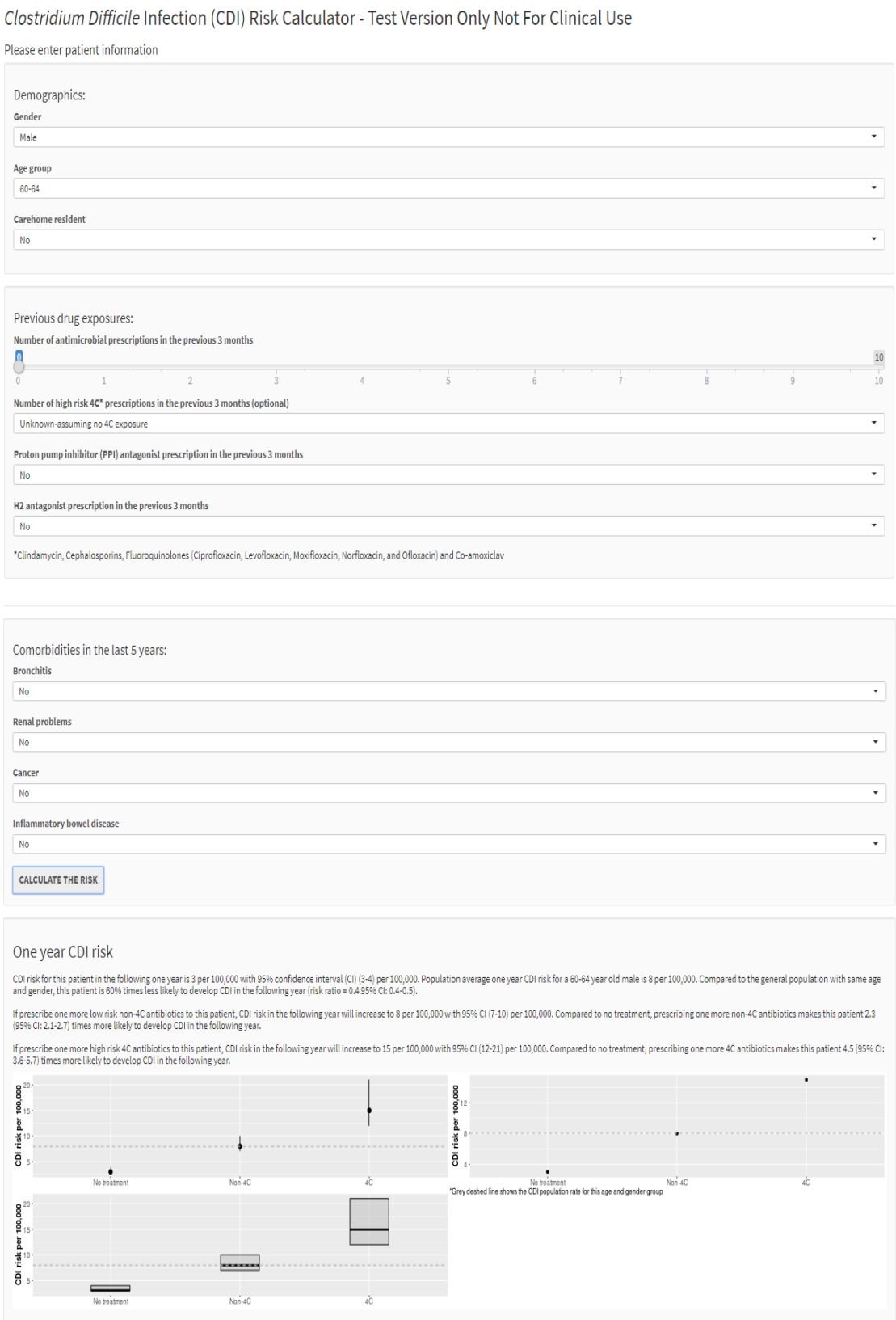


Figure 3. The CDI risk predictive tool Prototype 1 developed for testing by the statistical team at the University of Strathclyde

8. Computerised decision systems

As health care systems evolve, treatment options expand and clinical data becomes more digital the range of tools and resources to support clinicians in choosing the most appropriate treatment, weighing the benefits and the potential harms has increased. Although clinicians are trained to make treatment decisions, some can be unnecessary or harmful for the patient (Van de Velde *et al.*, 2016). To enhance and improve patient care delivery using patient data, computerized decision systems (CDS) have been introduced into the healthcare system. As the availability of patients' electronic health records (EHR) expands, the use of CDS tools that leverage a patient's EHR to generate disease prognosis or treatment recommendations has grown within the healthcare system (Garg *et al.*, 2005).

CDS tools are used for the prevention, diagnosis, and treatment of numerous diseases. There are two main types of risk prediction tools: (i) risk prediction of an undiagnosed condition in symptomatic individuals, and (ii) risk prediction of future condition development in asymptomatic individuals (Usher-Smith *et al.*, 2015). These prediction tools are created through multifactorial models that incorporate relevant risk factors or variables (Dent *et al.*, 2012). Risk factors can range from age to genetic biomarkers (Dent *et al.*, 2012) and can be either input by the clinician or automatically derived from the HER (Garg *et al.*, 2005).

CDS tools can provide recommendation by considering the patient's characteristics, as well as the risks and benefits associated with the available treatments (Thomson et al., 2005). The output of these tools can come in various formats, such as risk alerts, reminders, advice for drug treatment, and diagnostic support in numerical or graphical representations (Garg et al., 2005).

The use of CDS tools has facilitated shared decision-making, where patients and clinicians discuss the risks and benefits of individual treatments to choose the most appropriate therapy (Feldman-Stewart *et al.*, 2000)(Thomson, Edwards and Grey, 2005). Graphical illustrations of risk can enhance communication between patients and clinicians, leading to better treatment decisions (Pick, 2008).

8.1. Benefits of using Computerised decision systems

During consultations, clinicians are expected to provide prognoses to patients by analysing symptoms and laboratory test results. Their ability to provide precise diagnoses relies on previous experience, clinical judgment, and personal beliefs (Wasylewicz and Scheepers-Hoeks, 2019). Although clinicians are trained to make such predictions, their interpretations can sometimes be inaccurate, potentially leading to inappropriate treatments and the deterioration of a patient's health condition. To support clinical judgment, computerized decision systems (CDS) can assess patient data using mathematical algorithms to provide the likelihood of specific outcomes over time.

The intention of CDS is to assist clinicians while informing patients about their risks of disease development, considering the multifaceted treatment outcomes (Dagliati *et al.*, 2018). Often, due to the busyness of practice or limited understanding of a specific condition, clinicians may mishandle conditions, leading to overtreatment of low-risk patients and undertreatment of high-risk patients, resulting in medical complications (Rossello *et al.*, 2019). While many guidelines provide treatment suggestions for specific conditions, these are designed for the general population. Individual patients have different needs and risks, and a CDS tool that compares a patient's risk to that of the general population can refine treatment choices for individual patients, acknowledging the heterogeneity in risk (Billheimer *et al.*, 2014).

Using CDS tools can reduce unnecessary medical conditions caused by human error, benefiting the healthcare system by lowering financial costs. For example, treating a patient with CDI can cost around $24,000 (Zhang *et al.*, 2016), but a CDS tool that predicts the patient's risk can initiate preventive approaches to potentially avoid the infection. In addition to reinforcing the clinician's decision-making process with evidence, CDS tools can also reduce decision-making time. While a similar treatment choice might be reached without a CDS tool, the tool can facilitate a faster workflow (Pick, 2008).

Since COVID-19, technology in healthcare has been spotlighted as healthcare providers faced overwhelming demand due to the large number of patients needing care. A major advancement was the rapid adoption of remote healthcare services and digital tools to support virtual consultations. As a result, new tools were developed, and regulatory approval and adoption processes were expedited to meet urgent needs (Getachew *et al.*, 2023). Digital tools that previously saw limited use became essential for patient assistance during the pandemic (Fahy *et al.*, 2021). Athough digital tool usage surged during COVID-19, it is essential to implement active strategies to promote their continued use and integration, ensuring they remain beneficial in routine practice. These strategies might include training for healthcare providers, regular updates to maintain tool functionality and relevance, and ongoing evaluation of their impact on patient care and outcomes (Williams *et al.*, 2022).

8.2. Factors influencing the adoption of CDS tools

The integration of technology into the healthcare system has revolutionised traditional consultation and treatment approaches, particularly through the use of CDS tools. These CDS tools, capable of predicting disease development, enable preventive actions that reduce disease occurrence. Despite the documented benefits of risk prediction tools and CDS tools, their successful implementation and adoption remain limited (Kux *et al.*, 2017).

Several factors contribute to the reluctance of lead clinicians to adopt CDS tools, ranging from technological issues to implementation processes and personal attributes of the clinicians themselves. One major influence on adoption is the quality of the CDS tool, specifically its user-friendliness, usefulness, and contribution to alert fatigue (Kux *et al.*, 2017). Frequent and irrelevant alerts during consultations are a significant barrier, leading to a high rate of ignored alerts (49-96%) (Wadhwa *et al.*, 2008; Van de Velde *et al.*, 2016). Therefore, involving end users in the development of Clinical Decision Support (CDS) tools with alert features is essential to ensure that these alerts are both relevant and effective. When end users (typically healthcare providers) are actively engaged in the design and testing phases, they can provide insights into the types of alerts that are genuinely useful in clinical practice. This

collaborative approach helps to minimise “alert fatigue,” a common issue where excessive or irrelevant alerts are ignored, potentially leading to critical information being overlooked. By tailoring alerts to the actual workflow and preferences of users, CDS tools become more intuitive and impactful, enhancing patient care and supporting clinicians in their decision-making (Olakotan and Mohd Yusof, 2021).

User centred design has been shown to enhance the uptake of decision support tools, yet it remains underutilised. Involving end-users in the development process is crucial, as their non-involvement can lead to complex and poorly adopted tools (Kerr, 2004). For further information on the topic see user centred design. Compatibility with other systems is another critical factor; outdated CDS tools that fail to integrate with newer technologies disrupt workflows and foster negative perceptions towards CDS tools (Ross *et al.*, 2016).

Resource availability in healthcare settings also influences CDS tool adoption. Poor internet connectivity and time constraints can hinder performance, making the CDS tools appear cumbersome and aggravating the workload (Kux *et al.*, 2017). Additionally, concerns over patient privacy and cybersecurity must be addressed by ensuring compliance with medical software legislation (Shibl, Lawley and Debuse, 2013).

Training and ongoing support are essential for better uptake of CDS tools. However, clinicians may perceive these tools as threats to their autonomy, particularly if they feel that their roles are being substituted. This perception can be influenced by the clinician's relationship with technology, age, and previous experiences (Liberati *et al.*, 2017).

Implementation Science frameworks have been developed to guide the successful development and adoption of CDS tools. These frameworks, when combined with end-user involvement, show promise in improving adoption rates. The next section of this chapter will explore Implementation Science and the frameworks available for this study.

9. Implementation science

Historically, evidence-based practice (EBP) has taken approximately 17 years to be fully incorporated into the healthcare system, with only about half of the interventions being adopted and disseminated beyond their development settings (Bauer *et al.*, 2015). This lengthy timeframe highlighted the need for strategies to promote and facilitate the uptake of interventions in the healthcare system, leading to the development of the field of implementation science.

Implementation science aims to facilitate the rapid adoption and widespread dissemination of interventions. It is defined as a gateway to promote and employ research findings in routine healthcare systems by using systematic and scientific approaches to identify factors that facilitate or obstruct the adoption of interventions (Moir, 2018). Studies in implementation science draw on theories from various disciplines, including sociology and psychology, as well as new theories developed specifically within the field of implementation science (Nilsen, 2015).

These theories are designed to facilitate different stages of the implementation process. While each intervention may have a unique process depending on factors such as time, stakeholders, and resources, the general stages of the implementation process include planning, engaging, executing, and reflecting and evaluating (Damschroder *et al.*, 2009). Figure 4 provides definitions for each process stage.

Additional stages, such as designing, developing, and diffusing, may also be involved depending on the nature of the intervention. The lack of a consistent, defined implementation process or a one-size-fits-all framework for every intervention arises from the heterogeneity of interventions implemented in the healthcare system. Despite the availability of various implementation processes and frameworks, researchers often face challenges in selecting the appropriate framework or theory. This difficulty sometimes leads researchers to choose inappropriate frameworks based on convenience or prior experience (Birken *et al.*, 2017).

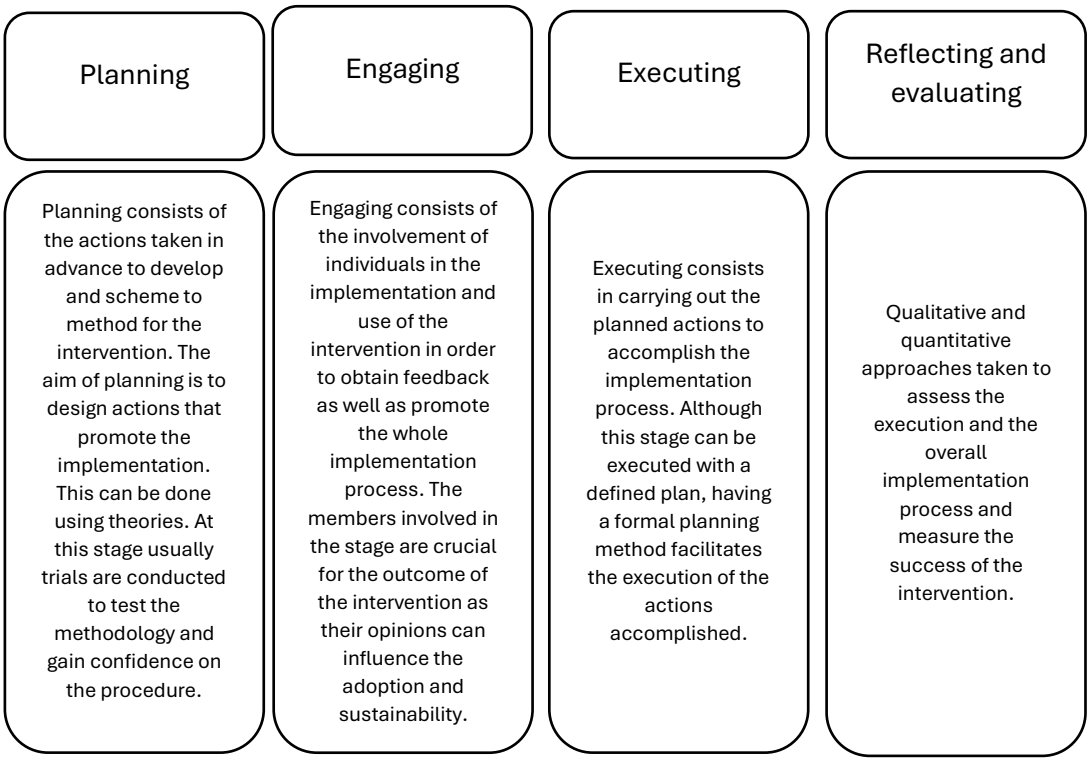


Figure 4. The implementation process stages according to the Consolidated Framework of Implementation Research (CFIR) framework (Damschroder *et al.*, 2009).

Nilsen et al. identified that all implementation frameworks or theories currently available serve one of three main aims, which should be considered during their selection. Frameworks that describe the implementation process are categorised as process models. These models outline the stages and steps necessary for implementing an intervention.

Frameworks that facilitate the identification of factors influencing implementation are categorised into determinant frameworks, classic theories, or implementation theories. Determinant frameworks focus on identifying factors that influence the implementation process, often considering barriers and facilitators. Classic theories are derived from established theories in disciplines such as sociology or psychology and are applied to the context of implementation. Implementation theories, on the other hand, are specifically developed within the field of implementation science to understand and explain implementation processes and outcomes.

Finally, frameworks that evaluate the implementation are categorised as evaluation frameworks. These frameworks are used to assess the effectiveness and outcomes of

the implementation process. According to Nilsen that at each stage of the intervention, at least one implementation theory should be used to guide the process (Nilsen, 2015).

Table 3 provides definitions for the classifications of implementation frameworks established by Nilsen.

Table 3 Definitions of the Implementation theories classification according to Nilsen (Nilsen, 2015)

Process models	Process models describe the actions that guide the implementation of an intervention. These process models describe the steps an intervention should go through for the translation of research into the practice. These steps guide from the detection of needing a change, development of the intervention and its dissemination. An example of process model is the Knowledge to action framework (Wilson *et al.*, 2011).
Determinant frameworks	Determinant frameworks describe factors that can influence the implementation. These determinants facilitate the identification of a number of enablers/facilitators or barriers that have an impact on the implementation outcome. An example of a determinant framework is the Consolidated Framework for Implementation Research (CFIR) (Damschroder *et al.*, 2009).
Classic theories	Classic theories are originated from the field of psychology, sociology or organisational theory. An example of classic theory is the Diffusion of Innovation which draws attention in involving intermediary actors that can drive the adoption and dissemination of the intervention (Everett M Rogers, 2013).
Implementation theories	Implementation theories are developed from other existing theories in the field with the aim to enhance understanding or a specific process/stage of implementation. An example is the Normalization Process theory (May and Finch, 2009).
Evaluation frameworks	Evaluation framework have been developed to evaluate the implementation stages or the outcomes of the intervention. An example of an evaluating framework is the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) (Glasgow,

	Vogt and Boles, 1999) that was developed with the intention to evaluate interventions implemented into health care.

10. User centred design

User centred design (UCD) involves developing an intervention by engaging potential end users at every stage of the design process (Rouke, 2017). The goal is to continuously capture their recommendations and feedback to develop an end product that reflects their requirements, thereby maximizing adoption. UCD is an approach widely used in computer science and follows the ISO 9241-210:2019 standards for human-centred design for interactive systems (ISO, 2019)

The UCS process is divided into four different stages:

- Analysis: This stage involves gathering requirements from the end users.
- Design: This stage focuses on designing the product to ensure it meets the users' requirements.
- Implementation: This stage involves integrating the product into the working system.
- Deployment: This stage includes continuous evaluation and amendment of the product to meet all user requirements (Wilkinson and De Angeli, 2014a).

The aim of UCD is to develop a product that avoids failure and underuse by end users due to complex design. By evaluating end users' requirements, the product is developed to match their expectations (Wever, van Kuijk and Boks, 2008). This approach has been shown to enhance commercial sales of the product, improve interaction with the tool, and decrease the need for training and support (Kujala, 2003).

11. Frameworks selected for this thesis

This thesis explores the development of a digital solution by integrating implementation science frameworks with computer science approaches and frameworks. Despite the common emphasis on end user involvement in

implementation frameworks, one major reason for the poor uptake of interventions is often the insufficient involvement of end users in all stages of the development (see section factors influencing the adoption of CDS tools). To address this, the User-Centred Design (UCD) approach was employed in various stages of this thesis (see figure 5 to see all the stages). UCD was combined with the Consolidated Framework for Implementation Research (CFIR), a determinant framework used to identify barriers and facilitators that informed the design stages of this programme. Two evaluation frameworks were selected to guide the testing stage: the Technology Acceptance Model (TAM) and Guideline Implementation with Decision Support (GUIDES). Although other evaluation frameworks were available, using frameworks from the computer science field was deemed logical due to the digital nature of the intervention. The next section will describe the three chosen frameworks and the rationale for their selection.

11.1. Consolidated Framework for Implementation Research

The Consolidated Framework for Implementation Research (CFIR) is a meta-theoretical framework introduced in 2009 by Laura Damschroder to identify contextual factors influencing implementation outcomes (Damschroder *et al.*, 2009; Kirk *et al.*, 2015). The CFIR framework, cited over 2,500 times in the past decade, was developed through a comprehensive review and synthesis of 19 existing implementation science theories and frameworks (Fernandez *et al.*, 2018). It is structured into 39 subdomains across five main domains, as detailed in Table 4 with definitions:

- Intervention Characteristics: Aspects of the intervention that influence its implementation.
- Inner Setting: Organizational factors that impact the intervention.
- Outer Setting: External or environmental factors influencing the implementation.
- Characteristics of Individuals: The influence of the people involved in the intervention.

- Implementation Process: Strategies that impact the intervention (Damschroder *et al.*, 2009)

According to Damschroder, the CFIR framework can be utilised to conduct evaluations at pre-, during-, and post-implementation stages to assess the needs of the intervention, the implementation process, and the implementation outcomes. Researchers are advised to selectively evaluate the relevant subdomains based on the nature of their intervention (Damschroder *et al.*, 2009)

CFIR was chosen as the primary framework for this study to identify factors influencing the development of the CDI Risk Predictor for the Scottish healthcare system. The framework facilitated the identification of enablers and barriers to inform the design of the tool. It guided data collection and analysis, ensuring that all factors influencing the development and implementation of the tool were captured comprehensively.

A systematic review by Kirk et al. highlighted that using CFIR for both data collection (to structure interview questions) and analysis resulted in a more thorough identification of factors influencing implementation compared to using CFIR solely for analysis. This was attributed to CFIR's role in structuring interviews as a checklist of potential influencing factors (Kirk *et al.*, 2015). This methodology was adopted for all data collection in this study.

Another reason for choosing CFIR is its broad consideration of influencing factors, designed to evaluate complex interventions comprehensively. Unlike some frameworks that are restricted to specific implementation stages, CFIR is applicable across all stages (Kirk *et al.*, 2015), making it suitable for this thesis' design stages and evaluation stage.

Finally, CFIR's development through the synthesis of 19 other implementation frameworks makes it robust and inclusive, suitable for this study. As a determinant framework, CFIR is also the most widely used among researchers, enhancing its credibility and appropriateness for this purpose (Birken *et al.*, 2017).

Table 4. Construct definitions of the Consolidated Framework for Implementation Research (CFIR) domains and subdomains (Damschroder *et al.*, 2009)

CFIR domains and subdomains	Construct Definition
Intervention characteristics	**Attributes that influence the intervention**
Intervention source	Stakeholders' perception on the intervention
Evidence strength and quality	This construct discusses the aspects that would support the desired outcomes of the intervention.
relative advantage	This construct discusses the participant's perception of the advantage of the intervention.
Adaptability	The construct discusses how an intervention can be adapted in order for users to find it useful. It includes suggestions for the improvement of the intervention.
Trialability	Testing the intervention with end users.
Complexity	The construct discusses the difficulty of the implementation of the intervention.
Design quality and packaging	The construct discusses quality and factors that do influence the quality of the intervention.
Cost	The construct discusses the cost related to the intervention
Outer setting	**External attributes of an organisation that influence the intervention**
Patients' needs and resources	This construct discusses the action the participants take in order to meet with the patient's needs.
Cosmopolitanism	Connection with other organisations
Peer pressure	Pressure to implement the intervention
External policies and incentives	Strategies to spread the intervention, such as guidelines, regulations…
Inner setting	**Internal attributes of an organisation that influence the intervention**
Structural characteristics	Composition of on organisation such as number of people, age…
Network and communication	The constructs discuss the communications channels within the organisation.
Culture	The construct discusses norms and assumptions of a practice.
Implementation climate	Perception of the intervention by the individuals involved
1. Tension of change	The construct discusses the perception of change need of the current situation.
2. Compatibility	The construct discusses aspects about the fit of the intervention with the interview's participants.
3. Relative priority	This construct discusses the importance of the intervention in their settings.

4. Organisational incentives and rewards	Incentivises that influence the performance of an organisation
5. Goals and feedback	This construct discusses objectives that would act in favour for the intervention.
6. Learning climate	The construct discusses participant's perception of an improvement need or actions they take in order to improve aspects of their consultation.
Readiness for implementation	Indication of an organisation decision for the implementation
1. Leadership engagement	Commitment of the managers in the implementation of the intervention
2. Available resource	Resources that can influence the development and implementation of the intervention.
3. access to information and knowledge	The constructs discuss about the accessibility to information that influence the adoption and implementation of tools, such as software training or consultation with experts.
Characteristics of individuals	**Attributes that influence an intervention by the individuals of an organisation**
Knowledge and beliefs about the intervention	The construct discusses participant's familiarity with truth and facts that linked with the intervention.
Self-efficacy	The construct discusses the participant's capability to conduct actions that are favourable for the intervention.
Individual stage of change	Progression of an individual in the use of the intervention
Individual identification with organisation	Individual's commitment with the organisation
Other personal attributes	An individual's characteristics such as motivation, tolerance, intellectual ability
Implementation process	**Steps for the implementation of an intervention**
Planning	A method development for the implementation of the intervention
Engaging	Involvement of appropriate individuals for the implementation
1. Opinion leaders	Individuals who have influence on the colleagues
2. Formally appointed internal implementation	Individuals from the organisations who has the role of a manager of the implementation
3. Champions	Individuals who support the implementation in an organisation
4. External change agents	Individuals connected to an external setting that influence the intervention.
Executing	Accomplish the implementation plan
Reflecting and evaluating	Quantitative and qualitative feedback of the intervention

11.2 The Guideline Implementation with Decision support (GUIDES checklist)

The Guideline implementation with decision support (GUIDES checklist) is a framework designed to help researchers in the development and implementation of computerised decision systems. The checklist has been designed to guide researchers in identifying factors that can affect CDS implementation through four different domains. The domains in the GUIDES checklist were created by Stjin Van de Velde and his team, in the Norwegian Institute of Public Health, by following four methods (Van de Velde *et al.*, 2016).

i) Reviewed available implementation frameworks and theories on factors influencing CDS (Van de Velde, Kunnamo, *et al.*, 2018).

ii) Synthesised the influencing factors reviewed in the first step, to create the first version of the GUIDES checklist. This was followed by involvement of experts in the field, clinicians, and patients to review the content of the GUIDES checklist.

iii) Following the review, they created a toolkit such as checklist and worksheet to be used during the use of the framework.

iv) Lastly, they conducted a pilot testing to investigate the usefulness of the GUIDES checklist by involving six researchers to use the checklist during the evaluation of CDS trial reports found during their research in step i). They also used the checklist to assess the development of a CDS tool for pain knee management (Van de Velde, Heselmans, *et al.*, 2018; Van de Velde, Kunnamo, *et al.*, 2018)

In addition, the GUIDES checklist was tested using the factors reported by Ross et al in the systematic review of factors influencing the implementation of e-health (Ross *et al.*, 2016). The testing demonstrated that the content of the GUIDES checklist was consistent to what was reported by Ross in the systematic review (Van de Velde, Kunnamo, *et al.*, 2018).

Differently from the CFIR, the GUIDES checklist is purely created to guide researchers for the designing, testing, and implementation of CDS tools only. The checklist was

created to be used in every health care setting around the world regardless of its size (Van de Velde *et al.*, 2016).

The GUIDES checklist is divided into four CDS domains, where each domain is tailored with definitions and recommendations.

1. The *CDS context domain* focuses on situations in which CDS can be potentially successful and beneficial.
2. The *CDS content domain* focuses on the factors shaping the success of the advice produced by the CDS system.
3. The *CDS system domain* focuses on functional features of the CDS tool.
4. The *CDS implementation domain* refers to the factors affecting the CDS integration in the health care practice.

Each of these four domains have other four subdomains that addresses possible situations and outcomes during each domain. The GUIDES checklist can be used as a guide during the development, evaluation, or implementation of CDS tools.

Although CFIR has been widely used, one limitation of the framework is its generality, its application across multiple fields. However, to better guide the research objectives of this thesis, a framework specifically tailored for (CDS) systems was required. Despite the GUIDES checklist being introduced only in in 2017, the methodology used to develop it is considered robust. One of the main advantages of the GUIDES checklist is its detailed explanations and sample questions, which enhance the understanding and practical use of the framework.

The entire GUIDES checklist can be found as part of the following website (https://www.guidesproject.org/) (de Velde, 2017).

11.2. Technology Acceptance Model

The Technology Acceptance Model (TAM) is an information systems theory developed by Fred D. Davis in 1989, which evolved from the Theory of Reasoned Action used in the psychological and sociological fields (Davis, 1989). TAM identifies key factors that influence users to adopt new technology: perceived usefulness and perceived ease of use.

Perceived Usefulness: This refers to the user's belief that using the technology will enhance their performance or facilitate their tasks.

Perceived Ease of Use: This is defined as the degree to which the user believes that using the technology will be free of effort.

As illustrated in Figure 5, TAM posits that the intention to use a technology is driven by these perceptions of usefulness and ease of use, which in turn lead to the actual usage of the technology (Kurniabudi, Sharipuddin and Assegaff, 2014). Additionally, perceived ease of use can directly influence perceived usefulness, as a tool that is easy to use is likely to be perceived as more useful due to the positive and enjoyable user experience (Davis, 1989).

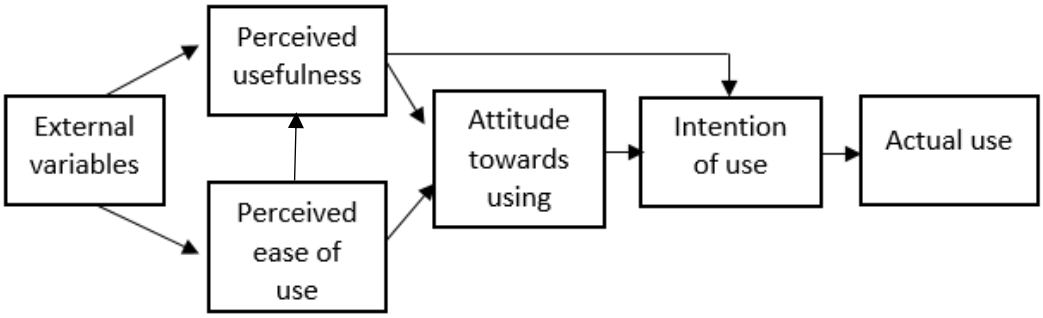


Figure 5. Technology acceptance model (Davis, 1989).

Furthermore, TAM suggests that external variables such as colleagues' opinions, system characteristics, individual preferences, and training can also impact users' perceptions of usefulness and ease of use (Dickman *et al.*, 2019).

TAM is one of the most widely used and cited frameworks for evaluating the development and implementation of CDS tools. Consequently, the concepts of ease of use and usefulness will be key factors measured in the testing stage of this thesis.

Although TAM has been widely used, it does not address the factors that can enhance the usefulness and ease of use of a CDS tool as comprehensively as the GUIDES checklist does. Despite the GUIDES checklist being a newly developed framework, it offers a more detailed approach compared to TAM. To balance the use of a widely recognized framework and a comprehensive one, both TAM and the GUIDES checklist

will be employed to develop interview questions and questionnaires for testing the tool in this thesis.

12. Thesis rationale

Clostridioides difficile infection (CDI) has become the leading cause of antibiotic-associated diarrhoea in North America and Europe. Although the prevalence was higher until the early 2010s, mandatory patient isolation and antibiotic stewardship have significantly reduced the incidence of CDI. However, cases still persist, with approximately 1,209 CDI cases reported in Scotland in 2023. The implementation of antibiotic stewardship has been effective in reducing the use of antibiotics classified as high-risk for CDI, but as shown in Figure 2, the overall usage of antibiotics did not decrease between 2008 and 2018 in Scotland.

Unnecessary antibiotic prescribing remains high, influenced by various factors including patient demand, practice business, and the clinician-patient relationship. The use of technology has demonstrated the ability to improve and facilitate disease communication, enhance the clinician-patient relationship, and expedite consultations (Garg *et al.*, 2005). Developing a tool to identify patients at high risk of CDI could support clinicians in antibiotic prescribing by providing a risk score for the current patient and the impact on risk when prescribing different classes of antibiotics (4C and non-4C antibiotics).

While numerous CDS tools are currently available to healthcare settings, poor uptake is often due to the lack of involvement from end users. Involvement of end users has been shown to improve the uptake, usefulness, and ease of use of these tools (Dickman *et al.*, 2019). Therefore, this thesis aims to develop a risk predictive tool for *Clostridioides difficile* tailored for the Scottish healthcare system through active involvement of end users.

13. Thesis aim and objectives

The overall aim of this thesis was to develop a digital tool for *Clostridioides difficile* for the Scottish health care system. The studies in this thesis explored clinician's perspective on CDI in primary and secondary care, their perception of using technology during consultation with patients, their preferred format for a digital tool for CDI, and finally developing and testing the tool following their feedback. The following stages of this thesis have aided the successful development of the CDI Risk Predictor (name of the digital tool for CDI).

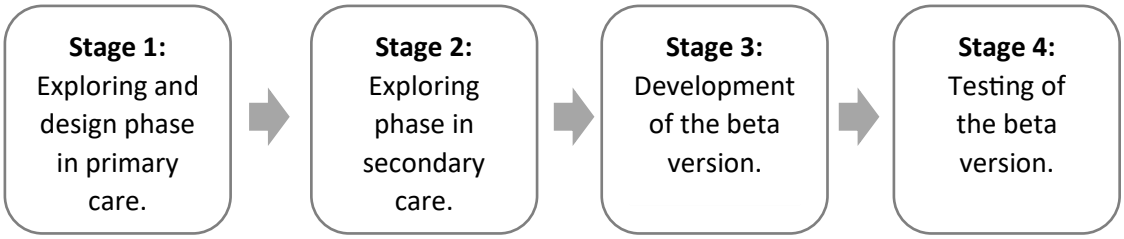


Figure 6 Overview of the different stages in this thesis

Each stage of this thesis has contributed to the development of the final version of the CDI Risk Predictor. The first part of Stage 1 of this thesis involved investigating the perspective of clinicians on CDI in primary care, their current relationship with technology, and their preferences for a digital tool for CDI. The first part concluded with some observations of clinician's consultation with patients to investigate at which stage the digital tool for CDI can be used. The second part of Stage 1 involved the development of a low fidelity prototype for CDI using the feedback that emerged from the first section.

Stage 2 investigated the perception of clinicians on CDI in secondary care, gathered feedback on the low fidelity prototype developed in stage 1, and investigated the potential implementation in secondary care.

Stage 3 involved working with a digital solution developing company named SWARMonline, to create a beta version (a version created for testing) of the CDI Risk Predictor using the feedback emerged in Stage 2.

Finally, Stage 4 involved testing the CDI Risk Predictor and gathering feedback on its layout, content, usefulness and ease of use with a range of clinicians from primary and secondary care.

Below presents the objectives for each stage in the thesis:

Stage 1: Exploring and design phase in primary care.

a) *Exploring phase in primary care*

Objectives:

- Investigate clinician's perspective of CDI in primary care.
- Investigate clinician's perspective of the use of technology in primary care.
- Investigate clinician's preferred format and features of a digital tool for CDI.
- Observe when in the consultation a digital tool for CDI can be used.

b) *Design phase in primary care*

Objective:

- Design a low fidelity prototype with the involvement of primary care clinicians and the feedback emerged in stage 1a.

Frameworks used:

- CFIR
- GUIDES checklist

Stage 2: Exploring phase in secondary care.

Objectives:

- Investigate clinician's perspective of CDI in secondary care.
- Investigate clinician's perspective of the use of technology in secondary care.
- Gather feedback on the low fidelity prototype developed in Stage 1.

- Investigate the potential implementation of the low fidelity prototype in secondary care.

Frameworks used:

- CFIR
- GUIDES checklist
- TAM

Stage 3: Development of the beta version.

Objectives:

- Create a requirements document which describes the layout and content of the digital tool for CDI.
- Manage the communication with SWARMonline to develop a precise beta version of the CDI tool.
- Monitor the output from SWARMonline to ensure the beta version meets the specifications indicated in the requirement document.

Stage 4: Testing of the beta version.

Objectives:

- Investigate clinician's perspective on the layout, content, usefulness, and ease of use of the CDI Risk Predictor
- Amend the CDI Risk Predictor using the feedback gathered from clinicians.

Frameworks used:

- CFIR

TAM**Project Team:** The Risk Predictor for CDI was developed through a collaborative effort across three key teams:

- Mathematics and Statistics Team: Chris Robertson, Kim Kavanagh, and Jiafeng Pan.

- Computer Science Team: Marilyn Lennon and Babis Kyfonidis.
- Implementation Science Team: Marion Bennie, Amanj Kurdi, and Ansu Joseph.

Decisions regarding project milestones and progress were discussed collectively, with team consensus guiding key developments. The study design and all data analyses were conducted by Ansu Joseph (AJ).

CHAPTER 2: Exploring and designing a digital tool for CDI with clinicians from primary care (stage 1)

1. Introduction

The introduction of technology into the health care system aims to support clinicians in reducing human errors, improving practice efficiency, improving clinical outcomes, and tracking patient data (Alotaibi and Federico, 2017). Although it is agreed that the use of technology can improve the overall performance of the healthcare system, its comprehension and adoption are extremely slow (Bauer *et al.*, 2015). It is believed that this slow adoption may be a consequence of product development pathways and/or the strategies used for technology implementation (Ross *et al.*, 2016). Additionally, if technology is not appropriately adopted into the healthcare system it may lead to adverse consequences such as loss of data, mislead illness detection and dosing errors (Wienert, 2019) that can negate any potential benefit(s) of the technology. For the simplification of this thesis, all types of technologies in the healthcare system will be referred as “digital tools”.

In order to inform the implementation process of digital tools, many implementation frameworks have been published with the aim of enhancing the uptake of the tools (see section on implementation science) (Nilsen, 2015). However, studies have demonstrated that the uptake of digital tools is not only influenced by the strategy used for the implementation, but it is also dependent on the performance, ease of use, and usefulness of the tool (Garavand *et al.*, 2016). The latter factors are often not met due to poor involvement of end users and implementation frameworks during the design and development stages (Dabbs *et al.*, 2009).

Involvement of end users is recommended throughout the development and implementation stages, commencing from the design, and concluding with the evaluation of digital tools. Involvement of users in the design phase is known as user-centred-design (UCD). The UCD approach (see section on user centred design) puts at the centre of the design the requirements of the users (de Beurs *et al.*, 2017). Some of the benefits of adopting the UCD approach, in the development of digital tools are improved quality of the tool, reduced development time, better functionality, and greater usability (Dabbs *et al.*, 2009). A further benefit of user involvement early in a

project is to verify the fit of the targeted users and setting for the adoption of the digital tool(s).

At the same time, the use of implementation frameworks during the design stages, has shown to facilitate the identification of factors influencing the adoption at multifaceted levels (Kirk *et al.*, 2015). Therefore, to maximise the adoption, the study in this chapter focused on involving end users and utilising implementation frameworks to understand factors that influence the development and implementation of a digital tool for CDI. Consequently, the findings from the study informed the development of a low fidelity prototype for CDI.

According to the ARHAI Scotland 2023 Annual Report, there were 1,209 cases of CDI in 2023, comprising 917 HA-CDI and 292 CA-CDI cases (ScotGov, 2024). Additionally. The 2018 Scottish One Health Antimicrobial Use and Antimicrobial Resistance Report indicates that 83.2% of total antibiotic use (DDDs) was prescribed in primary care settings, with of this total prescribed by 73.5% were by General Practitioners (GPs) (Health Protection of Scotland, 2018).

Therefore, for this study GPs from primary care were chosen as potential users of the digital tool for CDI, with the aim of understanding their perception of CDI, use of digital tools, and their preferences for a digital tool for CDI.

2. Aims and objectives

The aim of stage 1 (figure 7) of this study was to understand factors that influence the development and implementation of a digital tool for CDI in primary care and subsequently develop a low fidelity prototype. (For further details on the aims and objectives on this thesis aim and objectives)

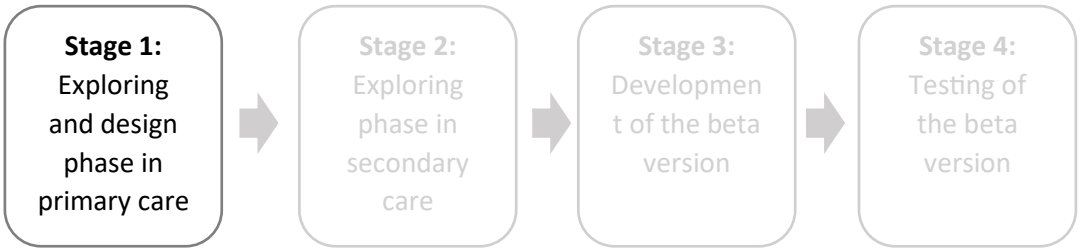


Figure 7. Stages involved in this thesis to develop the CDI risk predictor. Stage 1 discusses the exploring and designing of the low fidelity prototype with primary care clinicians.

The research question for this study was: "What are the barriers and facilitators that influence the development and implementation of a risk prediction tool for *Clostridioides difficile* in primary care?".

Stage 1 Study objectives comprised:

- Understand the clinician's perspective on the burden of CDI in primary care.
- Explore clinician's views on the use of digital tools in primary care.
- Understand the preferred format and features of a digital tool for CDI.
- Observe when during a consultation with patients the digital tool for CDI may be used.
- Design a low fidelity prototype with the involvement of primary care clinicians and using the feedback gathered in the study.

3. Method

3.1. Study design and participants

The study focused on understanding primary care clinicians perspectives of CDI, use of technology with patients, and their preferred format and layout of a digital tool for CDI. The feedback gathered in this study allowed development of a low fidelity prototype for CDI. The research activities that informed the design of the prototype, involved face to face semi structured interviews, observations of the consultations with patients and a co-design workshop. These research activities are widely used within user-centred design, especially for design requirements gathering, observing users in the use of existing digital tools, and sketching the design of the tool with end users (Maunder *et al.*, 2007; Dell'Era and Landoni, 2014).

Ethics was obtained through the Computer Science department, at University of Strathclyde (Ethics ID: 665 for the interviews; 704 for the observations; 794 for the co-design workshop).

The setting chosen for the study was Scotland covering a population of 5.5 million. Primary care GPs were chosen as the principal participants for the study as they are the primary prescribers of antibiotics (73.5%) compared to other prescribers (26.5%) (Health Protection of Scotland, 2018).

The study recruitment started few months before the start of this PhD, however the participants for the interviews were confirmed and the interview scheduled prepared and conducted only after the PhD started. Therefore, AJ's involvement was throughout the whole study expect for the recruitment process. The project team involved the Maths and Statistics Team, the Computer Science Team and the Implementation Team at the University of Strathclyde.

3.2. Participant recruitment strategy

The recruitment for the study was supported by the Scottish Antimicrobial Prescribing Group (SAPG) established by the Scottish Government in 2008. SAPG is a Scottish clinical network that supports and directs the antimicrobial stewardship agenda within NHS Scotland (Nathwani *et al.*, 2011). Through the SAPG Project

Officer an email communication highlighting that SAPG was supporting the development of a CDI risk prediction tool, was sent to all NHS Board antimicrobial management team (AMT) across Scotland, asking AMTs to encourage GPs within their NHS Board to come forward to participate in the study. Details of those interested to participate in the study were forwarded to the Project Officer, at SAPG, who then shared them with the project team at the University of Strathclyde.

The inclusion criteria for participation comprised of GPs practising within the primary care setting in clinical practice who are involved in prescribing of antibiotics without any restrictions or exclusion criteria in terms of demographics such as age, gender, and geography.

A letter (appendix A) discussing the study and its aim was distributed in late 2017 to the GPs that were recruited. The letter explained the research activities that were planned to be conducted. A monetary incentive of £210 for 3hr session was offered to each GP by the NHS Information Services Division (ISD) to compensate them for their involvement in the study. The initial idea was to recruit between 3 - 5 GPs. GPs who indicated an interest were contacted by the research team (either via phone or email) to arrange the interviews/visits.

3.3. Interview schedule

The first activity of this study was to conduct semi-structured interviews that aimed to understand the GP's perception of CDI, the use of digital tools in primary care, and preferred format and features for design of the CDI tool. An initial interview schedule was prepared by Babis Kyfonidis, a computer science researcher (BK) who was involved in the wider programme of work. The questions having been informed by previous experience in similar projects conducted in the computer science department. The initial interview schedule comprised of seven different sections (Table 5) and was then revised (AJ and BK) by analysing it in the context of two digital tool implementation frameworks (CFIR and GUIDES checklist), identified as part of the literature review (See frameworks selected for this thesis). This revision involved

matching of the proposed interview questions against the CFIR and GUIDES checklists to identify any key gaps. Consequently, the interviews schedule was revised to address any gaps identified (added a few questions) and this was further reviewed and approved by the project team (comprising academics with expertise in computing science, statistics, and pharmacy).

The interview schedule format was piloted by AJ and BK with a pharmacist working in primary care and a PhD student in a meeting room at the University of Strathclyde. Despite the fact the interviews were designed for GPs, due to limited access to GPs in this study, it was agreed that the piloting with the identified individuals would be helpful to test question flow and timing. Minor changes to the questions were suggested during the pilot, which were included in the final format of the interview schedule (see appendix B for interview schedule and mapping to CFIR and GUIDES checklist).

Table 5. Interview schedule topics

The interview schedule section	Themes of the section
1. Prescription process	Antibiotic prescribing process during consultations
2. Dynamics	Tension between clinician and patient for antibiotic prescribing
3. *C.diff* awareness	GP's perception on *C.diff*
4. Prescribing antibiotics and *C.diff*	GP's perception on the relationship between *C.diff* and antibiotic prescribing
5. Technology in workplace	GP's perception on using digital tools during consultations
6. Decision support	Factors that influence the adoption of digital tools
7. *C.diff* tool	Requirements for the CDI tool

**C.diff = Clostridium difficile*

3.4. Interview Data collection

The interviews were conducted (by AJ and BK) during February 2018 and lasted 90 – 120 minutes. The interviews were conducted at a convenient time for the GPs' and the option for face to face and telephone interview was offered. All GPs opted for

face to face interviews within their practices. On the day of the interview, an information sheet (appendix C) detailing the aim of the interview and data handling measures was given to the GPs. Permission for audio-recording, ensuring confidentially and anonymity was sought from each GP. A consent form (appendix D) was asked to be signed, with the option of withdrawal from the study at any time.

The interviews began by formally introducing the researchers (AJ and BK), giving a short overview of the project, and listing the aim of the interview. Subsequently, the participant was taken through the interview schedule by one of the researchers, while the other researcher took notes of the discussion. The questions were semi-structured allowing the conversation to flow and enable the participant to share any additional views not captured by the posed question. The interview was concluded by explaining the next research activities; seeking GP's permission to contact them for those activities and thanking them for their time.

3.5. Interview analysis

All interviews were recorded using Dictaphones and transcribed by (AJ) and (BK). Each transcript was carefully checked with the recordings to correct any mistakes by both AJ and BK. Personal identifiers were removed, and the transcript kept anonymised. The interview transcripts were all analysed by AJ using a thematic analysis approach, a recognised approach in qualitative research (Nowell *et al.*, 2017).Thematic analysis is used for identifying, analysing, and reporting themes that arise from transcripts (Vaismoradi, Turunen and Bondas, 2013) either inductively or deductively. Inductive thematic analysis allows the data to determine new themes derived from the transcript. In contrast, deductive thematic analysis, creates themes by fitting the data extracted from the transcripts into existing theories and coding frameworks (Roberts, Dowell and Nie, 2019).

Initially, AJ familiarised herself with the data by reading the transcript several times, then coded the transcript deductively using the CFIR codebook provided by Laura Damschroder (Damschroder *et al.*, 2009). The CFIR framework is a conceptual framework that is commonly used to identify factors that affect the development and

implementation process. Although the GUIDES checklist is a technology-oriented framework, CFIR was chosen as more comprehensive and better suited for the analysis of non-technology aspects discussed during the interviews. Additionally, CFIR is a well-known implementation framework that was similarly used in various papers (Kirk *et al.*, 2015; Keith *et al.*, 2017; Warner *et al.*, 2018; Lam *et al.*, 2021). The research question used for the analysis was: "what are the barriers and facilitators that influence the development and implementation of a risk prediction tool for *Clostridioides difficile* in primary care?".

The initial analysis was reviewed with two members of the project team (AK and MB) and an experienced qualitative researcher (RN). Following the review, the team agreed to customize the CFIR codebook with additional contextualised operational definitions, to support consistency of coding beyond the published CFIR codebook. This expanded CFIR codebook was created which incorporated the CFIR definitions with study operational definitions that serve as inclusion criteria for the coding (table 6). This expanded CFIR codebook was created to better inform the analysis for this study, as the author of the CFIR codebook used generalised definitions to enable fit for a variety of study topics. The codebook study operational definitions were created by AJ and reviewed and approved by AK, MB and RN. The original codebook contains five domains (Intervention characteristics, outer setting, inner setting, individual characteristics and process), however, as the study was at its initial stages of development, the domain "process", which discusses about the implementation approach, was not relevant and therefore not included in the new analysis. Furthermore, the application and use of this enhanced CFIR codebook was independently validated by a second qualitative researcher (KP) on one complete transcript and the output was compared, and any disagreement was discussed. Any unresolved disagreement was then presented to AK, MB, and RN (qualitative research expert) to achieve an agreement. Subsequently, AJ coded the remaining transcripts using the enhanced CFIR codebook (table 6). The validation process is essential to ensure the accuracy, reliability, and robustness of the analysis, minimizing potential biases and strengthening the validity of the results.

The definition is the actual CFIR definition, while the operational definition is meant to guide the researcher to code the transcript at a deeper level. While coding both definitions need to be consulted.

Table 6. Enhanced CFIR codebook with study operational definitions

CFIR Subdomain	CFIR Definition *	Study Operational definition (inclusion criteria)
Domain: INTERVENTION CHARACTERISTICS (Characteristics of technology)		
A. Intervention Source	Perception of key stakeholders about whether the intervention is externally or internally developed.	Clinician's perception that the tool is developed within or outside of the health system.
B. Evidence Strength & Quality	Stakeholders' perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes.	Published evidence on the subject matter of the digital solution. E.g. evidence base for *C.diff* and its risk factors. Additionally, could relate to evidence that a digital solution would be beneficial.
C. Relative advantage	Stakeholders' perception of the advantage of implementing the intervention versus an alternative solution.	Demonstrates an advantage of implementing a digital tool compared to other existing digital tools or methods used in practice.
D. Adaptability	The degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs.	Individual - flexibility in how a tool can be used by a clinician e.g. user interface. For example, clinicians are not constrained to use the tool in a set procedure/order but can adapt how they use the tool to meet clinical need. System - ability of a tool to fit in with different IT systems used by clinicians.
E. Trialability	The ability to test the intervention on a small scale in the organisation [8], and to be able to reverse course (undo implementation) if warranted.	The clinician or other individuals from the setting shows interest to be part of the testing (Early testing of the prototype).
F. Complexity	Perceived difficulty of implementation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement.	Describes the development or implementation of the CDI tool as complex. E.g. numerous steps required to implement or when educative training on the usefulness of the tool is required.

G. Design Quality and Packaging	Perceived excellence in how the intervention is bundled, presented, and assembled.	GPs perceptions on what the CDI tool should look like and/or features to be included in the tool e.g. designed to harvest information from other systems and resources (patients) to self-populate tool parameters.
H. Cost	Costs of the intervention and costs associated with implementing that intervention including investment, supply, and opportunity costs.	The perceived cost for the implementation of the CDI tool.
Domain: OUTER SETTING		
I. Patient Needs & Resources	The extent to which patient needs, as well as barriers and facilitators to meet those needs are accurately known and prioritized by the organisation.	Where there is a perceived need for the CDI tool based on the needs of the patients. Patient's response to digital tools as part of the consultation process - as perceived by GPs. E.g. does using digital tools meet patient's needs?
J. Cosmopolitanism	The degree to which an organisation is networked with other external organisations.	People workforce networking done outside of the GP setting.
K. Peer Pressure	Mimetic or competitive pressure to implement an intervention; typically, because most or other key peer or competing organisations have already implemented or in a bid for a competitive edge.	Perceived pressure from other organisation or GPs to implement digital tools in general. E.g. feeling pressurised to use an app from organisational / GP level.
L. External Policy & Incentives	A broad construct that includes external strategies to spread interventions including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaboratives, and public or benchmark reporting.	Strategies used to bring awareness in using a digital tool or about a disease. E.g. campaigns, messages in the news.
Domain: INNER SETTING (organisational / GP setting level)		
M. Structural Characteristics	The social architecture, age, maturity, and size of an organisation.	Describe characteristics of the GP setting E.g. organisation of the workforce / workforce profile.
N. Networks & Communications	The nature and quality of webs of social networks and the nature and quality of formal and informal communications within an organisation.	Describes the communication channels to inform the clinicians/individuals within a setting / organisation about digital tools.

O. Culture	Norms, values, and basic assumptions of a given organisation.	Individual's assumption on the GP setting. e.g. things that normally happen in a day-to-day situation, or certain behaviours within a setting that has transformed into something that is considered as normal to do or okay to do.
P. Implementation Climate	The absorptive capacity for change, shared receptivity of involved individuals to an intervention and the extent to which use of that intervention will be rewarded, supported, and expected within their organisation.	Statements supporting/ (or not), the perception of the CDI tool by everyone in the setting.
P – 1. Tension for Change	The degree to which stakeholders perceive the current situation as intolerable or needing change.	Statements that indicate the need for a change/ (or not) of the current situation and use of technology, or specifically to the use of antimicrobials and potential for CDI.
P – 2. Compatibility	The degree of tangible fit between meaning and values attached to the intervention by involved individuals, how those align with individuals' own norms, values, and perceived risks and needs, and how the intervention fits with existing workflows and systems.	Statements on the CDI tool fit with the clinician's workflow and workload at an individual operator level.
P – 3. Relative Priority	Individuals' shared perception of the importance of the implementation within the organisation.	Priority of CDI compared to other diseases and clinical activities.
P – 4. Organisational Incentives & Rewards	Extrinsic incentives such as goal-sharing awards, performance reviews, promotions, and raises in salary and less tangible incentives such as increased stature or respect.	Incentives/awards given by the setting when a certain action is performed. e.g. using a certain digital tool.
P – 5. Goals and Feedback	The degree to which goals are clearly communicated, acted upon, and fed back to staff and alignment of that feedback with goals.	Organisational goals. e.g. reduction of antibiotic prescribing.
P – 6. Learning Climate	A climate in which: a) leaders express their own fallibility and need for team members' assistance and input; b) team members feel that they are essential, valued, and	Clinicians are assisted or use a new method to improve their performance with patients during consultations.

	knowledgeable partners in the change process; c) individuals feel psychologically safe to try new methods; and d) there is sufficient time and space for reflective thinking and evaluation.	
Q. Readiness for Implementation	Tangible and immediate indicators of organisational commitment to its decision to implement an intervention.	Positive attitude for the implementation of the digital. Including, clinician's statement of wanting the tool or availability of the resources for the implementation.
Q – 1. Leadership Engagement	Commitment, involvement, and accountability of leaders and managers with the implementation.	Clinicians express interest in providing leadership within their organisation to engage with the implementation.
Q – 2. Available Resources	The level of resources dedicated for implementation and on-going operations including money, training, education, physical space, and time.	Clinicians indicate the availability of resources for the digital tool or the implementation of the tool. e.g. documents that could be useful for the tool.
Q – 3. Access to knowledge and information	Ease of access to digestible information and knowledge about the intervention and how to incorporate it into work tasks.	The access to documents that inform the use of the digital tool. e.g. training or handbooks on how to use the tool.
Domain: CHARACTERISTICS OF INDIVIDUALS (stakeholder level)		
R. Knowledge & Beliefs about the Intervention	Individuals' attitudes toward and value placed on the intervention as well as familiarity with facts, truths, and principles related to the intervention.	Clinicians knowledge and belief on *C.diff* infection, CDI tool and technology in general.
S. Self-efficacy	Individual belief in their own capabilities to execute courses of action to achieve implementation goals.	Individual autonomy to affect change through the tool to achieve reduction of CDI and clinician's belief of ability of reduction of CDI without the need of the tool. Also include quotes on computer literacy.
T. Individual Stage of Change	Characterization of the phase an individual is in, as he or she progresses toward skilled, enthusiastic, and sustained use of the intervention.	This subdomain is not relevant, as this can't be measured at this point of the study.
U. Individual Identification with Organisation	A broad construct related to how individuals perceive the organisation and their relationship and degree of commitment with that organisation.	The identification of the clinician within the GP setting and their willingness to participate in an implementation project or using a digital tool is affected.

V. Other Personal Attributes	A broad construct to include other personal traits such as tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style.	Discuss tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style.

***CFIR definitions are the actual CFIR definitions extracted by the CFIR codebook provided by Laura Damschroder** (Damschroder *et al.*, 2009)**.**

Abbreviations:

CDI: Clostridioides difficile infection

C.diff: Clostridioides difficile

Digital tool is used to refer to apps, websites software and risk prediction tools.

**If there are quotes that don't fit under any of the CFIR domains or subdomain please have a category named "Other".

3.6. Consultation observation

The second research activity was to observe the clinician's consultation process with patients. The observations aimed to capture the prescription process and the use (if used) of digital tools during the consultation, to consider at which stage of the prescription the digital tool for CDI may be used and to verify some of the themes that emerged from the interviews. The observations took place between May and June 2018 within the GP setting of two clinicians. Consent was obtained from each patient prior to the consultation. In situations where the patient was unwilling to be observed, both researchers (AJ and BK) left the consultation room. Both researchers recorded the observations by taking notes. The notes were gathered to create a consultation process and determine at which stage the CDI tool may be used.

3.7. Co-design workshop

The aim of the co-design workshop was to create a low fidelity prototype to be used to obtain feedback from clinicians prior to the development of a high-fidelity prototype. The co-design workshop was based on the participatory design, where the stakeholders (in this case end users) are invited into the design process to capture their needs and requirements. This allows the designers to customize and develop a digital tool that reflects the end user's requirements (Wilkinson and De Angeli, 2014b). The activities in the workshop led to the design of a paper low fidelity prototype.

All GPs recruited to the study were invited to attend the workshop. AJ and BK were present during the workshop. The activities were discussed and facilitated by AJ and BK, however, all the decisions on the design were taken by the participating GP. The workshop took place in October 2018 at the University of Strathclyde and lasted around 90 minutes. The workshop was audio and video recorded using Dictaphones and video camera. The workshop was divided into six stages, outlined in table 7 and workshop schedule (appendix E).

Table 7. Stages and activities of the co-design workshop

The Co-design workshop stages	Activities
Introduction	-The GP(s) was informed of the themes emerged during the interviews. -Aims of the workshop was discussed
Icebreaker	-An exercise was introduced to the GP(s) where simple geometrical figures are asked to be drawn e.g. rectangle, triangle etc.
Choose a platform	-Six different formats suggested during the interviews for the CDI tool were shown to the GP(s). -A card sorting exercise was followed, where the GP(s) was asked to sort the formats from most favourite to least favourite. -Pros and cons of each format were addressed and finally asked to card sort the formats again.
Design the outline	-The GP(s) was asked to design the favourite format chosen during the card sorting.
Design the specific feature	-The GP(s) was asked to design the features within the outline (e.g. button options, dropdown etc). -Write the message used within the tool. -Suggest the format for the risk score.
Conclusion	-The GP(s) was thanked for their time and asked to give a short feedback on the workshop.

4. Results

The characteristics of the clinicians involved in the research activities are presented in table 8. Three GPs agreed to participate in the interviews. The observation activity was undertaken with one GP and a prescribing nurse that was identified by another GP. The GP suggested to observe the nurse instead of the GP as the nurse was a key prescriber of antibiotics within their practice. For the co-design workshop, one GP was involved in the activity, while the remaining two GPs declined the invitation.

Table 8. Participants demographics (n= 4)

Demographic profiling	N (%)
Gender	
Female	3 (75%)
Male	1 (25%)
Age (years)	
35 – 44	1 (25%)
45 – 50	1 (25%)
51 – 55	1 (25%)
No response	1 (25%)
Role	
GP	3 (75%)
Nurse	1 (25%)
Years in current role	
0 - 10	1 (25%)
11 – 20	1 (25%)
21 – 30	1 (25%)
No response	1 (25%)
Location	
Glasgow	4 (100%)

4.1. Interviews

The GP (n=3) interview data is presented using the domains within the enhanced CFIR codebook (table 6), subdivided by the CFIR subdomains identified through the deductive thematic analysis.

Domain: Intervention characteristics

The CFIR domain “intervention characteristics” captures the characteristics of technology, in this case of the digital tool for CDI, that may influence the development and implementation outcomes. Of the eight subdomains available under this domain

(table 6), the interview data mapped across five subdomains: intervention source; relative advantage; adaptability; design quality and packaging; and cost.

Intervention source

This subdomain addresses the clinician's perception on the credibility of the developer of the digital tool (table 6). Credibility of the developer appeared to positively affect the uptake of a new technology. All three participants reported higher likelihood of adopting a digital tool suggested by authorities within the health care system, as this was perceived more trustworthy. The reported trust was attributed to participants' expectations that any tool developed by a credible source would be evidence based:

> *"…Probably anything that comes out of GGC [Greater Glasgow and Clyde]; anything it's been told to us by the GGC people I tend to trust more than anything else. "(GP2, 51-55 years)*

Relative advantage

This subdomain addresses the advantage (usefulness) of implementing a new digital tool compared to other already existing tools (table 6). All three GPs perceived a tool offering support to identify high risk patients for CDI as unnecessary. The tool would offer no advantages as the incidence of community-acquired CDI is relatively low in primary care compared to hospital-acquired CDI:

> *"…Give them a system that's got functionality added in and then they'll use it. Give them a system that's for predicting C.diff risk, on an elderly lady who they know is at high risk of C.diff already and they won't use it." (GP3, 45-50 years)*

Compared to a CDI specific tool, participants preferred a more generic tool, with a function to provide them with clinical decision support around safe antibiotic prescribing taking into consideration any possible risk the patient may have:

"..don't want a C.diff tool [I: Ok] so I don't want to tell me anything about C.diff [I: Ok] I wanted it to tell me the best, most appropriate and safest antibiotic to use in each circumstance." (GP3, 45-50 years)

Adaptability

This subdomain describes the flexibility to use the tool by clinicians according to their preference (table 6). One of the factors all GPs mentioned was that the uptake of digital tools was influenced by the autonomy given from the tool for decision making. In fact, clinicians during the interviews stated that they would like to use digital tools to support their decision making rather than being forced towards a decision:

"…'Cause you don't like to feel you're being pushed around by a computer; it's giving you the information and letting you decide, based on the information." (GP3, 45-50 years)

Design quality and packaging

This subdomain discusses the clinician's perception on the layout and functionality features of a tool including the provision/display of the risk score (table 5). Participants discussed the platform for hosting the CDI tool, the difficulty in accessing up to date patient data, the alert system and the time clinicians would spend using the tool. In term of platform, participants were asked whether they preferred the tool to be an app on their phones, a website or integrated into their prescribing system. All three clinicians stated a website or an app on the phone would require clinicians to search for the patient data and input into the tool to obtain the risk score. These actions were considered as time consuming since GP consultations were only 10 minutes:

"I just can't imagine that if that would go to a website and sort of typing characteristics you know, I wouldn't use it because we don't have that much time to make the decision…I just can't see that happening." (GP1, 35-44 years)

Instead, all three GPs suggested the tool needed to be integrated within their prescribing system:

> *"I think it has to be inside EMIS®."* (GP1, 35-44 years)

When asked about the layout for the tool, the three GPs mentioned Script-Switch® (commercial software package) as it notified the GPs with an alternative for the prescription. A feature of Script-Switch® is that it allows the clinician to choose whether to continue or change the prescription. As seen in the *Adaptability* subdomain clinicians dislike digital tools to impose a choice, instead they would like to be supported during decision making:

> *"out of all of those warning things that might make me change my prescribing is Script-Switch®. The Script-Switch® is probably the one I prefer, because you are sort of doing a prescription, you get a little flash up and you can either carry on with what you're doing, or you can take on board what it said."* (GP1, 35-44 years)

When asked about the format of the risk score, one GP stated they would prefer the tool to give a risk ratio comparing 4C antibiotics with non-4C antibiotics:

> *"…I mean if it was like "this patient from using this antibiotic was 5 times at risk for C.diff compared to amoxicillin" then I think that would make it quite clear that you are making a decision that's putting a patient potentially at risk, comparing them to average patients, I think we would need to see that kind of thing."* (GP1, 35-44 years)

A further point was suggested for the CDI tool to provide alternatives when a 4C antibiotic was chosen to be prescribed. Although providing an alternative to the 4C antibiotic could be a preferable feature, the mathematical algorithm supporting the evolving CDI tool cannot support this function:

> *"Particularly if it said what are the alternatives, you know, this patient is at high risk for C.diff have you considered xy&z"."* (GP1, 35-44 years)

One GP suggested to incorporate the option of generating a leaflet while using the tool, that would inform the patient about the risks of prescribing antibiotics. The GP suggested that the leaflet could be used as a backup during the discussion with the patient, when antibiotics are not being prescribed:

> *"A printout that advises the patient that actually it's the health authority's advice that they don't take antibiotics in these circumstances, that's at least a backup" (GP3, 45-50 years)*

In terms of patient data availability, participants were asked whether they have up to date patient data, as the risk predictive tool for CDI requires patient data in order to populate the risk score. All three GPs stated that most of antibiotic prescribing data was available within their prescribing system. However, in situations where any prescribing was conducted at the hospital or during home visits the data may not be recorded all the time within the GP's prescribing system:

> *"…any prescribing that I have done should be on there; but I won't necessarily have all the hospital prescribing on there, or maybe if somebody's done stuff on a house visit; but within this practice we tend to come and prescribe electronically so there should be an electronic record of acute and repeats." (GP2, 51-55 years)*

One participant added that out of hours prescriptions were also not recorded within EMIS® (GP prescribing system):

> "*The prescriptions from out of hours are not part of EMIS®, we get a document letter to say that the patient had an antibiotic, but it's not part of our EMIS® record." (GP1, 35-44 years)*

When participants raised the issue of alerts within their prescribing system, all three GPs indicated that the alerts for the CDI tool should be minimal and potentially only when a 4C antibiotic was being prescribed. Clinicians indicated that continuous alerts would aggravate their alert fatigue:

"…it's got to be relatively uncommon to give them warning." (GP3, 45-50 years)

Finally, when asked how much time the clinicians are willing to spend on a digital tool during a 10-minute consultation, all three GPs said only for one or two minutes:

"Out of a 10 minute appointment? You're probably talking 1 to 2 minutes max." (GP2, 51-55 years)

Cost

This subdomain addresses the costs to implement a digital tool within the GP's prescribing system (table 6). One GP stated that it can be expensive to implement a digital tool into EMIS® as it is a private company providing services to the NHS:

"…it's quite expensive to have computer systems which integrates with EMIS®." (GP3, 45-50 years)

Outer setting

The CFIR domain "outer setting" describes factors that may influence the development and implementation of the CDI tool that are outside the GP setting. Of the four subdomains available under this domain (table 6), the interview data was mapped across three subdomains: patient needs and resources; peer pressure; external policy and incentives.

Patient needs and resources

The subdomain describes the requirement for a CDI tool during consultation based on the needs of patients and the patient's response to digital tools as part of the consultation process - as perceived by GPs (table 6). Two GPs stated that patients were normally comfortable when clinicians were using digital tools during consultations, as the tools were evidence based:

"…I think actually they'll probably be reassured that you were using, as long as you explain to them what you're doing; that you're using some sorts of

electronic aid that's being recognised and its evidence based." (GP2, 51-55 years)

In contrast, one GP, perceived that patients would feel uncomfortable if clinicians used digital tools on their handheld devices, which would make patients question the clinician's competence:

"…the public are not quite used to us doctors using handheld devices, [I: Yes] to assist us with medicine. They're perfectly comfortable doctors with a book, more comfortable with doctors using the computer. Doctor with handheld device, may think they are rubbish." (GP3, 45-50 years)

Peer pressure

This subdomain addresses the perceived pressure for adopting digital tools from other organisations or GPs (table 6). When asked what would influence clinicians to adopt the CDI tool, one GP stated that clinicians have to be persuaded on the need of the CDI tool; especially pointing out that the need to improve antibiotic prescribing:

"I think you would need to persuade GPs of the need for more careful C.diff prescribing…So unless someone says to me that you are actually doing really badly here and there is loads of more scope for you to be doing better and I think, God! Alright, okay, and the way to get better is to type in all these numbers then I would probably do that ... but I'm quite like that and you know, not lots of GPs are like that." (GP1, 35-44 years)

External policy and incentives

The subdomain addresses the strategies used by policy makers to raise awareness about a disease and/or the use of digital tools (table 6). During the interviews, participants were asked about knowledge exchange channels that raise awareness of antibiotic prescribing and how that has affected the demand for antibiotic prescribing. Two GPs stated that since the health departments had made efforts to

organise public engagement and educational campaigns to raise awareness about antibiotic consumption and their adverse effects, more patients are less demanding towards antibiotic prescribing:

> *"…that expectation of an antibiotic or a real feeling of need for an antibiotic is a lot less than it used to be. I think some of the educational stuff that is going around in the news etc, has had an effect, and increasingly I think, especially with parents are coming in, and saying I'm hoping they don't need an antibiotic, but I just want to get them checked." (GP1, 35-44 years)*

Inner setting

The CFIR domain "inner setting" describes factors that influence the development and implementation of the CDI tool at the organisational level of the GP practice. Out of five subdomains available under this domain (table 6), the interview data was mapped across three subdomains. One subdomain comprised of additional sub-elements of which five out of six sub-elements were used from the Implementation climate subdomain. The following are the subdomains and sub-elements (found in brackets) used for mapping this domain: Network and communications, culture, implementation climate, (tension for change, compatibility, relative priority, goals and feedback, learning climate).

Network and communications

This subdomain described the channels of communication to promote new digital tools within a GP organisation (table 6). When asked how GPs learn about new digital tools, all three GPs stated that it was mainly through recommendations from colleagues or emails from the health boards:

> *"Yeah, just through word of mouth really [I: Ok]. And we get an email every so often … that alerts you to all the new developments every week." (GP3, 45-50 years)*

Culture

This subdomain describes day to day behaviours within a setting that have transformed into habitual actions (table 6). Firstly, when asked whether clinicians mention the risk of *C.diff* associated with antibiotic prescribing with the patient, one GP stated that they would mention it only while prescribing 4C antibiotics:

> "*I don't mention C.diff if I'm talking about amoxicillin as rule, but I always would if I would prescribe co-amoxiclav or Cipro." (GP1, 35-44 years)*

Secondly, when asked if antibiotic prescribing was influenced by the day of the week, two GPs stated that they prescribed more antibiotics on a Friday afternoon than a Monday morning to avoid patients going into the out-of-hours service since in the UK, GP settings only run from Monday to Friday:

> *"Actually, the decision to prescribe antibiotics or make errors in general It's related to how many patients the doctor has seen that week, how tired they are and where they are in the week, that's true" (GP3, 45-50 years).*

Lastly, when asked how clinicians deal with alert fatigue, all three GPs stated that they have become used to ignoring alerts or turning the notifications off:

> "EMIS® alerts, we hate it so, we switched them all off." *(GP2, 51-55 years).*

Implementation climate

The subdomain addresses the clinician's perception on the need for the CDI tool (table 6). In order to understand in depth, the reasons behind the statements given by the clinicians for this subdomain, four sub-elements were used to map the GP's perception on the need for the CDI tool. When asked whether their colleagues would adopt the CDI tool, one GP stated that the adoption of the tool is influenced by the perceived usefulness to ease clinician's workload:

> *"If it's useful regularly then people will use it because it will make their life easier." (GP1, 35-44 years)*

However, since community-acquired CDI cases were not frequent in primary care, all three GP stated that a tool for CDI was not necessary:

> *"if it was about C.diff I would think well that doesn't come up often enough in my day-to-day practice that I would justify an app on my phone." (GP1, 35-44 years)*

1. Sub-element: Tension for change

The sub-element indicates the need for a change of the current situation in terms of technology used in practice, the prescription of antibiotics, and CDI (table 6). Firstly, all three clinicians discussed issues that they faced with technology that they could not tolerate and that could negatively influence the adoption of the CDI tool. One of the issues was the difficulty in accessing hospital data, required for a comprehensive consultation or to be used for digital tools. The GP stated that if they needed to access hospital data, they would have to access it through a portal (software allowing to access patient's hospital and laboratory information) that timed them out if it was not used for a certain time:

> "*So, the one thing GP practices don't have easily is Portal. And we've got a limited access to portal so we can access what's on the hospital type stuff if we have to, but it's quite laborious I have to go in and open it up and all the rest of it and can't leave it open easily in the background for my whole surgery it'll sort of time me out*." *(GP2, 51-55 years)*

A second issue that could influence the adoption of new digital tools is delays caused by software updates and upgrades. During the interviews, a GP highlighted an issue with Docman®, a tool to manage patient's documents (such as hospital letters). The GP indicated that Docman® was unable to be used due to a recent upgrade, which caused delays to their work:

> *"If it goes down, it goes down badly. So, for instance, since we've got an upgrade in our Docman® last night, and it is virtually unusable. [I: Ooooh, ok..] Not so good. Because that just then takes time so…we're slowed up today."*

(GP2, 51-55 years)

One GP recognised that there was a need to educate patients about the risks of prescribing antibiotics in order to reduce unnecessary antibiotic prescribing, however this takes time away from their 10 minute consultation:

> *"I think we need to be brave enough to have those discussions; and yes that can take longer; it'll be easier to just if you come in "I've got chest infection" "That's fine here you go, that's the antibiotics" so yes I do think it takes longer and I think that's just good medical practice." (GP2, 51-55 years)*

When asked a GP how they dealt with conflict with patients they stated that when aggressive behaviours were observed, they tend to prescribe an antibiotic:

> "*Yes, people can be stubborn enough, people can be aggressive enough then yes, I'll give them. As long as I still don't think I'm doing them ultimate harm." (GP2, 51-55 years)*

2. Sub-element: Compatibility

The sub-element addresses statements on the suitability of the CDI tool with the clinician's workflow and workload (table 6). Two GPs stated that they were comfortable in using their phones during consultations:

> *"…I bring my phone out in front of patients, and I'll say, "I'm looking up the health board has given us an app which is really useful and I'm going to just double check" (GP1, 35 years)*

However, a third GP stated that digital tools developed for mobile phones would not be adopted by clinicians:

> *"…anything that's designed for a phone, probably wouldn't be routinely used during consultations" (GP3, 45-50 years)*

3. Sub-element: Relative priority

The sub-element discusses the priority of CDI compared to other conditions and clinical activities (table 6). All three clinicians stated that they understand the adverse effect of CDI, however when they prescribe antibiotics, they think more about the other consequences of antibiotics than CDI:

> *"'C.diff is not the most important thing I'm going to be thinking about, when I'm prescribing an antibiotic, primarily the most important thing is whether the patient is going to take antibiotic; have an anaphylaxis and die!" (GP3, 45-50 years)*

4. Sub-element: Learning climate

The sub-element discusses approaches used by clinicians to improve consultations with patients (table 6). A GP stated that in order to educate patients about certain health disorders, clinicians recommended apps to patients during consultations. This approach influenced the patient's perception towards the usefulness of digital tools as well as it educated them on their health disorders, leading to consultations to be easier:

> *"We will recommend certain apps to patients and one of the apps we're using in ours is the sepsis app…and I think that can influence, we'll also maybe use things like MSK app, headspace app, you know maybe patient friendly type stuff as well" (GP2, 51-55 years)*

Characteristics of individual

The CFIR domain "characteristics of individual" described the factors that influence the development and implementation of the CDI tool at the clinician level. Out of five subdomains available under this domain (Table 6), the interview data was mapped using two subdomains: self-efficacy and knowledge and belief about the intervention.

Self-efficacy

The subdomain addresses clinician's belief of making a change (e.g., reducing CDI) without the need of a digital tool (table 6). A GP during the interview stated that

although it was very rare, there were still some clinicians that refused to use technology in GP settings:

> *"…when I started there was still GPs refusing to use the computer at all. They are still getting bits of paper out and write in their handwritten notes and they retired without ever using a computer many years after the computer was introduced, in the general practice." (GP3, 45-50 years)*

One GP stated that their strategy was to avoid prescribing antibiotics and that the risk of CDI was not considered during antibiotic prescribing thus arguing the need for a digital tool for CDI:

> *"..so, it's not part of my overall strategy to identify high-risk patients and avoid drugs which may cause C.diff in high risk patients, that's not my strategy; My strategy is to avoid drugs in the first place if at all possible for everyone, and just apply that method to the entire population: high risk, low risk included." (GP3, 45-50 years)*

Knowledge and belief about the intervention

The subdomain addresses the clinician's knowledge and beliefs about CDI, the CDI tool and the use of technology primary care (table 6). When asked what the barriers are for adopting the CDI tool, a GP stated that they would not use the tool to obtain just a risk score:

> *"I think the barriers are, how long it takes; and how useful the information you get out of it is; you know, I don't know that I wouldn't do it just to get a score." (GP1, 35-44 years)*

Additionally, the same GP added that clinicians would prescribe 4C antibiotics if they considered that was the only antibiotic suitable to manage the infection:

> *"My feeling is that we only prescribe the 4Cs if we really feel that's the only option." (GP1, 35-44 years)*

One aspect that emerged from the interview was the differing views and knowledge of all three GPs on the relationship between 4C antibiotics and *C.diff*. In particular one GP believed that the only 4C antibiotic associated with *C.diff* was Co-amoxiclav:

> *"I think they should have focus on the drugs that really cause C.diff rather than taking more drugs than needed to, and saying, that can be associated with C.diff as well, 'cause even Metronidazole can cause C.diff, despite it being the treatment for C.diff… it left people with sense they didn't have a broad spectrum antibiotic to use cause ciprofloxacin is quite good and is rarely associated with C.diff but they managed to put that in the bucket of the 4c antibiotics." (GP3, 45-50 years)*

Additionally, when asked about the incidence of CDI in primary care, one GP stated that CDI is not prevalent in primary care because it's an infection caused by hospitals:

> *"..you don't see as much C.diff [I: Ok] but that's the hospital thing … you've got to remember that C.diff is a hospital acquired infection caused by hospital." (GP3, 45-50 years)*

4.2. Observations

The observations were conducted with one of the GPs and a prescribing nurse, identified by a second GP who participated in the interviews. The aim of the observation was to observe the interactions between patient and clinician and understand when digital tools are/could be used during consultation. A total of 13 observations were conducted in two GP practices between May and June 2018. Three observations were conducted with the nurse and 10 observations with the GP. From the 13 observations, six resulted in antibiotic prescribing while the other seven observations did not require antibiotic or further tests were needed to confirm the infection. During the observations, there were two episodes of disagreement between patient and clinician for antibiotic prescribing. In the first case, there was a language barrier for the patient, who could not understand the explanation of the clinician and insisted on an antibiotic. While in the second case, the patient entered the clinician's office distressed due to delay in the appointment and requested an antibiotic, which the clinician refused as it was not needed. The consultation process captured during the observation between clinicians and patients was captured and illustrated in figure 8:

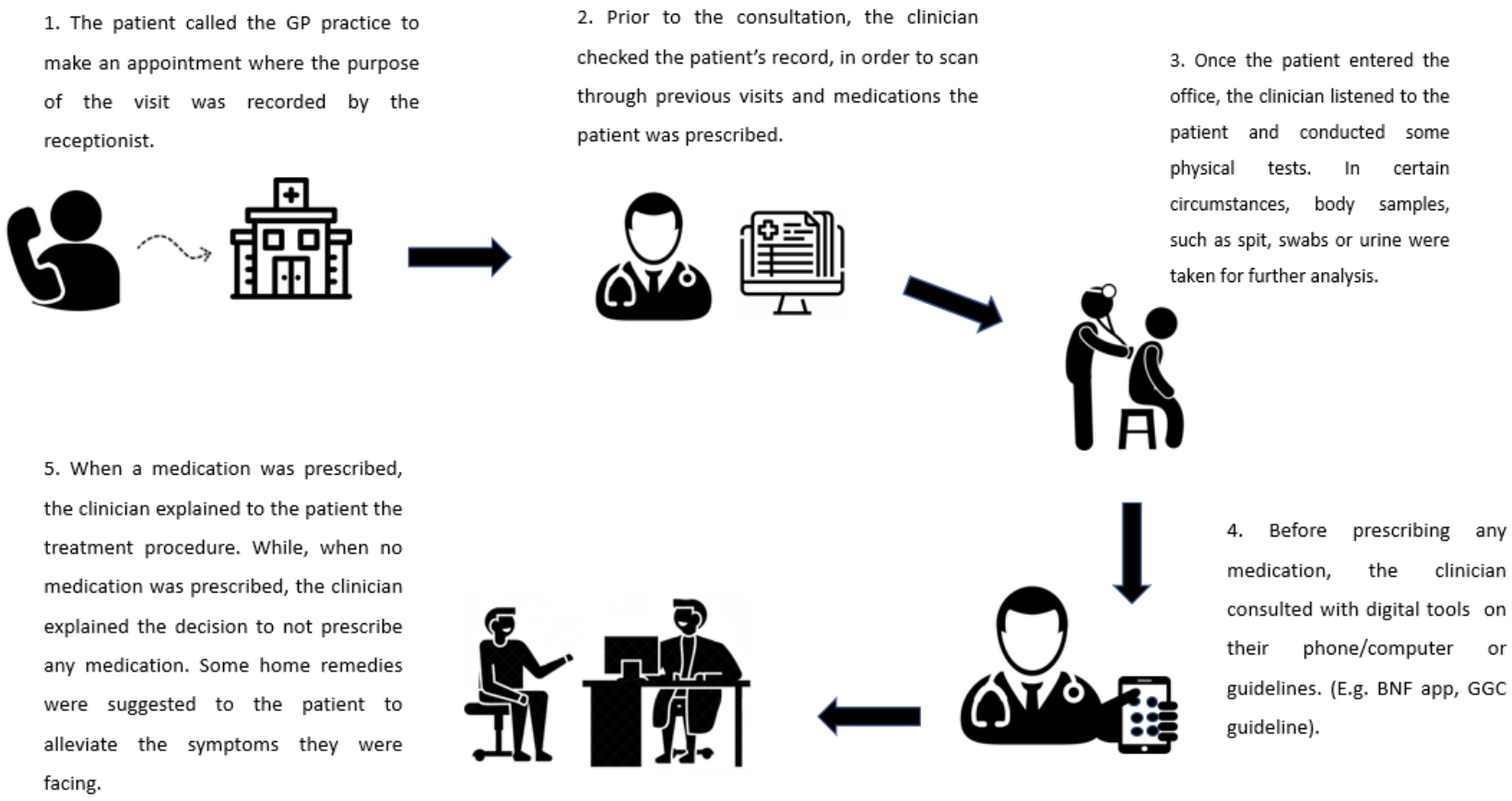


Figure 8. Diagram of consultation process captured during the observations conducted in primary care

4.3. Co-design workshop - Prototype

All three GPs who participated to the interviews were invited for the co-design workshop, however only one GP participated in this part of the study. The workshop took place in October 2018 at the University of Strathclyde. The entire workshop schedule can be found in Appendix E.

The workshop began by listing the below outcomes of the interviews:

- *C.diff* is not considered a threat.
- *C.diff* in primary care is rare.
- GPs tend to ignore EMIS®/InPS VISION® alerts.
- GPs don't want an app to inform about *C.diff* only.
- The tool should be implemented into the GP's system (within EMIS®/InPS VISION®).
- Script-Switch® is the good option.
- GPs like the printout's idea.

Perceived limitations for the proposed digital tool for CDI:

- The patient data need to be accurate.
- Alternatives cannot be provided.

Once the aim of the workshop and the ice breaker game was concluded, a card sorting exercise was conducted to determine the platform to insert the CDI tool. Below is the option given to the GP for the card sorting.

- Mobile app
- Website
- Script-Switch®
- Leaflet
- Combination → Script-Switch® + Website
  → Leaflet + Mobile app or Website or Script-Switch®
- Other

The GP chose Script-Switch® as format for the CDI tool and the initial sketch created by the GP with the content of the tool can be seen in appendix F.

The participant of the co-design workshop chose the preferred format of the CDI tool and drew the content of the format i.e. message boxes, buttons and risk score format. The hand drawings of the CDI tool's format designed by the participant can be seen appendix F (figures C – D). The hand drawing was used to create the low fidelity prototype that can be seen in figures 9 – 13.

Low fidelity prototype

A low fidelity prototype of the CDI tool was created following the co-design workshop using the sketches drawn by the GP. The prototype was drawn using a similar format to the Script-Switch® with the idea of implementing the prototype into the GP's prescribing system. The prototype was developed taking into consideration the fatigue alert clinicians experience. Therefore, in order to avoid frequent alerts, the window seen in figure 9 is meant to appear when the clinician is prescribing 4C antibiotics. As the tool is meant to be implemented into the GP's prescribing system, the tool would automatically extract the patient data from the medical record, avoiding the clinician's need to search and input the patient data into the tool. Once the tool extracts the data, the tool would compare the risk to develop CDI when 4C antibiotic vs non-4C antibiotics is prescribed. (The *C.diff* risk percentage shown in the low-fidelity prototype is merely an example of how a risk score might be displayed; it does not represent an actual risk assessment for either the antibiotic or the patient)

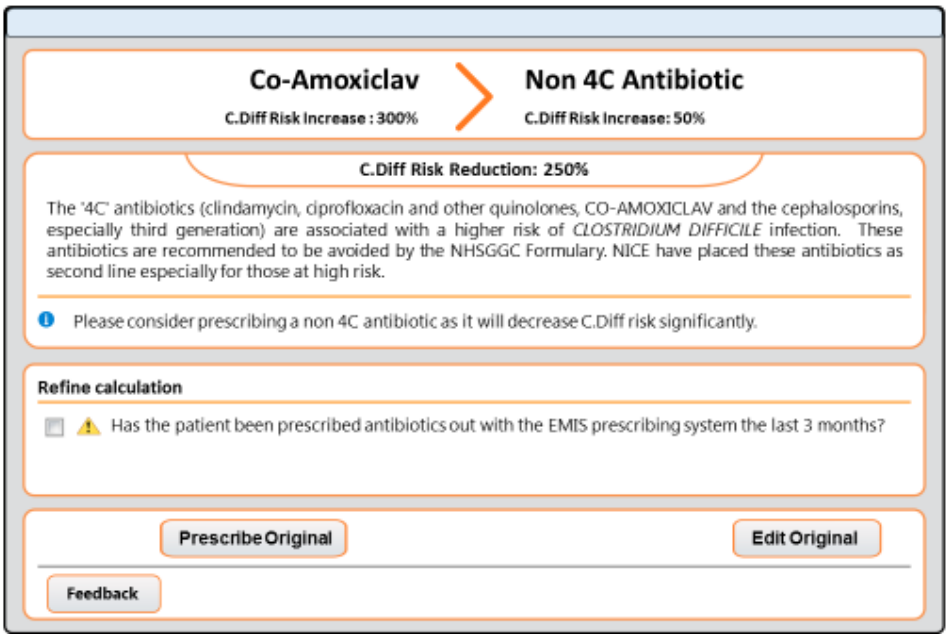


Figure 9. Prototype of the CDI tool (page one)

An issue discussed during the interviews was the incompleteness of the patient data within GP's medical records. This was due to prescriptions conducted in hospitals, dental settings or out of hours. Lack of complete patient medical record can lead to

inaccurate CDI risk prediction, as the tool automatically extracts the data required to generate the risk score. In the case the clinician knows that the patient had antibiotic prescriptions that have not been recorded within their medical record, there is the refine calculation option. The refine calculation provides a further accurate CDI risk prediction by inserting the additional number of antibiotic prescriptions the patient had outside the GP setting. As it can be seen in figure 10, the first step is to insert a tick mark on the refine calculation box.

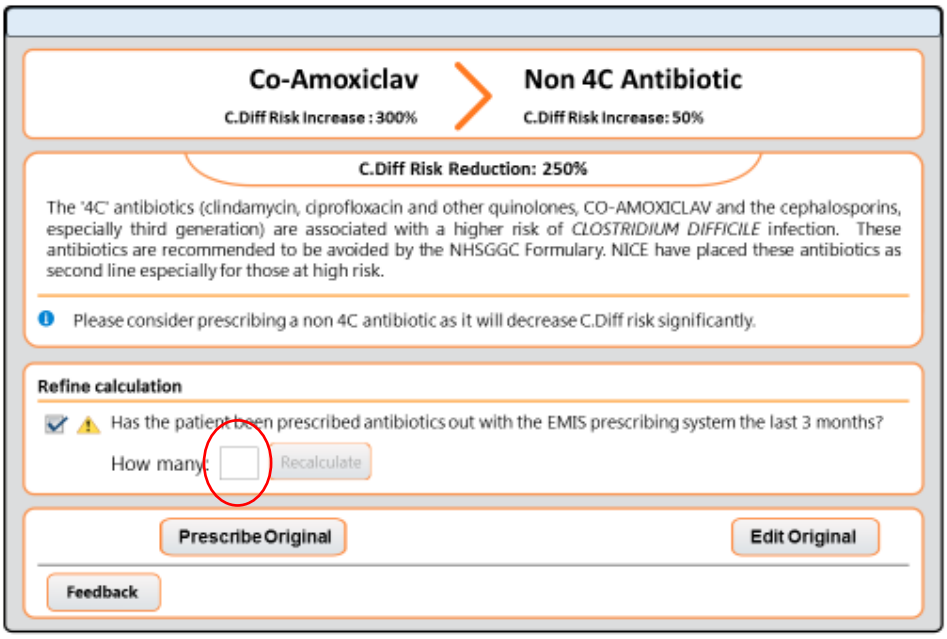


Figure 10. Prototype of the CDI tool (page two)

Following the tick in the refine calculation box, the clinician needs to insert the number of antibiotic prescriptions the patient had outside the GP setting and press the recalculate button to obtain the new risk score (figure 11).

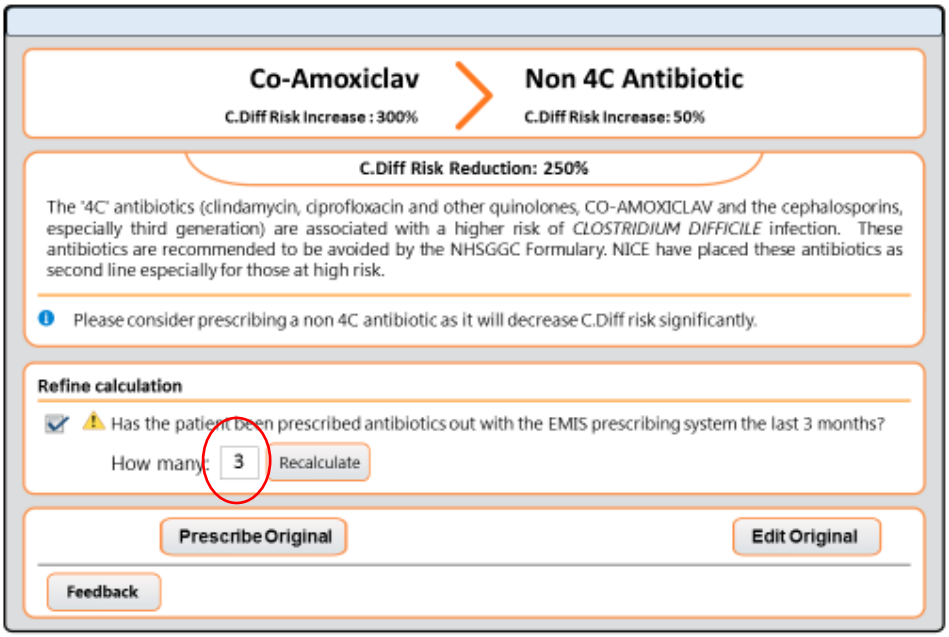


Figure 11. Prototype of the CDI tool (page three)

Following the calculation / recalculation in those cases where the patient is at high risk to develop CDI, the window seen in figure 12 will appear on the clinician's screen suggesting to prescribe a non-4C antibiotic with the hyperlink that takes the clinician to the online British National Formulary (BNF).

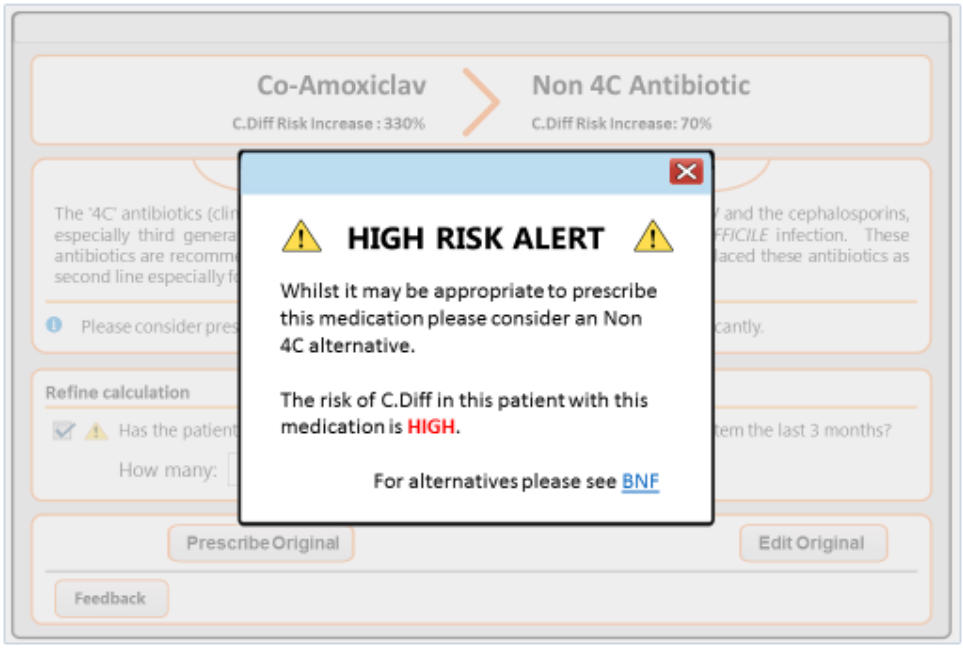


Figure 12. Prototype of the CDI tool (page four)

When the high-risk alert window has been closed, the clinician can then see the new risk score of the patient to develop CDI. The clinicians can decide whether to prescribe the 4C antibiotic chosen by clicking on “Prescribe original” or change the prescription into a non-4C antibiotic by clicking on “Edit original”. Unfortunately, the mathematical algorithm used for the prototype cannot provide an alternative to the 4C antibiotic, therefore the clinician would have to refer to the local antibiotic formulary or to the BNF for further details on the treatment choice.

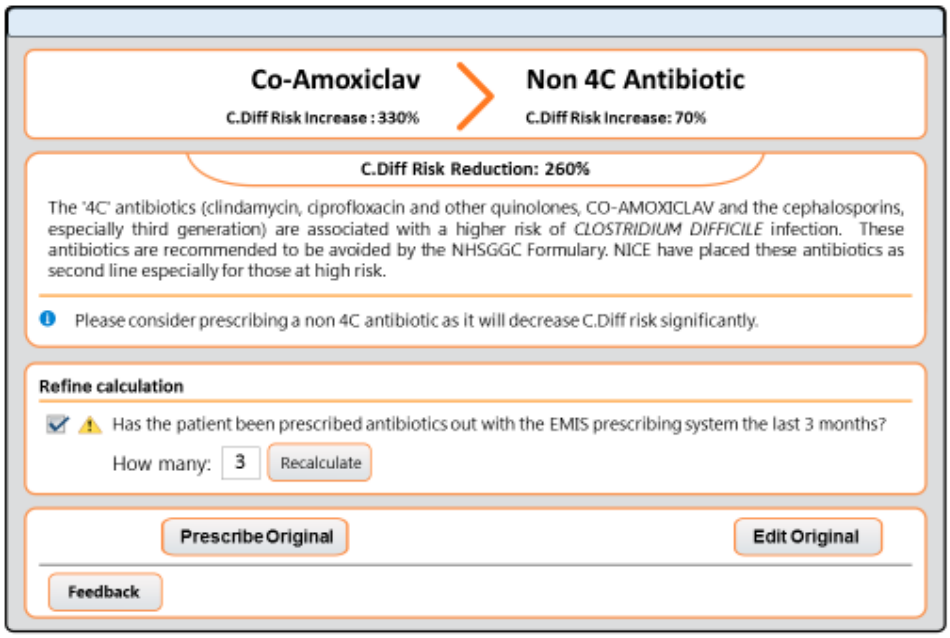


Figure 13. Prototype of the CDI tool (page five)

5. Discussion

This study aimed to identify factors influencing the development and implementation of a risk predictive tool for *Clostridioides difficile* in the primary care setting, with the ultimate goal to develop a low fidelity prototype. This involved a combination of semi-structured interviews, observation and finally a co-design workshop. Three GPs were interviewed to gather their perception/views on the burden of *C.diff* in primary care, use of digital tools in their clinical practice, and identify their preferred format and features of the digital tool for CDI. The idea behind this study was to develop a digital tool involving end-users to enhance/optimise uptake and implementation. The interviews were thematically analysed using the CFIR framework (table 6), and out of the five CFIR domains, the study's findings were mapped against four of the relevant domains. Following the interviews, two clinicians were observed with the aim of capturing the prescribing process including the use (if used) of digital tools during the consultation. The aim of the observation was to gain insights at which stage of the prescribing process the CDI tool may be used and verify some of the themes that emerged from the interviews. The study was then concluded with a co-design workshop with one GP which resulted in a low fidelity prototype for the CDI tool from the feedback gathered in the study.

5.1. Main Findings of the semi-structured interviews

Perception of CDI

Clostridioides difficile has been causing distress in the healthcare system for more than two decades (Depestel and Aronoff, 2013). The infection has been associated with increasing antibiotic consumption (Mullish and Williams, 2018), therefore, in order to support clinicians with appropriate antibiotic prescribing, a digital tool that could predict patient's risk to contract CDI (based on their demographic and clinical profile including the choice of prescribing no antibiotic versus 4C or non-4C antibiotic) appeared to be a useful endeavour to pursue. Although CDI is a serious healthcare burden, in Scotland, through antibiotic stewardship, clinicians have been able to tackle the incidence of CDI in the last decade (Nathwani *et al.*, 2012). Nevertheless,

according to Health Protection Scotland (HPS), there were roughly 1059 cases of CDI in 2019 (Health Protection of Scotland, 2020). While according to National Service Scotland in 2020 and in 2021 there were a total of 1,088 and 1,135 cases of CDI in Scotland (NHS National Services Scotland, 2021, 2022) indicating a lack of further decline in cases. Therefore, one of the research interests of this study was to investigate GP's perceptions of CDI and understand whether they would be interested in adopting a digital tool for CDI in primary care. From the interviews, when GPs were asked about the prevalence of CDI, all three GPs stated that there haven't been cases of CDI within their practice and hence they do not perceive CDI as a priority area (*Barrier - Implementation climate*). However, CDI is still considered a common issue and a priority for Public Health Scotland (PHS) with data showing 381, 253, 275, and 276 reported cases of community acquired CDI (CA-CDI) across Scotland in 2018, 2019, 2020 and 2021, respectively (Health Protection of Scotland, 2020; NHS National Services Scotland, 2021, 2022). The feedback on the low priority of CDI in this study could be because only 3 GPs from Glasgow were interviewed. Perhaps a higher perception of CDI would have been observed if more GPs across Scotland were recruited. A 2019 population data linkage and case-case study comparing the incidence of CA-CDI and HA-CDI in Northern Ireland between 2012 and 2016 found that there was a higher incidence of CA-CDI in rural areas (Maisa A, 2019). This was assumed to be due to higher exposure to farms and animals in rural areas. In another 2008 clinical study from Netherlands, CDI was found in porcine and bovine diarrhoeal sample, in retail meat, and in samples of people living in rural areas (Abraham Goorhuis Dennis Bakker and Kuijper, 2008). With this in mind perhaps recruiting clinicians from rural areas might have suggested different feedback to what has been captured.

An interesting point that emerged during the interviews was that although CDI's major risk factor is antibiotic prescribing, GPs stated that they do not think of CDI as a possible adverse consequence when prescribing antibiotics. GPs justified it by stating that the risk to develop CDI is lower than the consequences the patients might have if antibiotics are not prescribed (*Barrier - Relative priority*). In contrast, a

qualitative study conducted in England with 30 clinicians from 10 General Practices that aimed at understanding primary care clinician's perception on risk and safety concerns associated with reduced antibiotic prescribing, reported that English clinicians consider all the possible consequences of prescribing and not prescribing antibiotics, including the risk of CDI (Boiko *et al.*, 2020). This could be dependent on the incidence of CDI in England, which according to the Public Health England there were a total of 13,177 cases of CDI between April 2019 and March 2020 in England (Public Health England, 2020). Although it's important to remember that England has a population of around 60 million people compared to the 5 million people in Scotland. It's important to note that the digital tool for CDI is designed solely to provide guidance and support to clinicians in their antibiotic decision-making process. This tool is intended to streamline and assist with decisions, not to replace clinical judgment or the decision-making process itself. Clinicians remain fully responsible for using their expertise and judgment in making final antibiotic decisions by balancing the suggestions provided by the tool and any possible unintended consequences.

One of the key messages that emerged during the interviews was that clinicians may have a lack of awareness on how CDI is transmitted. The message was highlighted by one of the three GPs who reported that CDI is a hospital-acquired infection caused by hospitals (*Barrier and facilitator - Knowledge and belief about the intervention*). Although hospitalisation is one of the major causes of CDI, there are studies reporting the transmission of CDI within the community through tap water, from public areas or asymptomatic people (Guerrero *et al.*, 2013; Kotila *et al.*, 2013; Weber *et al.*, 2013; Durham *et al.*, 2016). Another factor that contributes towards the contraction of CDI is antibiotic prescribing. Although GPs might not encounter cases of CDI within primary care, they could be still indirectly contributing towards CDI through their antibiotic prescribing since in Scotland primary care clinicians prescribe 83.2% of the total annual amount of prescribed antibiotics while acute hospitals proscribe 14% of total annual amount (Health Protection of Scotland, 2020). This highlights the need for greater awareness of the risks associated with CDI and the advantages of utilising a digital tool for its management. Implementing such a tool could potentially shift

perspectives on CDI incidence and better address the patient risks tied to antibiotic prescribing.

Perception of digital technology in general

There is a lack of clarity when it comes to which factors influence the adoption of digital tools in health care. Researchers have identified several factors associated with the poor adoption of digital tools such as clinicians' busy schedules, age, computer literacy, and many more (Kilsdonk, Peute and Jaspers, 2017). Although a lot of research has been conducted in understanding the adoption of digital tools and interesting findings have emerged, there hasn't been "one size fits all" solution to overcome the poor adoption of digital tools. This is because there is multifactorial influences behind the adoption of a digital tool, and often these influences differ depending on the functionality of the tool and where it is being implemented (Jacob, Sanchez-Vazquez and Ivory, 2020). One of the research objectives of this study was to understand clinician's perception on the use of digital tools in primary care, including the proposed CDI tool. It was observed that the GP perceptions vocalised in this study influenced their potential willingness for adopting the CDI tool.

It is known that generally, users tend to adopt digital tools they had a positive experience with (Godoe and Johansen, 2012). However, there is limited evidence about whether negative experiences with digital tools affected the adoption of new tools. In terms of GPs perception of digital tools three main findings emerged during the interviews. The first related to the format of accessing/using the CDI tool. The proposal for the CDI tool was to create an app to use on a mobile device during clinical consultations and although two GPs expressed their willingness on using digital tools on their phones, one GP had the opposite opinion who stated that the use of phones in front of patients could question the clinician's competence in promoting the wellbeing of the patient (*Barrier - Patient needs and resources*). This seems to be a prominent concern among clinicians, which was also highlighted in a 2017 systematic review that focused on understanding factors that influence the implementation of digital tools (Kilsdonk, Peute and Jaspers, 2017). The study found that clinicians are

afraid that the use of digital tools may negatively affect their relationship with patients, especially the communication between the two (Kilsdonk, Peute and Jaspers, 2017). A 2012 qualitative study on digital tools for paediatric asthma with nine paediatric pulmonologist, also reported that the use of digital tools may limit the time and focus clinicians spend on patients during consultations, impacting the relationship between clinician and patient (Lomotan *et al.*, 2012). Although this a valid concern that clinicians have especially because consultations in primary care are only 10 minutes, there is evidence that the use of digital tools can ease their consultation with patients. A 2023 German qualitative study that aimed at investigating 30 patient's perception on the use of a digital tool for proton pump inhibitor during consultation, reported that the use of digital tools can improve and ease the conversation between clinician and patients and support shared decision making (Schmidt *et al.*, 2023). In another 2023 German simulated evaluation setting of a digital tool for the management of polytrauma patients in primary care, found that the use of digital tools notably reduced errors in patient treatment and improved guideline adherence (Vogel *et al.*, 2023).

The second main finding in our study was related to digital tool's functionality, especially the feature of triggering an alert system when using these digital technologies. All three GPs expressed their concerns of frequent and irrelevant alerts from the technologies which might act as a barrier for effective use/uptake of a digital tool *(Barrier - Design quality and packaging).* Similar findings were also reported in a cross-sectional online survey by 74 primary care and 106 secondary care Australian clinicians that aimed at understanding what factors influence the adoption of digital tools; clinicians in the study stated that digital tools that send frequent and irrelevant alerts are generally used less by clinicians (Laka, Milazzo and Merlin, 2020). In contrast, a Finnish qualitative study which involved 39 primary and secondary care physicians, that aimed at understanding clinician's perception on the barriers and facilitators to implementing digital tools, suggested that clinicians were keen on adopting the alert recommendations suggestions if they are coming from a strong evidence source rather than poor evidence (Varonen, Kortteisto and Kaila, 2008). This

suggests that when developing the digital tool for CDI it is important to focus on the quality / relevancy of the alerts to avoid poor uptake of the tool due to continuous irrelevant alerts. The above Finnish study also highlighted two main factors to why clinicians in Finland had a positive perception towards digital tools. Firstly, data suggests that Finnish clinicians follow guidelines more frequently than any other country in the world. Secondly, the author suggested that there was a greater favourable perception on digital tools by junior clinicians, since they felt the use digital tools aided them to avoid mistakes (Varonen, Kortteisto and Kaila, 2008). This is something to consider for future studies and during the implementation of the digital tool for CDI.

Nonetheless, the clinicians in the Finnish study were also not eager to adopt digital tools that sent out an excessive number of alerts as such reminders that could lead them to conduct unnecessary lab tests incurring cost and time to the healthcare system (Varonen, Kortteisto and Kaila, 2008). During the interviews with our study participants, GPs expressed that they would ignore or turn off notifications due to the alert fatigue they might experience *(Barrier - Culture).* Noteworthy is that this behaviour has been shown to lead to negative consequences where clinicians would miss out on important alerts leading to adverse consequences for patients (Kesselheim *et al.*, 2011). Consequently, all three GPs in our study were persistent in not aggravating potential alert fatigue with the CDI tool; one potential suggestion to address this issue was to design the tool in such a way that it will send alerts to use the tool only when 4C antibiotics were being prescribed since 4C antibiotics are associated with the highest risk of developing CDI *(Facilitator - Design quality and packaging).*

The last main finding was about persuading GPs on the need and usefulness of digital tools. From the interviews, it was observed that this could be influenced by the credibility of the digital tool developers; the autonomy the tool provides to the clinician; and ease of use and usefulness of the tool. All three GPs reported that they tend to trust digital tools developed or recommended by a credible and trustworthy

source such as the NHS or the health boards *(Facilitator - Intervention Source).* In fact, in the study described above conducted with Australian clinicians, 63% (113) of 180 clinicians indicated that they tend to not adopt digital tools due to trust-related issues (Laka, Milazzo and Merlin, 2020). Trustworthiness and quality of the content were also themes which emerged in a recent systematic literature review analysing 171 studies on social and organisational factors influencing the adoption of mhealth (Jacob, Sanchez-Vazquez and Ivory, 2020). The findings from the systematic literature review echoes what was reported by the three GPs in this chapter. The systematic literature review discussed how adoption and trust towards digital tools are influenced by recommendation and endorsement from reliable bodies such as scientific societies, the NHS, opinion leaders, internal champions, direct managers, or senior colleagues (Jacob, Sanchez-Vazquez and Ivory, 2020).

Another factor that could persuade GPs adoption of a digital tools, is ensuring when developing a tool that it allows clinician's autonomy in decision making while using the tools *(facilitator – Adaptability).* Likewise, perception was also expressed by clinicians in different studies, commenting that the use of digital tools should be in line with their decision making rather than being an enforced behaviour (Varonen, Kortteisto and Kaila, 2008; McDermott *et al.*, 2010; Kilsdonk, Peute and Jaspers, 2017; Jacob, Sanchez-Vazquez and Ivory, 2020) In the systematic review conducted by Kilsdonk et al. on factors influencing guideline-based digital tools, the reasoning behind clinician's need for autonomy was because there have been concerns that the use of digital tools, may cause mechanical decision-making leading to mistakes and endangering the patients. Additionally, concern were expressed towards the perception patients may have towards clinicians knowledge on the care provided (Kilsdonk, Peute and Jaspers, 2017).

Finally, the perceived ease of use and usefulness of digital tools have been also reported among the factors that influence clinician's adoption. These two factors have also been predominantly discussed in the literature (Zheng *et al.*, 2005; Varonen, Kortteisto and Kaila, 2008; Kilsdonk, Peute and Jaspers, 2017; Laka, Milazzo

and Merlin, 2020). In the 2020 systematic literature review conducted by Jacob et al. it was reported that tools that were quick and intuitive to use have been considered to be easy to use. While tools that facilitated the overall consultation with patients were reported to be useful (Jacob, Sanchez-Vazquez and Ivory, 2020).

Recommendations for the features of the CDI tool

The final research interest of this study was the recommendations that clinicians had for the desired features of the CDI tool that would potentially enhance its uptake and adoption. There were three main recommendations under this topic which were: integration of the CDI tool into the prescribing system; the need for alternatives to 4C antibiotics, and frequency of the alerts. Firstly, due to the low incidence of CDI, all three GPs expressed reservation for the CDI tool, especially if developed into an app format *(Barrier - Design quality and packaging).* However, clinicians were keener on having a digital tool for CDI if integrated into their prescribing system *(Barrier and Facilitator - Design quality and packaging)*. The advantage of integrating the tool into their prescribing system was that it would automatically extract the patient data and alert the clinician on the patient's risk to develop CDI without the need of manually inputting any data. Additionally, a tool that requires the clinician's data input may not be used as frequently, since it can be time-consuming and easy to forget to be used. Similar reservation on the manual input of data have also been reported in a mixed method study published in the USA in 2005, which included 41 primary care junior doctors on the implementation of a clinical reminder system named clinical cueing systems (Zheng *et al.*, 2005). Junior doctor's commented that inserting patient data can be time consuming and requiring a considerable amount of effort (Zheng *et al.*, 2005).

Secondly, additionally to the risk score that would be obtained through the digital tool for CDI, clinicians expressed the desire to incorporate the feature to provide alternatives of low-risk antibiotics while prescribing 4C antibiotics. Although the feature of providing alternatives is frequently met in digital tools within the health care setting, for example, notification of generic or cost-effective medications

(Sutton, 2020), this feature cannot be integrated into the proposed CDI tool as the mathematical algorithm does not currently support the option to provide alternatives to the 4C antibiotics to reduce the risk of CDI. Although this can be perceived as a barrier, as it had emerged in feedback, with certain patients, the only option is to prescribe a 4C antibiotic *(Barrier - Knowledge and belief about the intervention).* However, the tool could be used as a system to flag up high risk patients who need close monitoring, follow-up, and education about potential CDI symptoms.

The last feature for the CDI tool recommended by the GPs was to provide a patient's risk to contract CDI only on the occasion when clinicians were prescribing 4C antibiotics. This is mainly to not aggravate their existing alert fatigue discussed in the perception of technology in general. Although 4C antibiotics are highly associated with CDI, there has been evidence of non-4C antibiotics being associated with CDI, which would defeat the purpose of the CDI tool if clinicians are being notified only in the use of 4C antibiotics (Mullish and Williams, 2018). An important note to highlight is the fact that only three GPs were interviewed in this study and although they perceived that triggering an alert only when prescribing 4C antibiotic was enough, when developing the digital tool for CDI it's essential to obtain feedback from more clinicians to see if there is an agreement with the findings emerged in this study. It would be also relevant to investigate the risk non-4C antibiotics have on patients, to ultimately make the decision of providing alerts with any antibiotics that are high risk for the patient or just 4C antibiotics.

5.2. Main findings of the observations

The observations were conducted to capture and understand the consultations with patients and investigate at which stage of the consultation the digital tool for CDI may be used. One GP and a nurse from two different GP practices were observed. Both clinicians had similar consultation process. However, only the GP prescribed antibiotics to their patients, while the nurse did not prescribe any medication, instead took patient's samples for further tests. Although the nurse did not prescribe any antibiotics during the observation, they took us through their process of antibiotic

prescribing which was similar to the GP process observed. Although, there was a total of 13 consultations, 10 observations were with the GP, while only three were conducted with the nurse which could be a possible reason for the lack of antibiotic prescribing while observing the nurse. Both clinicians were pressurized to prescribe an antibiotic, however after examining the patient, both clinicians refused to prescribe antibiotics. One of the patients had a language barrier, therefore could not understand why the clinician was not prescribing the antibiotic. While in the second case, the patient arrived at the office distressed as the GP was running late from the previous consultations. In both cases the patient left the consultation distressed, however the clinicians did not think the antibiotic was necessary. Pressure from patients to prescribe antibiotics is very common within the health care, which was also observed in a 2021 literature review on managing patient pressure to prescribe antibiotics. The study described how patients use different strategies such as describing problems that are relevant to bacterial illnesses before the clinician could make a diagnosis or highlighting the positive outcome following a previous use of the antibiotic (Stivers, 2021). In difficult situations where patients are pressurising the clinicians for an antibiotic, the digital tool for CDI could be used as an aid to support the clinician's decision to not prescribe an antibiotic. In the systematic literature review by Jacob et al. describes that one of the factors that promotes the adoption of digital tools is in fact the usefulness of tools during conversations with patients (Jacob, Sanchez-Vazquez and Ivory, 2020). During the observations the clinicians used digital tools and guidelines towards the end of the consultation while deciding on the treatment to prescribe. As the aim of the observations was to investigate when clinicians would use the digital tool for CDI, the findings from the observations would suggest that the digital tool for CDI could be used towards the end of the consultation while deciding on the treatment for the patient and as well as discussing the treatment choice.

5.3. Main findings of the co-designed workshop

The aim of the co-design workshop was to develop a low fidelity prototype for CDI, and this was achieved through the involvement of one GP. Despite the small number

of participants in this study, it was important to run a co-design with clinicians. There are many benefits in running co-design workshops with end users in early stages of studies. The first benefit is the ability to understand what are the end users needs while using a digital tool. This would allow the content of the tool to be relevant and tailored to their needs and therefore perceived as useful. The second benefit is the ability of focusing on the layout of the tool, which could include drop downs, yes or no buttons or scrolling. Allowing end users to decide on the layout of digital tools could be beneficial towards the perception of ease of use (Davis, 1989). A 2017 systematic review on users experience of using mHealth for chronic noncommunicable diseases in young people, found that all the 12 studies discussed in the paper expressed importance of co-designing with end users as a fundamental principle to improve the adoption of digital tools (Slater *et al.*, 2017).

Despite the participation of only one GP during the co-design, all the proposed formats and features during the activities were informed from the themes emerged during the interviews. During the workshop the GP chose their preferred format for the CDI tool to be similar to Script-Switch®, which is a software that is implemented into the GPs prescribing system and provides the clinicians with a suggestion of a generic alternative medication for the same selected drug. The software is widely used within Scotland since it helps with the reduction of National Health Service (NHS) costs for medications. The Script-Switch® format was also suggested as the preferred format for the digital tool for CDI by all three GPs *(Barrier and facilitator - Design quality and packaging).* This strengthens the design of the prototype despite being designed by only one GP.

Although during the interviews, clinicians suggested the incorporation into the digital tool for CDI to provide alternatives to 4C antibiotics, as mentioned in the results, that feature is not supported by the algorithm. However, during the co-design workshop the GP suggested that having a link that would take end user into the BNF or the antibiotic formulary would facilitate search for an alternative antibiotic.

5.4. Strength and limitations

To our knowledge, this study is the first in Scotland to attempt to investigate GP's perception on CDI digital tools used in primary care and their preferred format and features for a digital tool for CDI. There are various strengths and limitations to this study. A strength was that the prototype was created following a rigorous use of different methods such as interviews, observations, and a co-design workshop that helped to shape the design of the prototype as seen in this chapter. A core element of the user-centred design is to involve end users in the development of digital tools to understand what is useful and easy to use. This is believed to be achieved in the activities conducted in this chapter. Another strength was that the findings have been analysed using known implementation framework such as the CFIR, which has been extensively studied and used since its publication. Using the CFIR allowed a structured examination of the potential barriers and facilitators for the development of the digital tool for CDI. Lastly, all the findings were validated by an independent researcher, giving a level of robustness to the findings.

Although the study resulted in a prototype, there are limitations to the sample size and the location of the participants. Only three GPs from Glasgow showed interest to the study, which could be argued to be a very small sample size, and that saturation might have not been achieved. Multiple recruitment processes were utilised to advertise the study and recruit more GPs, however possibly due to GPs busy schedules only three GPs were recruited for the study. Despite the sample size and the location, it can be argued that since NHS Greater Clyde and Glasgow, is the largest health board in Scotland, GPs in cities across Scotland may have similar feedback to the ones emerged in this study. Additionally, the healthcare system in Scotland uses similar prescribing systems within primary care. Therefore, similar themes might have emerged on the perception of digital tools and the preferred format and features of the digital tool for CDI. Additionally, similar findings on the use of antibiotics may emerge following the implementation of the antimicrobial stewardship programme in Scotland. The programme aims to ensure antibiotics are prescribed only when necessary, reduce overall usage, improve patient outcomes,

enhance monitoring and reporting of antibiotic use, and provide healthcare workers with up-to-date education and training on best prescribing practices.Whilst for the observations, the number of clinicians observed were only two, a total of 13 consultations were observed which had very similar processes and therefore it could be argued that saturation may have been achieved. Although only three GPs participated in the initial study, their feedback was instrumental in shaping its direction, providing key insights and laying a foundation for further investigation. Subsequent studies will aim to validate and build upon this initial feedback, allowing for a more comprehensive understanding and refinement of findings based on input from a broader group of clinicians.

A final limitation to this study is the fact that only one GP participated for the co-design workshop for the prototype. Although it would have been preferable to have all three GPs participating in the workshop, it can be counterargued that all the findings that informed the co-design workshop were extracted from the interviews and the shadowing. Therefore, the prototype was developed using a well known strategy that promotes adoption, which is the user-centred design method; the findings analysed using an established implementation framework (CFIR) that identifies barriers and facilitators to the implementation; and the use of multiple methods such as interview, observation, and a co-design workshop.

5.5. Future research

Future research to further confirm the above-mentioned findings is needed. Although GPs are the primary antibiotic prescribers (73.5%), it is important to explore the perception of other prescribers (26.5%) such as nurses and pharmacists who might also prescribe antibiotics. More and more non-medical professionals are being trained to prescribe antibiotics, due to the high demand of healthcare services and shortage of staff (Health Protection of Scotland, 2018).

Therefore, the next study aimed to recruit, and interview allied healthcare professionals from primary and secondary care. The findings will then be used as the

building blocks to produce the specification document required to develop the beta version of the CDI tool.

5.6. Conclusion

Although clinician's perception on the incidence of CDI in community is low, they agree that there is need for better antibiotic prescribing to reduce unnecessary prescribing. A digital tool for CDI implemented into their prescribing system that would automatically extract all the patient data, and alert clinicians on the patient's risk to contract CDI when they are about to prescribe a 4C antibiotic was emerged to be desirable. Emerged benefit of implementing the tool included the usefulness of educating patients on why they are not being prescribed an antibiotic. The findings from the interviews and observations informed the co-design workshop which resulted in production of a low fidelity prototype for CDI.

CHAPTER 3: Exploring and designing a digital tool for CDI for secondary care (stage 2)

1. Introduction

The previous chapter was aimed at identifying factors influencing the development and implementation of a digital tool for *Clostridioides difficile* in the primary care setting, with the ultimate goal to develop a low fidelity prototype. Two key findings from the previous chapter needed attention and further exploration. Firstly, GPs did not perceive CDI as a priority which they attributed mainly to the low prevalence of CDI in primary care. Furthermore, the participants (GPs) expressed reservation in adopting a CDI tool, especially if developed into an app format, as they wouldn't reach out for it.

Secondly, GPs expressed that CDI is a concern for secondary care as there is more incidence of CDI in hospitals rather than community. This perception was not a surprise since there is a vast amount of evidence on the incidence of CDI within hospital settings (Depestel and Aronoff, 2013). National Services Scotland reported that 78% (n=818/1,053) of all the CDI cases in Scotland in 2022 were healthcare associated CDI (NHS National Services Scotland, 2022). In contrast, Public Health of England reported a total of 13,177 CDI cases between 2019 and 2020, of which 35.70% (n=4,704) were healthcare associated (Public Health England, 2020). While in Wales between 2014 and 2018 a total of 4613 cases of CDI were confirmed (Tydeman *et al.*, 2021). In fact, transmission of CDI within hospitals was a great burden around the western world until the mid of 2010s (Balsells *et al.*, 2019).

One of the major key modifiable risk factors for CDI is the consumption of antibiotics, especially wide spectrum antibiotics (See section on pharmacological agents). Reduction of inappropriate use of antibiotics through stewardship has been a key strategy to reduce the incidence of CDI (Lawes *et al.*, 2017). Using digital tools is considered one of the key stewardship interventions to improve the appropriate use of antibiotics. This has been clearly demonstrated in a 2019 systematic review of 45 studies, which aimed at investigating the role and the effectiveness of digital tools on antibiotic stewardship (Rittmann and Stevens, 2019). The review highlighted that the use of digital tools was associated with a significant reduction of inappropriate

antibiotic prescribing including an increase in the use of narrow spectrum antibiotics compared to broad spectrum antibiotics. In one of the studies, it was highlighted that the use of digital tools was positively adopted if used on smartphones. While another study had contradictive findings suggesting that due to regular system updates and poor visibility, the use of digital tools on smartphones was poorly adopted (Rittmann and Stevens, 2019). Furthermore, an Australian 2017 interrupted time series study that aimed at assessing the impact of digital tools on multisite antimicrobial stewardship programs (Bond *et al.*, 2017), evaluated 12 hospitals sites across Australia and demonstrated significant impact of digital tools on enhancing appropriate antibiotic use including improvement in the cost of antibiotics usage, incidence of CDI rates and admission length (Bond *et al.*, 2017; Rittmann and Stevens, 2019). The findings from the Rittmann and Stevens systematic review and the Bond's study might be difficult to generalise, as it didn't include any British study and additionally Australia have a different healthcare structure and system compared to Scotland. Consequently, there is a need for more exploration on the role of digital tools on the antimicrobial stewardship outcomes in Scotland especially in the context of CDI within the secondary care setting.

Currently, the algorithm used for the CDI tool can only predict the risk of contracting CA-CDI, for this reason the initial focus of this project was directed towards primary care (see section on development of a mathematical algorithm for the CDI Risk Predictor). However secondary care patients who visit outpatients' clinics and A&E department could also be at risk of contracting CA-CDI if exposed to unnecessary antibiotics. Therefore, as there is potential scope and opportunity of using the digital tool for CDI in these settings, this chapter will include investigating and understanding the feasibility of implementing a digital tool for CDI in secondary care.

2. Aims and objectives

This chapter (stage 2 in figure 14) focused on understanding the perception of clinicians on the burden of CDI in secondary care and the feasibility and usefulness of implementing the proposed CDI tool developed in stage 1. Furthermore, it aimed to gather feedback on the prototype developed in the previous chapter regarding its layout, content, and functionality from primary care clinicians. The intention of this feedback on the prototype in this chapter is to validate the findings from the previous chapter that had limited participation of GPs in the development of the low fidelity CDI prototype.

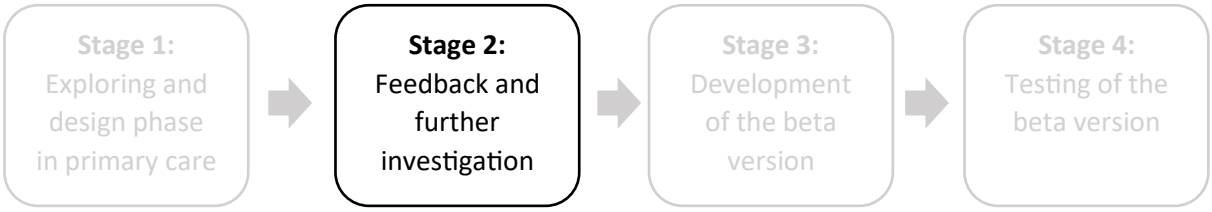


Figure 14. Stages involved in this thesis to develop the CDI risk predictor. Stage 2 discusses the exploring and designing a prototype for secondary care.

As both primary care and secondary clinicians were recruited in this stage of the study, some objectives are specifically for primary care clinicians, while other objectives are for secondary care clinicians or from both groups of clinicians. **Stage 2 study objectives comprised:**

- Objective 1: Understanding clinician's perspective on the burden of CDI in secondary care *(participants: secondary care clinicians)*
- Objective 2: Validating the key findings from chapter 2 regarding primary care clinicians' perceptions on the burden of CDI in primary care *(participants: primary care clinicians)*
- Objective 3: Obtaining feedback on the low fidelity prototype developed in chapter 2 *(participants: both secondary and primary care clinicians)*
- Objective 4: Exploring the feasibility and usefulness of implementing the low fidelity CDI prototype in a secondary care setting *(participants: secondary care clinicians).*

3. Method

3.1. Study design and participants

The study focused on understanding secondary care clinicians' perspectives of CDI, obtain feedback on the low fidelity prototype developed in chapter 2, and explore the feasibility and usefulness of implementing the prototype into secondary care.

The research activities in this study involved face to face semi structured qualitative interviews with clinicians from primary and secondary care in Scotland from April 2019 to May 2019. Ethics was obtained through the Strathclyde Institute of Pharmacy and Biomedical Science department, at University of Strathclyde (appendix G).

3.2. Participant recruitment strategy

Recruitment for the study was facilitated and supported by SAPG, the Scottish clinical network that supports and directs the antimicrobial stewardship agenda within NHS Scotland. The findings of the study with primary care clinicians (chapter 2) were presented to SAPG members at their regular quarterly meeting in February 2019. Having in mind the next stages for the project, members of the SAPG group were asked for their support and help recruiting clinicians to take part in this study. Subsequently, an advertisement information sheet, containing a brief summary about the study including background, aims and researcher's contact details, (appendix H) was disseminated by SAPG members to their corresponding Antimicrobial Management Teams (AMT) across Scotland; clinicians who were interested to participate were asked to contact the researcher to arrange for the interview. A reminder was sent by a SAPG member to gather more participants for the study.

The inclusion criteria for participation comprised:

- Physicians and allied health professional from primary and secondary care across Scotland
- Practitioners prescribing antibiotics

Following a low initial response to the advertisement, a reminder was sent out by SAPG after 2 weeks encouraging clinicians to participate in the study. This resulted in clinicians coming forwards to take part in interviews with the researcher. Reimbursement for participation was not provided in this phase of the study.

3.3. Interview schedule

The interview schedule was developed using the Consolidated Framework for Implementation Research (CFIR) framework, the Technology Acceptance Model (TAM) (Davis, 1989) and the Guideline Implementation with Decision Support (GUIDES) checklist (de Velde, 2017) because one of the main objectives of this study was to obtain feedback on the ease of use and usefulness of the developed low fidelity prototype; since CFIR lacked specific technology centred components to enable the latter, TAM and GUIDES were used to develop the interview schedule as complementary to CFIR.

Consequently, the interview schedule comprised of two sections (appendix L). Firstly, section 1 focused on exploring clinicians' perception on the burden of CDI in primary and secondary care and identifying their perception on how the CDI tool should look like. Section 1 was informed by the Consolidated Framework for Implementation Research (CFIR). The interview questions used in section 1 were four introductory questions each containing sub questions that aimed at achieving objective 1 and 2. Most questions used in this section were similar to the questions used in chapter 2, however there were five additional questions that weren't in the interview schedule of the previous chapter. The five new questions were added to this study to understand the perception of the CDI burden in secondary care as well as to address emerging themes from chapter 2. The questions used in section 1 can be seen in appendix K.

Section 2 of the interview schedule consisted of questions related to obtaining feedback on the low fidelity prototype (objective 3 and 4). Following the first five interviews, it was clear that the low fidelity prototype developed in chapter 2 (prototype 1) would be difficult to implement in secondary care as the prototype

would require to be implemented into an electronic system that embedded up to date patient data. Unfortunately, at the time of the interviews, the Scottish secondary care sector lacked an up to date/complete electronic data, as most of patient data was retained in paper format. Therefore, for the remaining five interviews, it was decided to investigate the feasibility of implementing a digital tool for CDI that would require manual input of patient data. As part of the interviews prototype 2 was shown to participants which was created by the University of Strathclyde to test the algorithm (as seen in section development of a mathematical algorithm for the CDI Risk Predictor). Additionally, to prototype 2, there was interest in understanding whether clinicians preferred the risk score (output) to be shown in different formats than the one presented in prototype 2. In order to identify risk formats commonly used in other digital tools that were favoured among clinicians and patients, a literature review was conducted (appendix N). The literature review revealed that bar charts and population diagrams are favoured among clinicians and patients for digital tools. Consequently, the CDI risk score was also presented in a bar chart and population diagram formats during the last five interviews.

In summary, the first five participants only provided feedback on prototype 1; while the last five participants provided feedback on both prototype 1 and 2. Both prototype format can be seen in appendix M.

3.4. Interview Data collection

The interviews were conducted from April to May 2019 at a convenient time for the clinicians and the option for both face to face and telephone interview was offered. All clinicians opted for face-to-face interviews within their clinical practice. On the day of the interview, an information sheet (appendix I) detailing the aim of the interview and data handling measures was given to the clinicians. Permission for audio-recording, ensuring confidentially and anonymity was sought from each clinician. A consent form (appendix J) was asked to be signed, with the option of withdrawal from the study at any time.

The interviews began by formally introducing the researcher, giving a short overview of the project, and outlining the aim of the interview. The questions were semi-structured allowing the conversation to flow and enable the participant to share any additional views not captured by the posed questions. The interview was concluded informing the clinicians about the next phase of the study; seeking the permission to contact them for those activities and thanking them for their time.

3.5. Interview analysis

All interviews were recorded using Dictaphones and verbatim transcribed. Each transcript was carefully checked with the recordings to correct any mistakes. Personal identifiers were removed, and the transcript kept anonymised. Thematic analysis was used to analyse the interviews transcripts including deductive analysis. This involved a series of steps:

- Familiarised with the data by reading the transcript several times (Nowell *et al.*, 2017).
- The first section of the feedback was coded deductively using the enhanced CFIR codebook (Table 9) and CFIR codebook provided by Laura Damschroder (Damschroder *et al.*, 2009) (See section on Consolidated Framework for Implementation Research). While the second and third sections that captured feedback on the two prototypes were analysed using the TAM framework.
- Validation of the coding involved a second independent qualitative researcher coding the quotes from two randomly selected transcripts; the output was compared, and any disagreement discussed.

3.6. Presentation of findings

The interview findings gathered with the 10 clinicians, their perception on the burden of CDI in secondary care, feedback on the layout, usefulness, and ease of use of the prototype in secondary care and its possible implementation. Following the first five interviews it was understood that the prototype developed in the previous chapter is difficult to be implemented into secondary care as for its optimal functionality it would require to pull out patient data from one platform which was unavailable in

secondary care at the time of the interviews. Therefore, a second prototype was also introduced for the remainder five interviews to understand whether the new prototype would be feasible to be used in secondary care. Due to the introduction of the second prototype to the interviews the finding section will be presented as follows:

- **First section:** Clinicians perception on the burden of CDI in secondary care (Findings from 10 interviews)
- **Second section:** Feedback on prototype 1 (Findings from 10 interviews)
- **Third section:** Feedback on prototype 2 (Findings from last 5 interviews)

The definition is the actual CFIR definition, while the operational definition is meant to guide the researcher to code the transcript at a deeper level. While coding both definitions need to be consulted.

Table 9. CFIR subdomain, definition and operational definition used to code the interview transcript (Damschroder *et al.*, 2009).

Subdomain	Definition	study Operational definition (inclusion criteria)
INTERVENTION CHARACTERISTICS (Characteristics of technology)		
A. Intervention Source	Perception of key stakeholders about whether the intervention is externally or internally developed.	Clinician's perception that the tool is developed within or outside of the health system.
B. Evidence Strength & Quality	Stakeholders' perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes.	Published evidence on the subject matter of the digital solution. E.g. evidence base for *C.diff* and its risk factors. Additionally, could relate to evidence that a digital solution would be beneficial.
C. Relative advantage	Stakeholders' perception of the advantage of implementing the intervention versus an alternative solution.	Demonstrates an advantage of implementing a digital tool compared to other existing digital tools or methods used in practice.
D. Adaptability	The degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs.	Individual - flexibility in how a tool can be used by a clinician e.g. user interface. For example, clinicians are not constrained to use the tool in a set procedure/order but can adapt how they use the tool to meet clinical need. System - ability of a tool to fit in with different IT systems used by clinicians
E. Trialability	The ability to test the intervention on a small scale in the organisation [8], and to be able to reverse course (undo implementation) if warranted.	The clinician or other individuals from the setting shows interest to be part of the testing (Early testing of the prototype).
F. Complexity	Perceived difficulty of implementation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement.	Describes the development or implementation of the CDI tool as complex. E.g. numerous steps required to implement or when educative training on the usefulness of the tool is required.

G. Design Quality and Packaging	Perceived excellence in how the intervention is bundled, presented, and assembled.	GPs perceptions on what the CDI tool should look like and/or features to be included in the tool e.g. designed to harvest information from other systems and resources (patients) to self-populate tool parameters.
H. Cost	Costs of the intervention and costs associated with implementing that intervention including investment, supply, and opportunity costs.	The perceived cost for the implementation of the CDI tool.
OUTER SETTING		
I. Patient Needs & Resources	The extent to which patient needs, as well as barriers and facilitators to meet those needs are accurately known and prioritized by the organisation.	Where there is a perceived need for the CDI tool based on the needs of the patients. Patient's response to digital tools as part of the consultation process - as perceived by GPs. E.g. does using digital tools meet patient's needs?
J. Cosmopolitanism	The degree to which an organisation is networked with other external organisations.	People workforce networking done outside of the GP setting.
K. Peer Pressure	Mimetic or competitive pressure to implement an intervention; typically, because most or other key peer or competing organisations have already implemented or in a bid for a competitive edge.	Perceived pressure from other organisation or GPs to implement digital tools in general. E.g. feeling pressurised to use an app from organisational / GP level.
L. External Policy & Incentives	A broad construct that includes external strategies to spread interventions including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaboratives, and public or benchmark reporting.	Strategies used to bring awareness in using a digital tool or about a disease. E.g. campaigns, messages in the news.
INNER SETTING (organisational / GP setting level)		
M. Structural Characteristics	The social architecture, age, maturity, and size of an organisation.	Describe characteristics of the GP setting E.g. organisation of the workforce / workforce profile.

N. Networks & Communications	The nature and quality of webs of social networks and the nature and quality of formal and informal communications within an organisation.	Describes the communication channels to inform the clinicians/individuals within a setting / organisation about digital tools.
O. Culture	Norms, values, and basic assumptions of a given organisation.	Individual's assumption on the GP setting. e.g. things that normally happen in a day-to-day situation, or certain behaviours within a setting that has transformed into something that is considered as normal to do or okay to do.
P. Implementation Climate	The absorptive capacity for change, shared receptivity of involved individuals to an intervention and the extent to which use of that intervention will be rewarded, supported, and expected within their organisation.	Statements supporting/ (or not), the perception of the CDI tool by everyone in the setting.
P – 1. Tension for Change	The degree to which stakeholders perceive the current situation as intolerable or needing change.	Statements that indicate the need for a change/ (or not) of the current situation and use of technology, or specifically to the use of antimicrobials and potential for CDI
P – 2. Compatibility	The degree of tangible fit between meaning and values attached to the intervention by involved individuals, how those align with individuals' own norms, values, and perceived risks and needs, and how the intervention fits with existing workflows and systems.	Statements on the CDI tool fit with the clinician's workflow and workload at an individual operator level.
P – 3. Relative Priority	Individuals' shared perception of the importance of the implementation within the organisation.	Priority of CDI compared to other diseases and clinical activities.
P – 4. Organisational Incentives & Rewards	Extrinsic incentives such as goal-sharing awards, performance reviews, promotions, and raises in salary and less tangible incentives such as increased stature or respect.	Incentives/awards given by the setting when a certain action is performed. e.g. using a certain digital tool.

P – 5. Goals and Feedback	The degree to which goals are clearly communicated, acted upon, and fed back to staff and alignment of that feedback with goals.	organisational goals. e.g. reduction of antibiotic prescribing.
P – 6. Learning Climate	A climate in which: a) leaders express their own fallibility and need for team members' assistance and input; b) team members feel that they are essential, valued, and knowledgeable partners in the change process; c) individuals feel psychologically safe to try new methods; and d) there is sufficient time and space for reflective thinking and evaluation.	Clinicians are assisted or use a new method to improve their performance with patients during consultations.
Q. Readiness for Implementation	Tangible and immediate indicators of organisational commitment to its decision to implement an intervention.	Positive attitude for the implementation of the digital. Including, clinician's statement of wanting the tool or availability of the resources for the implementation.
Q – 1. Leadership Engagement	Commitment, involvement, and accountability of leaders and managers with the implementation.	Clinicians express interest in providing leadership within their organisation to engage with the implementation.
Q – 2. Available Resources	The level of resources dedicated for implementation and on-going operations including money, training, education, physical space, and time.	Clinicians indicate the availability of resources for the digital tool or the implementation of the tool. e.g. documents that could be useful for the tool.
Q – 3. Access to knowledge and information	Ease of access to digestible information and knowledge about the intervention and how to incorporate it into work tasks.	The access to documents that inform the use of the digital tool. e.g. training or handbooks on how to use the tool.
CHARACTERISTICS OF INDIVIDUALS (stakeholder level)		
R. Knowledge & Beliefs about the Intervention	Individuals' attitudes toward and value placed on the intervention as well as familiarity with facts, truths, and principles related to the intervention.	Clinicians knowledge and belief on *C.diff* infection, CDI tool and technology in general.
S. Self-efficacy	Individual belief in their own capabilities to execute courses of action to achieve implementation goals.	Individual autonomy to affect change through the tool to achieve reduction of CDI and clinician's belief of ability of reduction of CDI without the need of the tool. Also include quotes on computer literacy.

T. Individual Stage of Change	Characterization of the phase an individual is in, as he or she progresses toward skilled, enthusiastic, and sustained use of the intervention.	this subdomain is not relevant, as this can't be measured at this point of the study
U. Individual Identification with Organisation	A broad construct related to how individuals perceive the organisation and their relationship and degree of commitment with that organisation.	The identification of the clinician within the GP setting and their willingness to participate in an implementation project or using a digital tool is affected.
V. Other Personal Attributes	A broad construct to include other personal traits such as tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style	Discuss tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style.

Abbreviations:

CDI: *Clostridioides* difficile infection

C.diff: Clostridioides difficile

Digital tool is used to refer to apps, websites software and risk prediction tools.

**If there are quotes that don't fit under any of the CFIR domains or subdomain please have a category named "Other".

1. Results

Overall, 10 clinicians participated in the study. The results for this study are divided into three sections: the first section describes all 10 clinician's perception on the burden of CDI and their perception on how the CDI tool should look like without being presented with the prototype; the second section (Cohort 1, n=5) describes the feedback on the low fidelity prototype developed in the previous chapter (prototype 1), and; the third section (Cohort 2, n=5) describes the feedback from the participants who were shown prototype 1 and 2 (see appendix L).

The characteristics of the 10 clinicians involved in this study are presented in table 10. Ten clinicians agreed to participate in the interviews, from four different health boards in Scotland, of which there were two physicians, one nurse, three pharmacists and four podiatrists.

Table 10. Participant's demographic profiling (n=10)

Demographic profiling	N (%)
Role	
Physician	2 (20%)
Nurse	1 (10%)
Pharmacist	3 (30%)
Podiatrist	4 (40%)
***Setting**	
Primary care	5 (50%)
Secondary care	9 (90%)
Area of work	
Out of hours/ unscheduled care (Nurse)	1 (10%)
Antimicrobial care (Pharmacists)	2 (20%)
General internal medicine/renal medicine (Physician)	1 (10%)
GP/Medical receiving ward (Physician)	1 (10%)
Clinical pharmacist/e-prescribing (Pharmacist)	1 (10%)
Diabetes and wound care (Podiatrists)	4 (40%)
Years in current role	
0 – 10	5 (50%)
11 – 20	3 (30%)
21 – 30	2 (20%)
Location	
Greater Glasgow and Clyde	3 (30%)
Ayrshire and Arran	2 (20%)
Fife	4 (40%)

Dumfries and Galloway	1 (10%)
Gender	
Female	5 (50%)
Male	5 (50%)
Age	
30 – 39	2 (20%)
40 – 49	5 (50%)
50 – 59	3 (30%)

*The total number of clinicians who participated in this study were 10, however the number of participants in the setting section is higher because some of them worked in both primary and secondary care.

4.1. First section: Perception on the burden of CDI and perceived aesthetics / content of a CDI tool

(feedback prior to the presentation of the prototype)

This first section of the results gathers findings on the clinician's perception of the CDI burden and their thoughts on how the CDI tool should look like. For the study, it was important to gather clinician's thoughts on the CDI tool prior to showing the prototypes as it would allow capture of their initial views without being influenced by the prototypes.

This section of the results is presented using the domains within the enhanced CFIR codebook (table 9), subdivided by the CFIR subdomains analysed deductively. CFIR is composed of four domains, however for the purpose of this study only three domains were identified and therefore applied for the analysis. The three domains are composed of subdomains that were used to understand whether the quotes were facilitators or barriers towards the implementation and adoption of the tool in secondary care. The analysis in the result sections was categorised into either barrier or facilitators that affects the implementation and adoption of the CDI tool.

Domain: Characteristics of individuals

Knowledge and belief about the intervention

This subdomain addressed the clinician's knowledge and beliefs about CDI, the CDI tool and technology in general (table 9). The themes that emerged addressed clinicians' knowledge on 4C antibiotics. When asked who contributes more towards

CDI between primary and secondary care, some clinicians had specific knowledge on the percentage and type of antibiotics prescribed in primary and secondary care. (Facilitator).

> *"I think primary care has higher impact on C.diff because they prescribe 80% of antibiotics. So, in that case there is a higher burden from that side, into secondary care that are obviously antibiotics, which are not just oral. So, there's IV (intravenous) antibiotics which aren't 4Cs that patients could get. And so, we (secondary care) prescribe fewer antibiotics." (P1, 30-39 years, secondary care)*

When discussing about the prescription of 4C antibiotics, a clinician mentioned that they prescribe a lot of 4C antibiotic in the renal unit. (Facilitator).

> *"We in renal medicine use quite a lot of 4C antibiotics, um, more than in other settings, certainly more than I would be prescribing in a general medicine environment. Um, and so I'm quite conscious of that with elderly patients with significant co-morbidity and cumulative of antibiotic exposure. But I think that it's a gut feeling rather than a confidence in my scientific knowledge." (P2, 30-39 years, secondary care)*

When asked whether all 4C antibiotics contribute equally to CDI, most clinicians weren't sure about it. This suggests that there is a lack of knowledge on the association of 4C antibiotics and CDI. (Barrier).

> *"I'm not entirely sure." (P6, 40-49 years, primary/secondary care)*

Domain: Inner setting

Culture

This subdomain describes day to day behaviours within a setting that have transformed into habitual actions (table 9). The themes that emerged were on clinician's antibiotic prescribing method and use of digital tools. Most clinicians stated

that they are cautious when prescribing 4C antibiotic and think about CDI when prescribing. (Facilitator).

> *"But obviously that's something when we review patients on antibiotics and if they are on antibiotics strongly associated with C.diff we will try to get them off the antibiotics or make sure the durations are reviewed and documented so that patients are not continuing them and make sure they are appropriate in terms of choices. We are working closely with microbiologists, the ones I work with, are very conscious of C.diff as well." (P10, 40-49 years, secondary care)*

One participant mentioned that they search for digital tools on google when they need support during consultations. (Facilitator).

> *"What I would ordinarily do is Google it, and then there's several sites which you've got kind of interactive, you click in different symptoms and then it gives you a score. And I wouldn't necessarily go to the same one each time. I just click till I find one and then go. I'm going through a kind of web browser really." (P3, 50-59 years, primary/secondary care)*

Implementation climate

1. *Sub-element: Tension for change*

The sub-element indicates the need for a change of the current situation in terms of technology used in practice, the prescription of antibiotics and CDI (table 9). The themes that emerged in this sub-element discuss the incidence of CDI in secondary care and prescription of antibiotics in Scotland. When asked if CDI is a burden, most clinicians stated that they do come across CDI in secondary care. (Facilitator).

> *"I come across it quite a lot in general medicine, yeah, a reasonable amount. (P2, 30-39 years, secondary care)*

When asked whether primary or secondary care contributes towards CDI, half of the clinicians mentioned that primary care prescribe more antibiotics, however the other

half of clinicians stated that secondary care comes across patients with more complex conditions than the patients in primary care, therefore most patients are prescribed with antibiotics in secondary care. (Facilitator).

> *"I imagine secondary care; I imagine it contributes more just because of the nature of the patients. So, people are in a worse position, presumably you know, they're not in the greatest of health as they've got to secondary care." (P9, 40-49 years, primary care)*

During the discussion about 4C antibiotics, a clinician mentioned that compared to other places in the world where they worked, the prescription of 4C antibiotics is well controlled in the UK. (Facilitator).

> *"Compared to other places, uh, I think probably quite low as well. I've worked in Australia for a while where 4C antibiotics were still given like tap water, compared to peers working in England." (P2, 30-39 years, secondary care)*

Furthermore, a clinician stated that although there has been a great reduction of 4C antibiotic prescribing, it is still prescribed unnecessarily. (Facilitator).

> *"Co-amoxiclav was the guilty secret. Many people just hide that they do it, but they do." (P4, 50-59 years, primary/secondary care)*

Readiness for implementation

The subdomain discusses the positive attitude towards the implementation of the CDI tool (table 9). All participants agreed that the CDI tool could be useful during consultations with patients. A clinician stated that they would use the CDI tool during the discussion of antibiotic prescribing with patients. (Facilitator).

> *"Yeah, I think they'd be useful. Um, yeah. Uh, I think even just for just having the discussion with patients." (P2, 30-39 years, secondary care)*

Another clinician mentioned that they would like the CDI tool to improve their knowledge of the infection. (Facilitator).

"I actually think I would because I don't think I know that much about that, I would, I'd like to have an idea, you know, and even it may not necessarily be something that would use all the time, but I still think the learning that I would get it to begin with, you know, and looking for certain risk factors that they haven't acknowledged before." (P8, 40-49 years, primary/secondary care)

Domain: Intervention characteristics

Design Quality and Packaging

This subdomain discusses the clinician's perception on the layout and functionality features of a tool including the provision/display of the risk score (table 9). The themes that emerged in this domain discuss the data storage method across secondary care, their perception on how the CDI tool should present the risk score and where they currently use digital tools. The listed themes were discussed before the clinicians were presented with the prototype, and therefore the following feedback is around their perception on how the CDI tool should look like rather than the feedback on the prototypes presented later to participants.

Although, different electronic systems were used in different wards at the time of the interviews, all secondary care clinicians stated that their system and the GP's system weren't interconnected. (Barrier).

"There is not a link between the two system currently, over here you have the GP system, and over there you have the pharmacy system. We try to pass the information but it's a manual process." (P5, 40-49 years, secondary care)

Even though the primary and secondary care systems are not electronically interconnected, there is still transfer of information between the two settings. It often happens through discharge letters or referral letters. Some clinicians mentioned that the prescriptions completed in secondary care would be notified to the patient's GP, however there is lack of recording the data into the GP system. (Barrier)

"We use Tiara so we record what we prescribe on our wound record on Tiara, but we also notify the GP practice what we have prescribed to their patient and then they can record that on to their EMIS® system or VISION® system so it will get uploaded onto their emergency care summary." (P6, 40-49 years, primary/secondary care)

"I think so. I hope so. I don't always check to make sure that they've done it, (GPs recording prescriptions done in secondary care) but that has certain of why we let them know so that it can be put into the system. [I:Okay]. I've heard that it doesn't always happen. "(P7, 50-59 years, secondary care)

Often in secondary care microbiologist examine patient's biological samples to determine whether an antibiotic should be prescribed or not. It was mentioned during the interviews that the microbiologists also have access to patient data and therefore determine which antibiotic to prescribe. Microbiologists have also additional patient data compared to clinicians. (Facilitator)

"They have the same as me in more actually, they've got more on paper data." (P7, 50-59 years, secondary care)

When asked where the clinicians use their current digital tools, nine clinicians mentioned that they use them on their phones (Facilitator). Only one clinician stated that they don't use phones during consultations with patients.

"Yeah they are on an iPhone." (P2, 30-39 years, secondary care)

During the interviews all clinicians were asked how the CDI tool should show the risk score (output). Most clinicians requested the risk score to be a numerical score or be divided into categories of low, medium and high-risk format. (Facilitator)

"…A numerical risk I think will be quite useful, and a time bounce or you have an X risk over the next Y number of days. I think it would quite useful." (P2, 30-39 years, secondary care)

"Just a risk, you know, if it said high risk category I guess caution or, yeah, almost like a.. You know when you put in your medication and to the BNF and it'll come up red if it's like a warning, be careful because just because of this, this and this, something like that. So, a warning and whether there's like mild chance or there is a significant risk." (P7, 50-59 years, secondary care)

Cost

This subdomain addresses the costs to implement a digital tool within clinician's prescribing system (table 9). When asked a clinician whether the CDI tool would be useful, the clinician mentioned that it would be useful in secondary care, however it would be costly to implement. (Barrier)

"Yeah useful, particularly in secondary care. But yeah, I would think that's costly [to implement]. But it would make a lot of sense" (P4, 50-59 years, primary/ secondary care)

4.2. Second section: perception on prototype 1

(following presentation of the prototype)

Cohort 1

This section of the study describes the clinician's feedback on prototype 1 from the perspective of all 10 interviews. Prototype 1 (appendix M) was shown to the clinicians and feedback on its usefulness and ease of use was gathered. The findings for this section are presented using the TAM usefulness and ease of use domains.

Usefulness

When asked if the prototype shown can be implemented into secondary care, clinicians stated that prescriptions are not done electronically, therefore the tool wouldn't be able to automatically extract the patient data to produce the risk score. (Barrier)

"The problem is you don't prescribe electronically in hospital." (P4, 50-59 years, primary/secondary care)

When asked whether clinicians would use a tool on their phones (where they would need to manually insert patient data), there were mixed views. One clinician stated that as junior doctors do rotations every six months, it would become a burden for clinicians to train them on the use of digital tools that are active formats. (Barrier)

"The question is would people do it? So, for the juniors every six months you'd have to tell another bunch of doctors what to do." (P4, 50-59 years, primary/secondary care)

In contrast another clinician stated that it could be useful for junior doctors while they are on their training. (Facilitator)

"I think it'd be good for junior doctors to sort of look at all of these things individually to see, well I should be like, you know, for their training." (P1, 30-39 years, secondary care)

When asked whether the shown prototype can be implemented in hospitals that had the hospital electronic prescribing and medicines administration system (HEPMA), one clinician who worked with the HEPMA system stated that having many risk alerts or notification that clinicians have to read might lead them to ignore the message. (Barrier)

"I mean it certainly looks like it looks like something you could have, […] but it needs to be discussed with the HEPMA team, […] because the more high risk notes you have, the less risky it seems because they (clinicians) are reading it at all the time." (P1, 30-39 years, secondary care)

When asked whether clinicians in secondary care would change their 4C prescriptions when a high-risk message was shown, the clinician stated that if they knew they are increasing the patient's risk then they would think twice about prescribing it. (Facilitator)

"If I knew a patient's C.diff risk been increased by so much, then certainly in this sort of elderly population you would maybe think twice about prescribing it." (P1, 30-39 years, secondary care)

When asked whether having a CDI tool would allow to prescribe, when necessary, with more confidence 4C antibiotics for low-risk patients. A clinician stated that it would, as the tool would be doing a calculation for the clinician and save their time. (Facilitator)

"Now if you're doing a full track that's time. So, if that's just calculating it for you, then yeah." (P1, 30-39 years, secondary care)

When asked whether the message on the CDI tool is enough for decision making, the clinician stated that it might help change their prescription. (Facilitator)

"I think it helps with your decision. Yeah. I think there's obviously a lot of other factors that would contribute to your final decision. But if you decided co-amoxiclav is the right option and then that comes up, you might change your decision. So yeah it helps." (P1, 30-39 years, secondary care)

One respondent stated that some clinicians prescribe co-amoxiclav without thinking and they doubted a risk prediction tool can change their decision making. (Barrier)

"I think there's probably a cohort of us clinicians who don't do a lot of thinking and prescribe Co-amoxiclav because we think that's a good antibiotic if you don't know what to do. […] I think if you've kind of reached that stage of decision making anyway, my guess is you're not going to be influenced by, you're not going to then look up what the individual risk of C.diff is before you do that." (P2, 30-39 years, secondary care)

One respondent stated that the CDI tool considers only the patient's risk to contract CDI and no other disorders, which could lead clinicians to prescribe drugs that can increment the risk of other disorders. (Barrier)

"The only thing about it is that is interested only in C.diff, if a patient had penicillin allergy […] it doesn't take any advance considerations, […] so my only thought there would be what if this process let them select a drug that is less

susceptible to C.diff but more risky to the patient for other reasons". (P5, 40-49 years, secondary care)

Easy to use

When asked whether the tool would be easy to interact for clinicians in secondary care, the clinician stated that clinicians might have to look at their notes to see if all the information for the risk calculator is present within HEPMA. (Barrier)

"I guess with HEPMA for the last three months we would require them to then go back to the notes. They might not have that information at hand." (P1, 30-39 years, secondary care)

When asked if they would prefer the CDI tool to be a standalone app or integrated into a system, the clinician stated that it would be used if integrated into a system that is already being used. (Barrier)

"I think it would be most likely to be used if it was integrated into something that's already used." (P2, 30-39 years, secondary care)

When asked whether the refining calculation feature is easy to use, the clinician stated that it is simple and straight forward. (Facilitator)

"I think it looks quite simple. No, I think really it looks good." (P1, 30-39 years, secondary care)

While another clinician suggested to change into buttons with yes or no option instead of the tick box. (Facilitator)

"You would have just yes or no. Why not just have the button?" (P7, 50-59 years, secondary care)

One respondent stated that having a standalone app that requires to put in patient data shouldn't be a challenging task as it can be done quickly. (Facilitator)

"Having a tool on your phone that you could quickly access, set in the details cause I don't think would be that enormous to put in these kind of details cause these are all just kind of drop downs and tick boxes on the tick box, aren't they? To me it would take a few seconds to set those into your calculator." (P2. 30-39 years, secondary care)

When asked whether the prototype was easy to understand, one clinician stated that they have difficulties in understanding the risk score format. (Barrier)

> *"It's quiet easy, the only thing I suppose it's not easy is you have co-amoxiclav, c.diff risk increase 330% so I can understand that and then the non-4C antibiotic c.diff risk increase is 70% and what does that mean in practice I'm not sure, presumably it's an additional 70% over the baseline risk, but I have no idea what the baseline risk for C.diff is". (P3, 50-59 years, primary/secondary care)*

4.3. Third section: perception on prototype 2

(following presentation of the prototype)

Cohort 2

This section of the study describes the clinician's feedback on prototypes 2 from the perspective of clinicians who attended the last five interviews. Prototype 2 (appendix M) was only shown during the last five interviews. The feedback was collected and presented using the TAM usefulness and ease of use domains.

Usefulness

When asked if the CDI tool would be useful as an app format, a clinician stated that it could slow down the appointment however it could increase patient safety. (Facilitator/ barrier)

> "*it would slow down the appointment, but I don't see that as a negative thing if it's going to increase patient safety*." (P7, *50-59 years secondary care)*

When asked if they would use prototype 2 during their consultation, a clinician stated that anything that can help them keep in mind the risk factor can be useful. (Facilitator)

"So, anything that can help you keep the risk factors at the front of your mind? I think that's a positive thing." (P9, 40-49 years, primary care)

When asked whether microbiologists would use the tool when making their decisions on which antibiotic to prescribe to the patient, a clinician stated that they would use it. (Facilitator)

"I would think they absolutely would" (P8, 40-49 years, primary/secondary care)

When asked which format of the CDI tool they would prefer, the clinician stated that the population diagram would be useful to discuss the antibiotic prescribing with patients. (Facilitator)

"I think this is useful for patients if you were to discuss antibiotic prescribing with patients [I: so, the population diagram] […] I think this is quite a visual aid for patients to show them. I think for us [clinicians] they all work because they all show the risk". (P10, 40-49 years, secondary care)

When asked if there is a clear benefit using the CDI tool, the clinician stated that they rarely prescribe 4C antibiotics as a guideline has been developed to reduce the prescription of the 4C antibiotic. (Barrier)

"There would be, but however because the guidelines have been developed actually really to reduce the use of for the 4C we do limit". (P6, 40-49 years, primary/secondary care)

When asked which format would be useful to have for the CDI tool, the clinician stated that having the risk presented in a population of 100 people would be easier for patients to understand than the percentage. (Facilitator)

"I think from a patient point of view, probably numbers over hundred. There's a lot a bit easier. Just thinking about some of my patients, you know, any percentage seems to be a risk to them versus you know, 12 out of hundred. So, if you sort of said like, you know, 4 percent chance, they might not understand

the significance of that. So yeah, I would probably say in a hundred". (P8, 40-49 years, primary/secondary care)

Easy to use

One clinician stated that depending on the understanding of the patient they would either use the bar chart or the population diagram to explain their choice of prescription. (Facilitator)

> *"I quiet like them both equally. And it just, I'm think if you were sitting discussing that with a patient, it would depend on your patient and how much they would understand". (P6, 40-49 years, primary/secondary care)*

One respondent highlighted that if prototype 2 was implemented it would be time consuming as clinicians would have to search and input all the patient data manually for the risk score. (Barrier)

> *"But very time-consuming cause you're gonna put all the previous medic, well the medication and previous antibiotic history, which is time consuming". (P7, 50-59 years, secondary care)*

While when asked whether prototype 2 could be implemented into secondary care, the clinician stated, that it looks simple and easy to use. (Facilitator)

> *"When I initially saw it, I wasn't keen on it. But then when you explained that it is pretty simplistic and it does make absolute sense, you know, it's pretty easy to use a slider bar for the age, a simple yes and no selectors and things. Um, yeah. And then quite simple to calculate the risk". (P8, 40-49 years, primary/secondary care)*

One respondent stated that the bar chart is too academic, and it would be difficult for patients to understand. (Barrier)

"So, I think that one looks too academic so, I can understand that, but I don't think if you want to use it with patients on a day to day basis, people don't look at things like this, most of the time". (P9, 40-49 years, primary care)

5. Discussion

This chapter aimed at understanding clinicians' perception on the burden of CDI in secondary care, validate feedback captured on CDI from the previous chapter, obtaining feedback on the low fidelity prototype developed in chapter 2 and understanding the feasibility of implementing a tool in secondary care. This involved semi-structured interviews with 10 clinicians from primary and secondary care across Scotland. As seen in the previous chapter only three GPs from primary care were engaged in the search activities. Although the engagement led to the development of the low fidelity prototype (prototype 1), for this chapter it was important to engage with more allied health professional to observe any discrepancies from the feedback obtained in the previous chapter. Although one of the objectives of this chapter was to investigate the possible implementation of prototype 1 in secondary care, due to lack of patient data in one electronic system it was evident that the prototype could not be implemented. Therefore, possible implementation of prototype 2, which required clinicians to input patient data manually was investigated during the last five interviews. The interviews were thematically analysed using the CFIR framework (table 9), and out of the five CFIR domains, the study's first section of findings was mapped against three of the relevant domains. While the second and third sections were analysed using the TAM's usefulness and ease of use domains.

5.1. Perception on the burden of CDI and perceived aesthetics / content of a CDI tool

One of the objectives (objective 1) of this study was to understand clinicians' perceptions of the burden of CDI in secondary care and to validate the findings from the previous chapter regarding the perspectives of primary care clinicians (objective 2). The results revealed wide variations in participants' knowledge and awareness of CDI prevalence and its associated risk factors, including the contentious issue of antibiotics being a significant risk factor for CDI. Some secondary care clinicians encounter CDI regularly, while others, including those in primary care, rarely encounter it (Tension for Change). Additionally, there was a divide in opinions on unnecessary 4C antibiotic prescribing, with some clinicians identifying it as a problem

in secondary care, while others indicated it was more prevalent in primary care (Knowledge and Belief about the Intervention).

Discrepancies in the reported incidence of CDI might be attributed to the varying population sizes and healthcare practices across different regions in Scotland, a country with around five million people. The 2020 NHS National Services Scotland report on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) indicated higher incidences of HA-CDI in NHS Ayrshire and Arran and NHS Highland, with CA-CDI being higher in NHS Ayrshire and Arran (NHS National Services Scotland, 2020). The 2022 ARHAI report further noted that NHS Ayrshire and Arran, NHS Highland, and NHS Lanarkshire had the highest incidences of HA-CDI, with NHS Highland showing the highest rates of CA-CDI (NHS National Services Scotland, 2022).

Although two clinicians from NHS Ayrshire and Arran were interviewed, there was a notable lack of representation from other health boards with higher incidences of CDI as reported by ARHAI. This limited representation may have contributed to variations in clinicians' perspectives on CDI incidence.

During the interviews, clinicians were also asked to share their perceptions of a potential digital tool for CDI and their ideas about its design. All participants agreed that a digital tool for CDI could be useful during discussions of antibiotic prescribing with patients. One clinician noted that such a tool could enhance their knowledge about the infection (Readiness for Implementation).

The use of digital tools in healthcare has many demonstrated benefits, including improving the clinician-patient relationship, enabling faster diagnoses, and promoting better communication and shared decision-making. For instance, a 2020 review analysing the progression of technology in healthcare highlighted the significant impact of telemedicine during the COVID-19 pandemic. Telemedicine facilitated remote appointment booking, diagnosis, and treatment, thereby minimising direct contact with the virus and maintaining continuity of care (Senbekov *et al.*, 2020). Although many are the benefits of using digital tools it’s vital for its

successful implementation and adoption to develop a tool that is user-friendly and useful.

Despite not being shown prototypes when discussing design ideas for the CDI tool, nine clinicians indicated that they use digital tools on their mobile phones during consultations. This suggests a positive likelihood of accepting a mobile-based digital tool for CDI. This sentiment was further reinforced when clinicians highlighted that patient data is not fully accessible through their current prescribing systems.

The clinicians interviewed used different systems: podiatrists used Tiara9©, some clinicians used the Hospital Electronic Prescribing and Medicines Administration system (HEPMA), and others relied on a combination of clinical portals and paper prescribing. Additionally, at the time of the interviews, the prescribing systems in primary and secondary care were not electronically interconnected. Communication between these systems was primarily conducted through discharge or referral letters. Some secondary care clinicians mentioned that when they issued a prescription, they notified the patient's GP practice, but there was often a lack of data recording into the GP's system (Design Quality and Packaging). A 2015 narrative review of the literature on healthcare communication between different settings highlights the significant issues healthcare professionals face, such as incomplete discharge letters or errors in referral letters. These communication problems can lead to negative outcomes like discontinuity of care, compromised patient safety, and increased costs (Vermeir *et al.*, 2015).

5.2. Perception on prototype 1

The next objective of this study was to gather feedback on the low-fidelity prototype developed in Chapter 2 (Objective 3) and investigate its implementation in secondary care (Objective 4). Overall, all clinicians liked the format of Prototype 1. However, they provided some negative feedback regarding the risk score format (percentage), expressing uncertainty about its clinical relevance and noting the absence of the population's baseline risk (Ease of Use). One clinician suggested changing the risk

refining calculator from its current tick-box format to a yes-or-no button (Ease of Use).

When discussing the implementation of the tool in secondary care, clinicians emphasized that while they appreciated its integration into a prescribing system, the fact that patient data is recorded in different systems within secondary care would make its implementation as a passive tool challenging (Usefulness). Accurate patient data consolidated in a single electronic system is crucial for the accuracy of the risk score and to prevent misleading results. A 2020 literature review on the benefits, risks, and strategies for successful digital tool implementation highlights how data quality can significantly impact treatment decision-making, leading to potential poor adoption of the tool (Sutton, 2020).

Although it became clear after the first five interviews that Prototype 1 could not be implemented in secondary care, a second prototype (Prototype 2) was proposed during the last five interviews. This iterative approach aimed to address the feedback and challenges identified with Prototype 1, potentially enhancing the tool's feasibility and acceptance in the secondary care setting.

5.3. Perception on prototype 2

Prototype 2 was developed as an active format, requiring clinicians to input all patient data to obtain the risk score. Initially, some clinicians were sceptical about its practicality, as searching for and inputting all the patient data seemed time-consuming. However, after receiving a demonstration and understanding how to use and interpret the results, they became more receptive, recognising its potential to facilitate patient consultation (Easy to use).

Opinions on the result format were mixed. Some clinicians found the population diagram easier to understand and useful for explaining risks to patients, while others preferred the bar chart, which included confidence intervals (Easy to use). One respondent appreciated both formats, using the population diagram for patient discussions and the bar chart for personal decision-making (Usefulness). A 2008 exploratory study on risk communication by Dolan and Iadarola suggested that

patients better understood their risk when multiple formats were used to communicate it (Dolan and Iadarola, 2008). This highlights the potential benefit of incorporating both formats into the CDI tool, catering to different preferences. Nonetheless, further investigation is needed to determine the preferred format among clinicians, given the small sample size in this study.

Compared to the GP interviews in Chapter 2, clinicians in this study expressed a greater willingness to use the digital tool for CDI on their mobile phones during patient consultations, the majority indicating they would use it to verify their decision-making and discuss their decisions with patients. A 2015 multicentred survey, which aimed to understand phone ownership rates among clinicians in five hospitals, found that 92.6% of physicians and 53.2% of nurses found their phones useful for performing clinical duties. Additionally, 89.6% of physicians and 67.1% of nurses used digital tools on their phones as part of their clinical practice and decision making (Mobasheri *et al.*, 2015).

This suggests a promising adoption rate for the CDI tool if it is optimised for mobile use, potentially improving clinical decision-making and patient communication.

5.4. Strengths and limitations

A strength of this study was the perceived positivity towards a digital tool for CDI. Although the implementation of prototype 1 into secondary care was deemed challenging, clinicians showed enthusiasm for using prototype 2 as an app or website. Despite only the last five of the ten interviewed clinicians being presented with prototype 2, the positive feedback received indicates substantial scope for further investigation.

A limitation of this study was that the clinicians recruited were from only four of the 14 health boards in Scotland. While including more clinicians from a broader range of health boards would have been ideal, this study represents significant progress compared to the previous study, which engaged only three GPs from a single health board. Furthermore, this round of interviews included a mix of allied health

professionals, providing insights into prescribing methods and systems across different professions.

Lastly, despite clinicians' support for prototype 2, challenges in accessing patient data between primary and secondary care mean that essential data might not be entered into the tool, or clinicians might have to rely on patients to provide the data. This situation is not ideal and could lead to misleading risk scores. However, these interviews were conducted in mid-2019, and there is a possibility that intercommunication between primary and secondary care has since improved. Nevertheless, further investigation is needed to understand the evolution of communication between these two settings.

5.5. Future work

The findings suggest that clinicians in secondary care are keen on using prototype 2 either on their phones or as a website during their patient consultations. To further understand the ease of use and usefulness of a digital tool for CDI, the next step would be to create a beta version of the CDI tool. The feedback collected to date will inform the design, layout, and content of this tool. Additionally, engaging with a digital development company to support this development will bring industry expertise and insight, ensuring the tool is both functional and user-friendly.

5.6. Conclusion

The study findings reveal varied perspectives among the interviewed clinicians on the burden of CDI, antibiotic prescribing practices, and the impact of 4C antibiotics. Despite these differences, there was a clear interest in having a digital tool to support antibiotic prescribing.

Although there was initial enthusiasm for prototype 1, its implementation in secondary care was deemed challenging due to discrepancies in patient data. Consequently, prototype 2 was introduced during the last five interviews. While manually entering all patient data is time-consuming, secondary care clinicians recognized the potential benefits the tool could bring to their consultations with patients. They appreciated the tool's capacity to enhance decision-making and

improve patient communication. This feedback highlights the importance of developing a user-friendly and efficient digital tool to support clinicians in managing CDI and antibiotic prescribing.

CHAPTER 4: The journey of developing the beta version of the CDI tool (Stage 3)

1. Introduction

Chapter 3 was aimed at understanding clinicians' perception on the burden of CDI in secondary care, obtaining feedback on the low fidelity prototype developed in chapter 2 and understanding the feasibility of implementing a tool in secondary care. The findings from chapter 3 suggest that although there are mixed feelings towards the burden of CDI in secondary care, clinicians are supportive of having a digital tool for CDI to support their clinical decision making. When exploring the possibility of implementing the low fidelity prototype developed in chapter 2, it was apparent that it would not be feasible since secondary care lacked up to date patient data in one electronic system (at the time of the interviews, data were collected in multiple electronic systems and in paper records). Therefore, a second prototype that required clinician's manual input of patient data was introduced during the last five interviews. In addition to prototype 2, two risk score formats (bar chart and population diagram) were also presented during the last five interviews to understand clinicians preferred risk format. Upon understanding how prototype 2 works, clinicians supported the idea of implementing an active system which requires manual input of patient data. Furthermore, when asked which risk score format clinician preferred, both formats were equally chosen during the last five interviews. As the interview sample size was small to decide on the risk format, it is apparent that there is a need to further investigate the preferred risk format among clinicians.

From the findings gathered in chapter 2 and 3 on a digital tool for CDI, the next step was to create a beta version to test the ease of use and usefulness of the tool with clinicians. A beta version is a pre-release of a tool that is used for testing its functionality before a final version is developed ready for implementation (Kumar and Abraham, 2017). To develop the beta version a digital tool development company was engaged as part of this programme of work. This chapter aims to describe the journey that was involved to develop the beta version of the CDI tool from the low fidelity prototypes.

2. Aims and objectives

This chapter (stage 3, figure 15) focused on developing the beta version for the CDI tool in collaboration with a digital development company. The findings from chapters 2 and 3 were used to inform the design of the beta version. A procurement document was created summarising in detail all the requirements and formats for the tool.

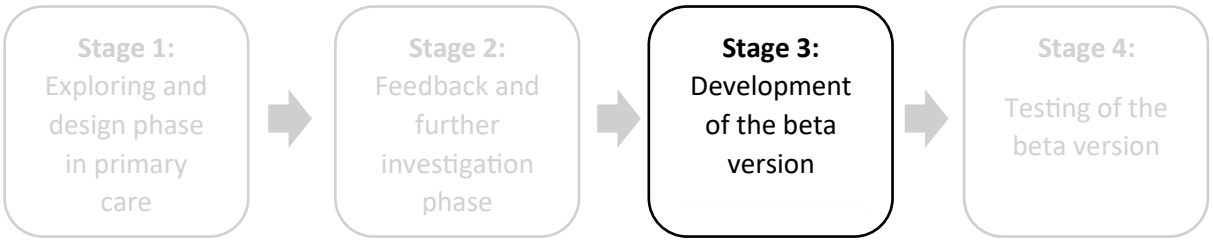


Figure 15. Stages involved in this thesis to develop the CDI risk predictor. Stage 3 discusses the development of the beta version of the CDI tool with a digital developing company.

The stage 3 study objectives comprised of:

- Objective 1: Create the procurement document that feeds all the requirements and format choices for the beta version of the CDI tool
- Objective 2: Project manage the process of developing the beta version
- Objective 3: Ensure the beta version incorporates all the requirements and formats addressed in the procurement document

3. Method

3.1. Digital tool development company

The study involved engaging a digital tool development company to create the beta version of the CDI tool. The company was chosen following a positive outcome in developing a digital tool for another project by a member of the project team. The company was contacted in April 2019 and a meeting was arranged between AJ, the project team and the project manager of the company. The conversation discussed what was the vision for the CDI tool and what would be possible to develop considering the budget and the time. The company suggested that creating a website for the beta version would be the optimal option as clinicians would easily be able to test it on their computers or phones through a link instead of having to download an app. Therefore, for the purpose of testing it was decided a website would be created for the beta version of the CDI tool. The funding to develop the beta version of the CDI tool was secured through the Scottish Healthcare Associated Infection Prevention Institute (SHAIPI).

3.2. Procurement document

A comprehensive procurement document outlining the requirements and formats for the beta version was created and shared with the digital development company. The company provided a template of the procurement document to the project team, which contained all the necessary information for developing the beta version. This document detailed the scope of the CDI tool, functional requirements (e.g. the ability to launch the digital tool for CDI from a link), variables with inputs (e.g. variable - gender; input - female or male), non-functional requirements (e.g. text should be readable and clear), and a storyboard illustrating how the CDI tool would be used.

Along with the procurement document, a supplementary document illustrating the result formats was also shared. This included examples of bar charts, population diagrams, and the explanatory text used to present the results. Additionally, the mathematical model for the digital CDI tool, developed by the University of Strathclyde, was provided for the development of the beta version.

3.3. Project management

The study and conversation with the company was managed by AJ and shared with the project team. Although, the documents were shared with the company by the end of June 2019, due to other work commitment of the company and summer holidays, the beta version wasn't created until October 2019. Unfortunately, the first version of the tool missed many factors that were specified in the documents shared. Therefore, another face-to-face meeting was arranged with the company's project manager and the web site creator. During the meeting all the errors in the beta version were addressed and resolved, resulting the beta version being ready to be tested with clinicians.

4. Results

This section presents the procurement document shared with the company to create the beta version. The document contains the purpose, format, content, functional requirements, non-functional requirements and the storyboard.

4.1. Procurement document

Purpose of the product/service

The purpose of this application is to allow clinicians to identify patients that are at risk of contracting the *Clostridioides difficile* infection (CDI) as a result of antibiotic prescribing.

The application should be in web app format, where clinicians obtain a risk score (to the screen) for the patient after the input of a set of N variables (listed below). The app should indicate the risk the patient has when: no antibiotic is prescribed, 4C antibiotics (Antibiotics associated with CDI) are prescribed and non 4C antibiotics are prescribed, therefore 3 risk scores should be presented. The presentation of the risk will be both numerical and graphical formats.

Scope

The risk score web-app should be stand-alone and executable/runnable from either a desktop PC or a mobile platform such as tablet or smartphone (cross platform). A link should take the clinician into the risk prediction tool home page and instructions should appear on the landing screen, where a set of pre-defined variables can be input manually (drop down). Following the input of these N variables clinicians should be able to click a “Calculate risk score” button, which will be followed by the displaying of the numerical and graphical risk for that given patient.

The risk score will be calculated using an existing algorithm which was developed by the Strathclyde team and a spreadsheet with the possible outcomes will be supplied for embedding within the web app.

Hardware

Since the web app will be running on desktop or a mobile/tablet, the tool should be able to run on Windows, IOS and Android if possible.

Software

The application should be written using cross platform tools and languages of the developer's choice to maximise the requirements set out in this document while staying within budget. The University of Strathclyde will provide the underlying risk score algorithm which has already been developed and tested.

Communications

The web app should have the ability to communicate with other linked websites or apps that will be defined from the team (e.g. BNF, medicines formulary).

The web app will store data of the user's usage. Once the clinician inserts the set of variables, the risk score should be immediately displayed without any pop-ups or dialogues. After the consultation, the clinician should have the option to clear the risk score outcome and use the calculation tool again for another patient with new input variables.

No advertisement, or any other kind of pop-ups should appear on the app.

Functional requirements

Functional requirements are desired operations or behaviours, which includes features, what it does, how it behaves, input, output, calculations, displays/presentations, user interface (e.g. scroll bar, clickable icons). More details of the functional requirements that were requested for the digital tool for CDI can be seen in table 11.

Table 11. List of functional requirements.

Functional Requirements for the digital tool for CDI
FR1: Be cross platform (IOS, Android, windows).
FR2: Be able to launch from link
FR3: The risk score tool (data entry screen) should be displayed after tapping the link
FR4: The app should be scrollable
FR5: The clinicians must be able to enter the variables in drop down format
FR6: The clinicians click the "calculate risk score" to display the risk for a single patient
FR7: Numerical and graphical risk should be displayed on one screen
FR8: No dialogues or Pop-ups should be present
FR9: input variables and output should be cleared easily so the tool can be easily used for another patient.
FR10: have a copy paste option

FR11: Need a hidden requirement on the 4C antibiotic variable drop down (in the variable table) – Number of 4C course <= Number of antibiotic courses. Either showing an error message if hidden requirement doesn't fulfil or automatically adjust the max value for number of 4C according to number of antibiotics.

Variables

The variables are patient's data used to calculate the patient's risk to contract CDI. The table 12 below shows all the variables that clinicians have to insert into the digital tool for CDI to obtain the risk score. The inputs are the options to clinicians have to choose from when inserting the patient data. The below variables and iputs were used to create the algorith for the CDI tool, hence accurate patient data is required to obtain an accurate risk score. Next to each variable in brackets there is a description on the functional requirement of how the input will be shown in the calculator page.

Table 12. List of variables and inputs.

Variables	**Inputs**	
Demographics		
Gender (binary drop down)	Female	Male
Age group (drop down)	15-19 20-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 65-69 70-74 75-79 80-84 85+	
Care home resident (drop down)	Yes	No
Previous drug exposure		
Number of antibiotic courses prescribed in the previous 3 months (drop down)	0 (minimum)	10 (maximum)

Number of 4C antibiotic courses prescribed in the previous 3 months (drop down)	Unknown-assuming no 4C exposure Unknown-assuming 4C exposure 0 1 2 3 4 5	
Proton pump inhibitor (PPI) antagonist prescription in the previous 3 months (drop down)	Yes	No
H2 antagonist prescription in the previous 3 months (drop down)	Yes	No
Comorbidities in the last 5 years		
Bronchitis (drop down)	Yes	No
Renal problems (drop down)	Yes	No
Cancer (drop down)	Yes	No
Inflammatory bowel disease (drop down)	Yes	No

*list of comorbidities ICD-10 (to be displayed as an information box). The ICD-10 were used to develop the mathematical model for the digital tool for CDI. To see which are ICD-10 for each comorbidity, please see table 13 below.

Comorbidities – Content for the information boxes

Table 13 below shows the comorbidities and the ICD-10 codes with their description. The information in the table is to be used as information boxes in the first calculator page. The information boxes are to be used by clinicians to understand which conditions are categorised under each comorbidity when inputting patient data. The ICD-10 codes were used to develop the mathematical model for CDI.

Table 13. List of comorbidities with the ICD-10 to be displayed as information boxes.

Comorbidities	ICD-10 codes with description
Bronchitis	- I27.8, Other specified pulmonary heart diseases - I27.9, Pulmonary heart disease, unspecified - J40.x–J47.x, Chronic lower respiratory diseases - J60.x–J67.x, Lung diseases due to external agents - J68.4, Chronic respiratory conditions due to chemicals, gases fumes and vapours. - J70.1, Chronic and other pulmonary manifestations due to radiation - J70.3, Chronic drug-induced interstitial lung disorders.
Renal problems	- I12.0, Hypertensive renal disease with renal failure - I13.1, Hypertensive heart and renal disease with renal failure - N03.2–N03.7, Chronic nephritic syndrome: diffuse membranous glomerulonephritis, diffuse mesangial

	proliferative glomerulonephritis, diffuse endocapillary proliferative glomerulonephritis, diffuse mesangiocapillary glomerulonephritis, dense deposit disease, diffuse crescentic glomerulonephritis - N05.2–N05.7, Unspecified nephritic syndrome: diffuse membranous glomerulonephritis, diffuse mesangial proliferative glomerulonephritis, diffuse endocapillary proliferative glomerulonephritis, diffuse mesangiocapillary glomerulonephritis, dense deposit disease, diffuse crescentic glomerulonephritis - N18.x, Chronic kidney disease - N19.x, Unspecified kidney failure - N25.0, Disorders resulting from impaired renal tubular function - Z49.0–Z49.2, Care involving dialysis - Z94.0, Transplanted organ and tissue status - Z99.2Dependence on renal dialysis
Cancer	- C00.x–C26.x, Malignant neoplasms of: lip, oral cavity and pharynx, digestive organs - C30.x–C34.x, Malignant neoplasm of: nasal cavity and middle ear, accessory sinuses, larynx trachea, bronchus and lung - C37.x–C41.x, Malignant neoplasm of: thymus, heart, mediastinum, pleura, neoplasm of other and ill-defined sites in the respiratory system and intrathoracic organs, bone and articular cartilage. - C43.x, Malignant melanoma of skin - C45.x–C58.x, malignant neoplasm of: breast, female genital organs - C60.x–C76.x, male genital organs, urinary track, eye, brain and other part of the central nervous system, neoplasm of other and ill-defined sites - C81.x–C85.x, Hodgkin lymphoma, follicular lymphoma, non-follicular lymphoma, mature T/NK-cell lymphomas, Other and unspecified types of non-Hodgkin lymphoma - C88.x, Malignant immunoproliferative diseases - C90.x–C97.x multiple myeloma and malignant plasma cell neoplasms, lymphoid leukaemia, myeloid leukaemia, monocytic leukaemia, other leukaemia of unspecified cell type, other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue, malignant neoplasms of independent (primary)multiple sites
Inflammatory bowel disease	- K50 Crohn disease (regional enteritis) - K51 Ulcerative colitis - K52.9 Noninfective gastroenteritis and colitis, unspecified

Non-functional requirements

Non-functional requirements are critical to the overall user experience and system performance. They define the attributes and conditions a system must have, rather than specific behaviours or functions. Examples include Availability, Reliability, Performance, Safety, Security, Quality.

Attributes required for the digital tool for CDI included:

a) Following the insertion of variables such as age, number of antibiotics, etc, a risk score for the patient should be presented in numerical format and graphical format for the following cases: no antibiotic, non-4C antibiotic, 4C antibiotic is prescribed.

b) The platform infrastructure will be designed to enable external links with related mobile apps (e.g. the NHS Scotland sepsis app) and other online resources (e.g. formularies).

c) The solution will be extensible, providing foundations for a national mobile CDS infrastructure and having the capability to expand to incorporate other types of content in future.

d) The solution will be designed to work with IOS and Android, windows operating systems in the first instance. Specific versions are detailed in the NHS National Education Scotland (NES) technical design and development standards

at:
http://www.central.knowledge.scot.nhs.uk/nesdigital/nesdigitalmobileappstechnicaldevelopmentguide.pdf
(**note:** the link does not work anymore, at the time it was a requirement to insert the above link that detailed the technical design and development standard. NES did not have any direct involvement in this project).

f) The solution should support reports of usage levels and analysis of usage behaviour – e.g. which areas and functionality are used most frequently.

Additional non-function requirements for the digital tool for CDI can be seen in table 14.

Table 14. List of non-functional requirements.

Non-functional Requirement for the digital tool for CDI
NFR1: Text should be readable and clear (AAA format)
NFR2: buttons and drop downs easy to click and insert variables
NFR3: free from errors
NFR6: There should be no option to amend the app from any user's side.

Storyboard

The storyboard (figure 16) was created to give an illustrative idea of when, why and how the digital tool for CDI (beta version) would be used.

When: During clinician and patient consultation, it is clear that the patient may need an antibiotic.

Why: The clinician is concerned whether prescribing an antibiotic could increase the patient's risk to contract CDI.

How: The clinician takes their phone and clicks on the digital tool for CDI, puts the patient's data and upon clicking on calculate, the patient's risk to contract CDI is being shown in a bar chart format and a population diagram. Both formats show the patient's current risk for CDI (without prescribing any antibiotics), the risk when non-4C antibiotics are prescribed and the risk when 4C antibiotics are prescribed. The digital tool for CDI helps the clinician make a decision whether prescribing antibiotics increases the patient's risk of contracting CDI in the next 12 months.

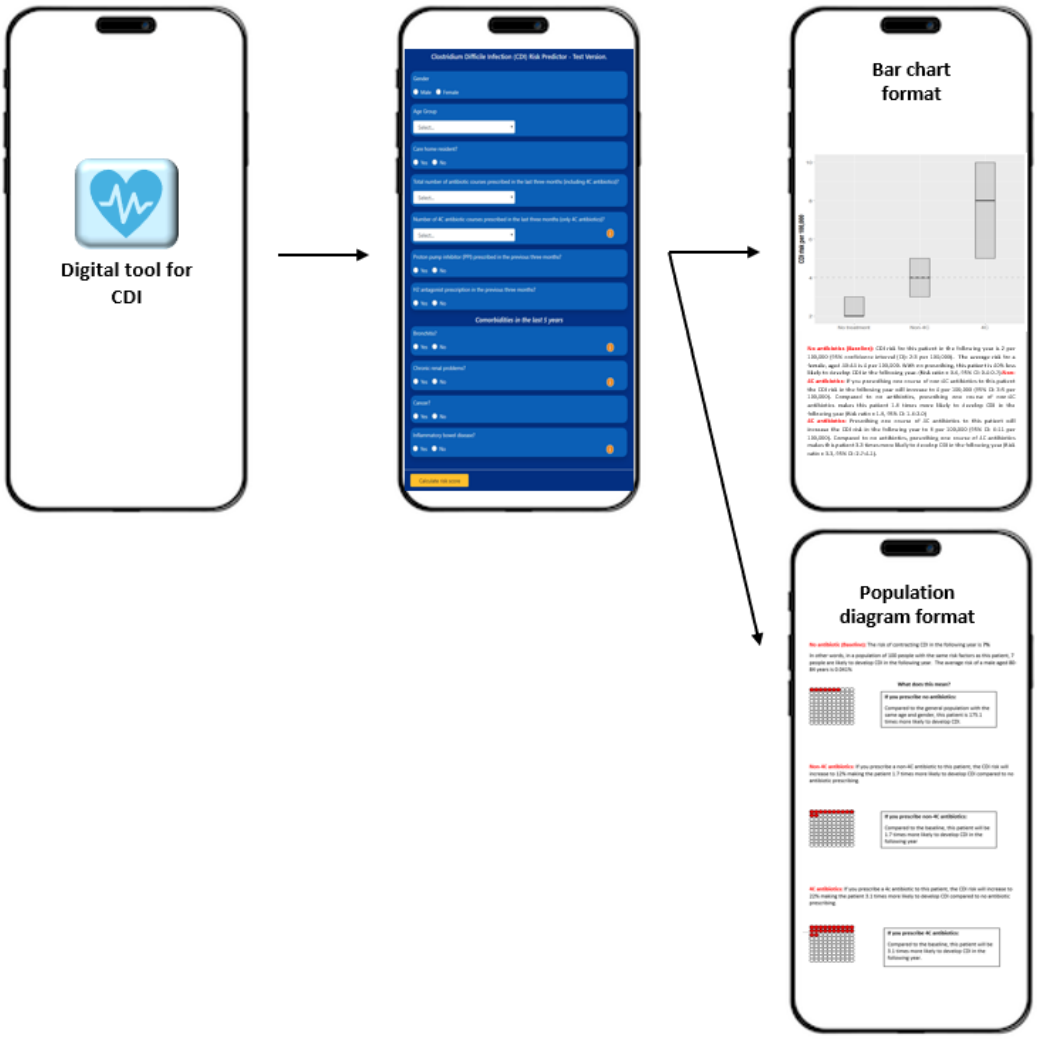


Figure 16. Storyboard that showcases how the digital tool for CDI should look like. The first screen shows that upon clicking on the digital tool for CDI, a page to insert the patient data will appear on the screen. Upon completing the screen with patient data and clicking calculate at the bottom, two risk score formats are presented as bar chart or population diagram. Both risk formats inform the clinician the patient's risk of contracting CDI in the next 12 months.

4.2. Result formats

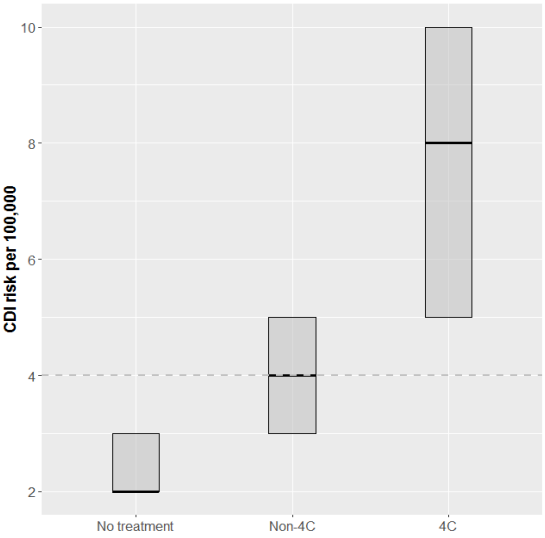
The section illustrates the patient's risk score of contracting CDI using two different result formats. The first result format is the bar chart diagram while the second result format is the population diagram. Both results formats display the baseline risk (the patient's current risk without prescribing antibiotics), the risk when non-4C antibiotics are prescribed and the risk when 4C antibiotics are prescribed. The patient's risks to contract CDI are presented for a timeline of 12 months. In this

section three case scenarios are presented so that it is possible to observe how the risk is presented of patients with low, medium and high risk to contract CDI.

Case scenario 1 (low risk patient):

Female, 40-44 years old, in the past 3 months no antibiotics, no other medication, non care home resident and in the past 5 years had no comorbidities.

Option 1 - Bar chart diagram:



*Grey dashed line shows the CDI population rate for this age and gender group. The black line represents the mean estimate of the risk, the grey bar represents the 95% confidence interval surrounding the estimate reflecting the variability in the estimate for the population.

No antibiotics (Baseline): CDI risk for this patient in the following year is 2 per 100,000 (95% confidence interval (CI): 2 - 3 per 100,000). The average risk for a female, aged 40-44 is 4 per 100,000. With no prescribing, this patient is 40% less likely to develop CDI in the following year. (Risk ratio = 0.6, 95% CI: 0.4-0.7).

Non-4C antibiotics: Prescribing one course of non-4C antibiotics to this patient the CDI risk in the following year will increase to 4 per 100,000 (95% CI: 3 - 5 per 100,000). Compared to no antibiotics, prescribing one course of non-4C antibiotics makes this patient 1.8 times more likely to develop CDI in the following year (Risk ratio = 1.8, 95% CI: 1.6-2.0)

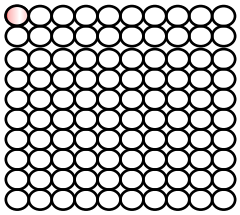
4C antibiotics: Prescribing one course of 4C antibiotics to this patient will increase the CDI risk in the following year to 8 per 100,000 (95% CI: 5 -10 per 100,000). Compared to no antibiotics, prescribing one course of 4C antibiotics makes this patient 3.3 times more likely to develop CDI in the following year (Risk ratio = 3.3, 95% CI: 2.7-4.1).

Option 2 - Population diagram:

No antibiotics (Baseline): The risk of contracting CDI in the following year **is 0.002%**.

In other word, in a population of 100 people with the same risk factors as this patient, 0.002 person are likely to develop CDI in the following year. The average risk of a female aged 40-44 years is 0.004%.

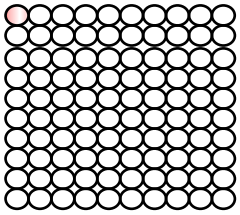
What does this mean?



If you prescribe no antibiotics

Compared to the general population with the same age and gender, this patient will be 40% less likely to develop CDI in the following year.

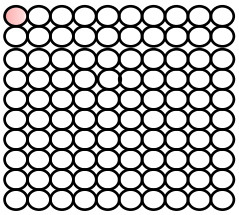
Non-4C antibiotics: If you prescribe a non-4C antibiotic to this patient, the CDI risk will increase to 0.004%, making this patient 1.8 times more likely to develop CDI compared to no antibiotic prescribing.



If you prescribing non-4C antibiotics:

Compared to the baseline, this patient will be 1.8 times more likely to develop CDI in the following year.

4C antibiotics: If you prescribe a 4C antibiotic to this patient, the CDI risk will increase to 0.008% making this patient 3.3 times more likely to develop CDI compared to no antibiotic prescribing.



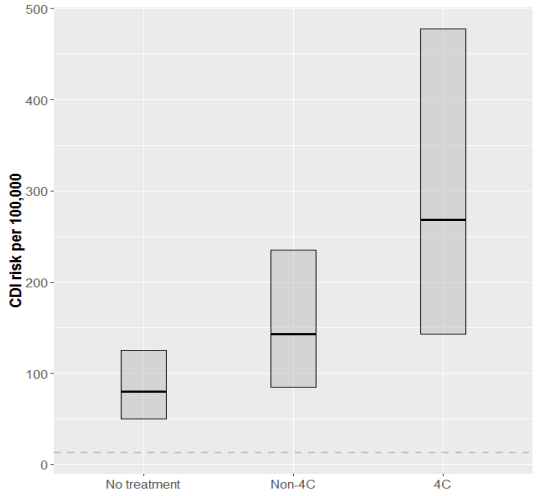
If you prescribe 4C antibiotics:

Compared to the baseline, this patient will be 3.3 times more likely to develop CDI in the following year.

Case scenario 2 (medium risk patient):

Male 65-69, in the past 3 months had 2 antibiotics of which 1 4C antibiotics, prescribed PPI, but non care-home resident and in the past 5 years had bronchitis.

Option 1 - Bar chart diagram:



*Grey dashed line shows the CDI population rate for this age and gender group. The black line represents the mean estimate of the risk, the grey bar represents the 95% confidence interval surrounding the estimate reflecting the variability in the estimate for the population.

No antibiotics (Baseline): CDI risk for this patient in the following one year is 87 per 100,000 (95% confidence interval (CI): 55 - 132 per 100,000). Compared to the CDI risk of the general population with same age and gender of 13 per 100,000, this patient is 6.6 times more likely to develop CDI in the following year. (Risk ratio=6.6, 95% CI: 4.2-10)

Non-4C antibiotics: Prescribing one course of non-4C antibiotics to this patient will increase the CDI risk in the following year to 154 per 100,000 (95% CI: 93 - 243 per 100,000). Compared to no treatment, prescribing one more course of non-4c antibiotics makes this patient 1.8 times more likely to develop CDI in the following year. (Risk ratio=1.8, 95% CI: 1.6-2)

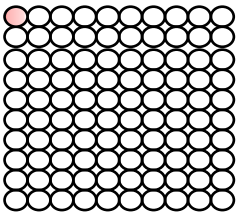
4C antibiotics: Prescribing one course of 4C antibiotics to this patient will increase the CDI risk in the following year to 292 per 100,000 (95% CI: 154 - 507 per 100,000). Compared to no treatment, prescribing one course of 4C antibiotics makes this patient 3.3 times more likely to develop CDI in the following year. (Risk ratio=3.3, 95% (CI): 2.7-4.1).

Option 2 - Population diagram:

No antibiotic (Baseline): The risk of contracting CDI in the following year is **0.087%**

In other words, in a population of 100 people with the same risk factors as this patient, 0.087 person are likely to develop CDI in the following year. The average risk of a male aged 65-69 years is 0.013%

What does this mean?



If you prescribe no antibiotics:

Compared to the general population with the same age and gender, this patient is 6.6 times more likely to develop CDI.

Non-4C antibiotics: If you prescribe a non-4C antibiotic to this patient, the CDI risk will increase to 0.154% making the patient 1.8 times more likely to develop CDI compared to no antibiotic prescribing.

If you prescribe non-4C antibiotics:

Compared to the baseline, this patient will be 1.8 times more likely to develop CDI in the following year

4C antibiotics: If you prescribe a 4c antibiotic to this patient, the CDI risk will increase to 0.292% making the patient 3.3 times more likely to develop CDI compared to no antibiotic prescribing.

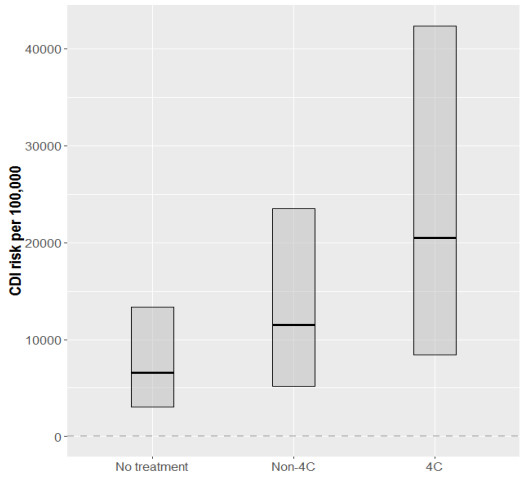
If you prescribe 4C antibiotics:

Compared to the baseline, this patient will be 3.3 times more likely to develop CDI in the following year.

Case scenario 3 (high risk patient):

Male 80-84 years, in the past 3 months had 4 antibiotics of which 2 4C antibiotics, prescribed PPI and is a care home resident. In the past 5 years he had bronchitis and cancer.

Option 1 - Bar chart diagram:



*Grey dashed line shows the CDI population rate for this age and gender group. The black line represents the mean estimate of the risk, the grey bar represents the 95% confidence interval surrounding the estimate reflecting the variability in the estimate for the population.

No antibiotics (Baseline): CDI risk for this patient in the following one year is 7119 per 100,000 (95% confidence interval (CI): 3238-14604 per 100,000). Compared to the CDI risk of the general population with same age and gender of 41 per 100,000, this patient 175.1 times more likely to develop CDI in the following year. (Risk ratio = 175.1, 95% CI: 79.6-359.1)

Non-4C antibiotics: Prescribing one course of non-4C antibiotics to this patient will increase the CDI risk in the following year to 12338 per 100,000 (95% CI: 5404-25604 per 100,000). Compared to no antibiotic, prescribing one more course of non-4c antibiotics makes this patient 1.7 times more likely to develop CDI in the following year. (Risk ratio = 1.7, 95% CI: 1.6-1.9)

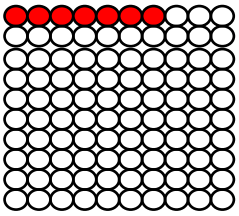
4C antibiotics: Prescribing one course of 4C antibiotics to this patient will increase the CDI risk in the following year to 21894 per 100,000 with (95% CI: 9140-44573 per 100,000). Compared to no antibiotic, prescribing one course of 4c antibiotics makes this patient 3.1 times more likely to develop CDI in the following year. (Risk ratio = 3.1, 95% CI: 2.6-3.5)

Option 2 - Population diagram:

No antibiotic (Baseline): The risk of contracting CDI in the following year is **7%**

In other words, in a population of 100 people with the same risk factors as this patient, 7 people are likely to develop CDI in the following year. The average risk of a male aged 80-84 years is 0.041%

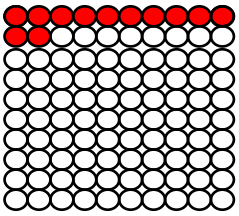
What does this mean?



If you prescribe no antibiotics:

Compared to the general population with the same age and gender, this patient is 175.1 times more likely to develop CDI.

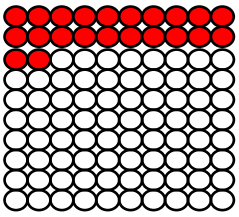
Non-4C antibiotics: If you prescribe a non-4C antibiotic to this patient, the CDI risk will increase to 12% making the patient 1.7 times more likely to develop CDI compared to no antibiotic prescribing.



If you prescribe non-4C antibiotics:

Compared to the baseline, this patient will be 1.7 times more likely to develop CDI in the following year

4C antibiotics: If you prescribe a 4c antibiotic to this patient, the CDI risk will increase to 22% making the patient 3.1 times more likely to develop CDI compared to no antibiotic prescribing.



If you prescribe 4C antibiotics:

Compared to the baseline, this patient will be 3.1 times more likely to develop CDI in the following year.

4.3. Beta version

First look of the digital tool for CDI

Once the procurement document and the result formats documents were shared with the developing company, a first version of the digital tool for CDI was shared with the project team (See figures 17 - 19). Figure 17 presents the first page of the digital tool for CDI which is the calculator page requiring all the patient information. While figure 18 shows the result page with both the bar chart and the population diagram on the same page. Although both diagrams look like the diagrams shared in the results document, the text explaining the risk score was missing. Figure 19 shows an error message that was displayed on the first page of the digital tool. The error message would be displayed when selecting the option “Unknown” on the variable “Number of 4C antibiotics courses prescribed in the last three months (only 4C antibiotics)”. When the procurement document was shared with the company, it was indicated that there would be two “Unknown” options for the variable “Number of 4C antibiotics courses prescribed in the last three months (only 4C antibiotics)”, the first one as “Unknown-assuming no 4C exposure” and “Unknown-assuming 4C exposure”. This allowed the clinician to make an informed decision with the patient and choose either one of the options appropriately. However, in figure 18 only the option “Unknown” was given and an error message would be displayed without allowing to calculate the risk score.

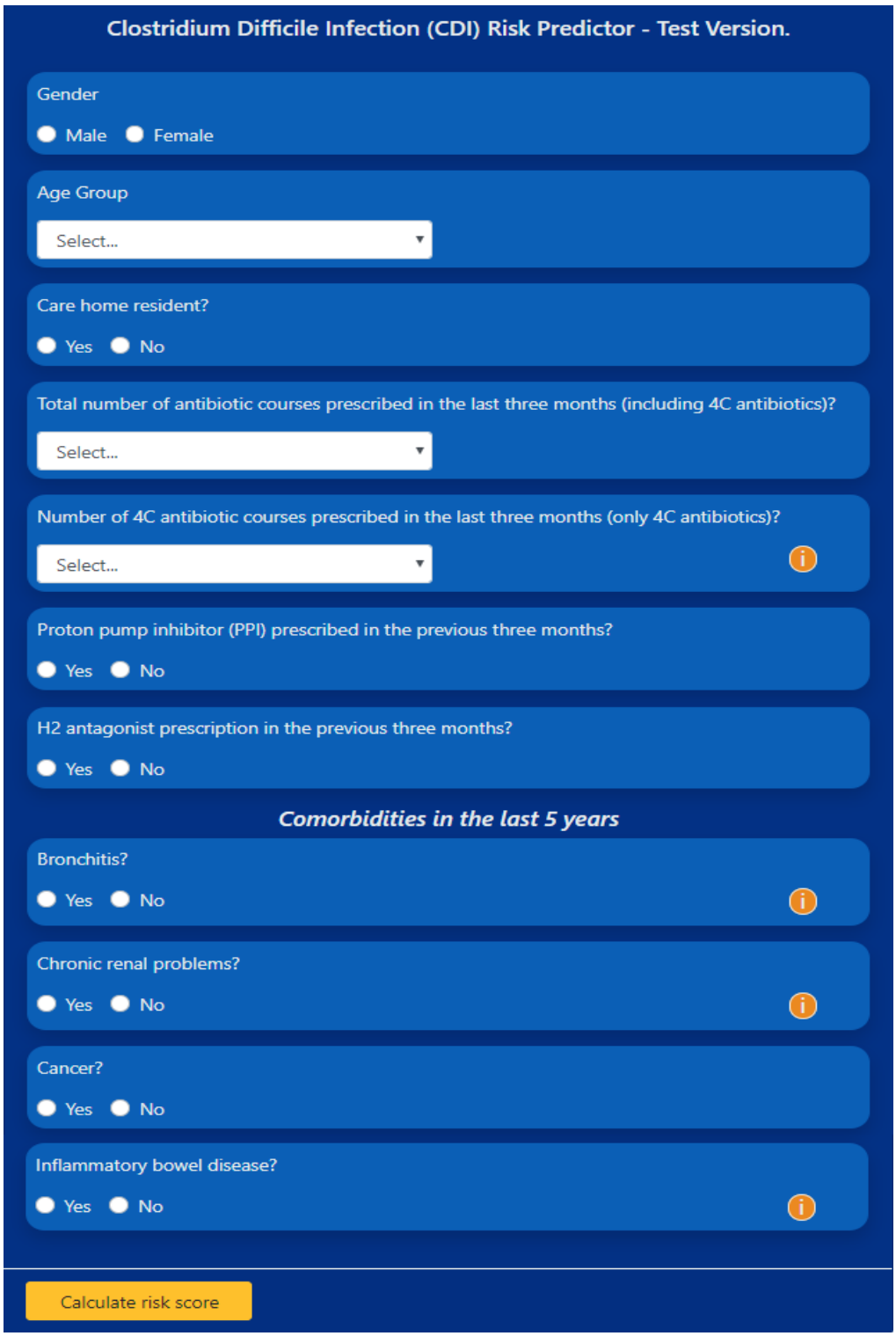


Figure 17. First page of the digital tool for CDI (beta version). The first page is used to insert all the patient data required to calculate the patient's risk score to contract CDI. This was v1 of the beta version.

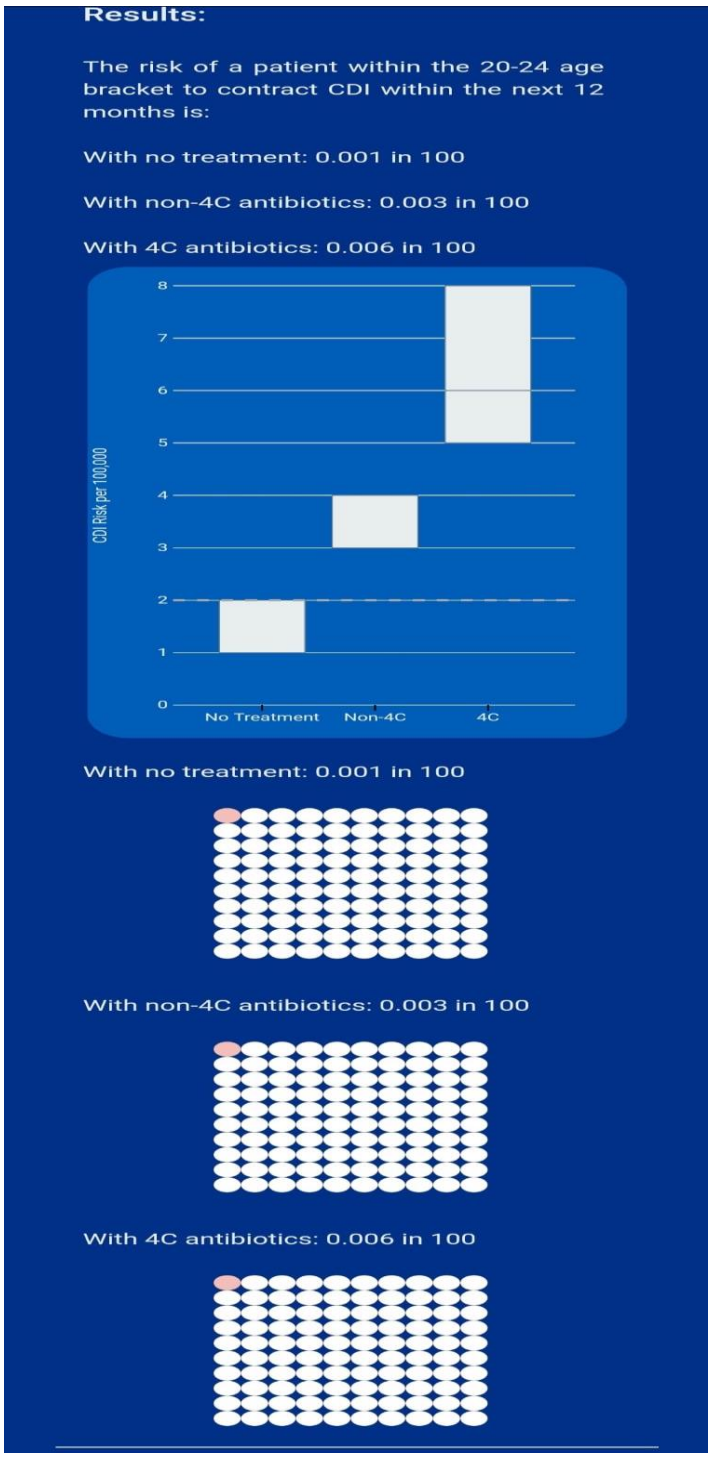


Figure 18. Result page of the digital tool for CDI (beta version). In this beta version of the digital tool for CDI, both the bar chart and the population diagram are displayed on the same page. Currently, explanatory text to help clinicians better understand the results is not included. This was v1 of the beta version.

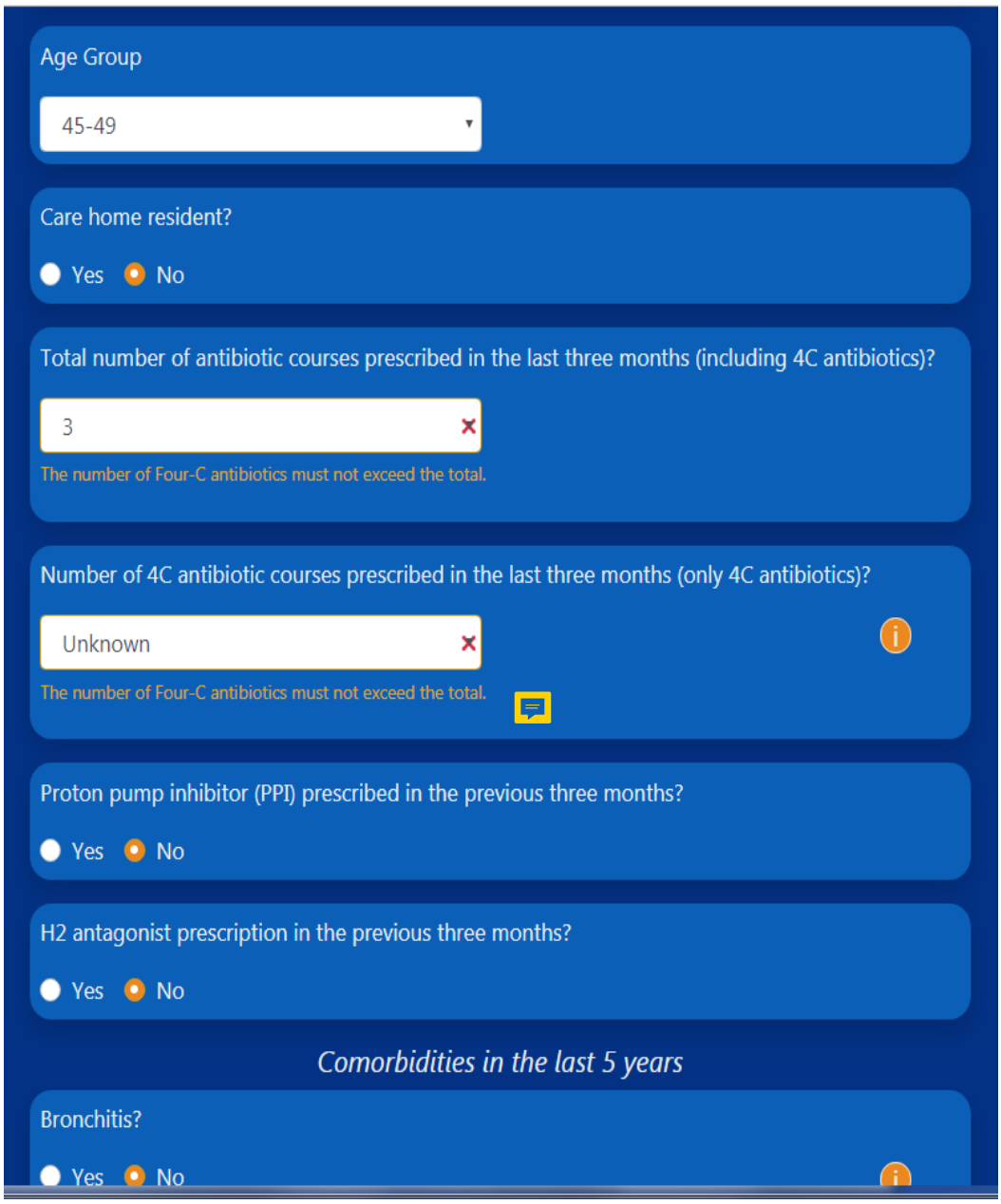


Figure 19. An error message appears when the "Unknown" option is chosen for the number of 4C antibiotics courses prescribed in the last three months. Selecting "Unknown" prevents the user from continuing with the calculation. This was v1 of the beta version.

4.4. Amendments to v1 of the beta version for CDI

Once the project team reviewed the beta version shared by the developing company, the team created a document listing all the changes required to the digital tool for CDI. Table 15 below shows all the changes that were requested for the first page and to the two results formats.

Amendments to the first page (variables page) of the digital tool for CDI

Table 15. Changes for the first page (variable page) of the digital tool for CDI

Current header	New header (to be actioned)	Feature	Variable description changes (to be actioned)	Programming notes
Clostridium difficile Infection (CDI) Risk Calculator – Test Version, only for clinical trials	*Clostridium difficile* Infection (CDI) Risk Predictor - Test version.		A “L" is missing in Clostridium	
Number of antibiotics courses prescribed in the last three months	Total number of antibiotic courses prescribed in the last three months (including 4C antibiotics)	Drop down required	Include a drop down select option with a rating (increment = 1) from 0 to 10+	For the 10+ group, use the results for 10 in the look up file.
Number of 4C antibiotic courses prescribed in the last three months	Number of 4C antibiotic courses in the past three months (only 4C antibiotics)	Drop down	- Remove “unknown-assuming no 4C antibiotics” – not required. - Change label “unknown 4C exposure” to “Unknown” using the same existing row in the look up file. - Change upper limit from “5” to “5+”. - Include an information box “i” to define 4C antibiotics - text to read “clindamycin, cephalosporin, fluoroquinolones and co-amoxiclav”.	For the 5+ group use the result for 5 in the look up file.
Proton pump inhibitor (PPI) antagonist prescribed in the previous three months	Proton pump inhibitor (PPI) prescribed in the previous three months		Remove “antagonist” from header.	
Bronchitis		Information icon	Remove current text in information icon and replace with: - Specified and unspecified pulmonary heart disease	

			- Chronic lower respiratory diseases - Lung diseases due to external agents (chemicals, gases, fumes, vapours, radiation, and drugs)	
Renal problems	Chronic renal problems	Information icon	Remove current text in information icon and replace with: -Chronic nephritic syndrome -Chronic kidney disease -Unspecified kidney failure	
Cancer		Information icon	Remove icon	
Inflammatory bowel disease		Information icon	Remove current text in information icon and replace with: - Crohn's disease - Ulcerative colitis	
Submit	Calculate risk score		Change the labelling of the button to “calculate risk score”	

Layout features / capabilities

- Place the variables and the input options on the same line, rather than below each other.
- Insert an error message if the variables are inserted incorrectly, or any inputs are missing. e.g. an error would come up if the clinician entered a total number of antibiotics which is less than the number of 4C antibiotics.
- The tools format/layout on the phone looks good. However, on the computer, the tool looks squeezed in the middle of the page. Configure a better format for the computer view

Results page

- Insert two separate results presentation formats on separate pages/screens ideally with the option for clinicians to view as a bar chart and then as a population diagram – this should be located at the end of the variables screen. (This is important in the prototype so we can get feedback on what may be the preference of clinicians or if we should have both. It will also allow us to better accommodate the text needed with the graphics to provide interpretation – see below).
- On the result page insert two buttons for the following actions:

    - To allow the clinician to go back to the inserted variables for the current patient and edit a variable if incorrect e.g. entered no to cancer but this is not correct and wants to recalculate without re-entering all variables.
    - Retain the present “clear“ button for a new patient.

Bar chart presentation

- Change the colour of the bar chart background to allow a better contrast between the background of the app and the bar chart background. It is presently blue on blue.

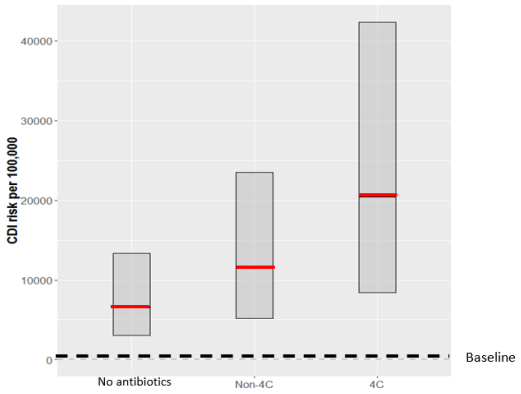
- The mean estimate risk score in the bar chart (the middle line) should be bold or in a different colour so it can be seen more easily as shown below as a red line.
- The baseline should be a different colour, bolder and there should be a label to identify this is the baseline - as shown below.
- There should be a text explanation (to the bar chart "Key" – as shown below). If you change the colours in bar chart, please amend the colours indicated in the text.
- Can we have the ability when the mouse is on the bar chart to have a pop up window providing the actual figure for the bar i.e. the mean estimate and the 95% confidence interval (or an alternate format to accommodate these data)

E.g.

  - **No antibiotics:** For your patient the risk to contract CDI with no antibiotic is 7119 per 100,000. **(95% confidence interval (CI): 3238-14604 per 100,000)**

- Below is an example of the bar chart again and also the text that needs to accompany the bar chart on the app view.

Bar Chart:



Key – the black dashed line shows the CDI population rate for this age and gender group. The red line represents the mean estimate of the risk, the grey bar represents the 95% confidence interval surrounding the estimate reflecting the variability in the estimate for the population.

Bar chart text

Please place the text below the chart in the following format and text. Please note the risk score for the bar chart should be in 100,000 and not 100. We want to have this different in the different results options.

The **baseline risk** of a male aged 80-84 to contract CDI within the next 12 months is 41 per 100,000. For your patient if you prescribe:

No antibiotics: the risk to contract CDI with no antibiotic is 7119 per 100,000. Compared to the baseline risk, your patient is 175.1 times more likely to develop CDI.

Non-4C antibiotics: The risk to contract CDI with a non-4C antibiotic is 12338 per 100,000. Compared to no antibiotics, prescribing one more non-4C antibiotics makes your patient 1.7 times more likely to develop CDI.

4C antibiotics: The risk to contract CDI with a 4C antibiotic is 21894 per 100,000. Compared to no antibiotics, prescribing one more 4C antibiotics makes your patient 3.1 times more likely to develop CDI.

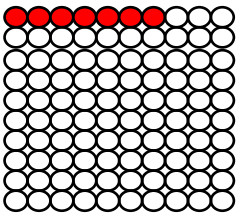
Population diagram:

- Please place the text as shown in the example below i.e. some of the text alongside the population plot

The **baseline risk of** a male aged 80-84 to contract CDI within the next 12 months is 0.041%.

No antibiotics: For your patient the risk of contracting CDI in the following year is **7%** i.e. in a population of 100 people with the same risk factors as your patient, 7 people are likely to develop CDI in the following year.

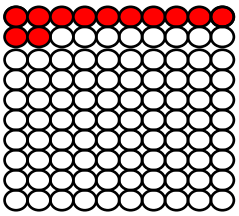
What does this mean?



If you prescribe no antibiotics:

Compared to the baseline risk with the same age and gender, your patient is 175.1 times more likely to develop CDI.

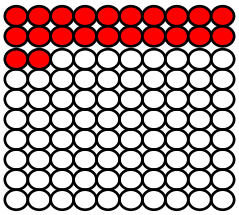
Non-4C antibiotics: If you prescribe a non-4C antibiotic to your patient, the CDI risk will increase to 12%.



If you prescribe non-4C antibiotics:

Compared to no antibiotics, your patient will be 1.7 times more likely to develop CDI in the following year

4C antibiotics: If you prescribe a 4C antibiotic to this patient, the CDI risk will increase to 22%.



If you prescribe 4C antibiotics:

Compared to no antibiotics, your patient will be 3.1 times more likely to develop CDI in the following year.

4.5. Version 2 of the beta version for CDI

The below screenshots of the beta version for CDI were taken after the amendments to version one of the tool. Figures 20 – 22 show the updated first page of the tool and the two risk score formats, which are now in two different screens. The user can switch between the two formats by clicking on the top left button which reads as "Switch to population diagram" or "Switch to bar chart". Differently to version one, the result pages of version two have all the text explaining the result.

Figure 20. Front page of v2 the beta version with example scenario of female patient aged between 65 – 69 who had two antibiotics in the past three months of which one 4C antibiotic. The patient has been prescribed with Proton pump inhibitors in the past three months and had cancer and inflammatory bowel disease in the past five years.

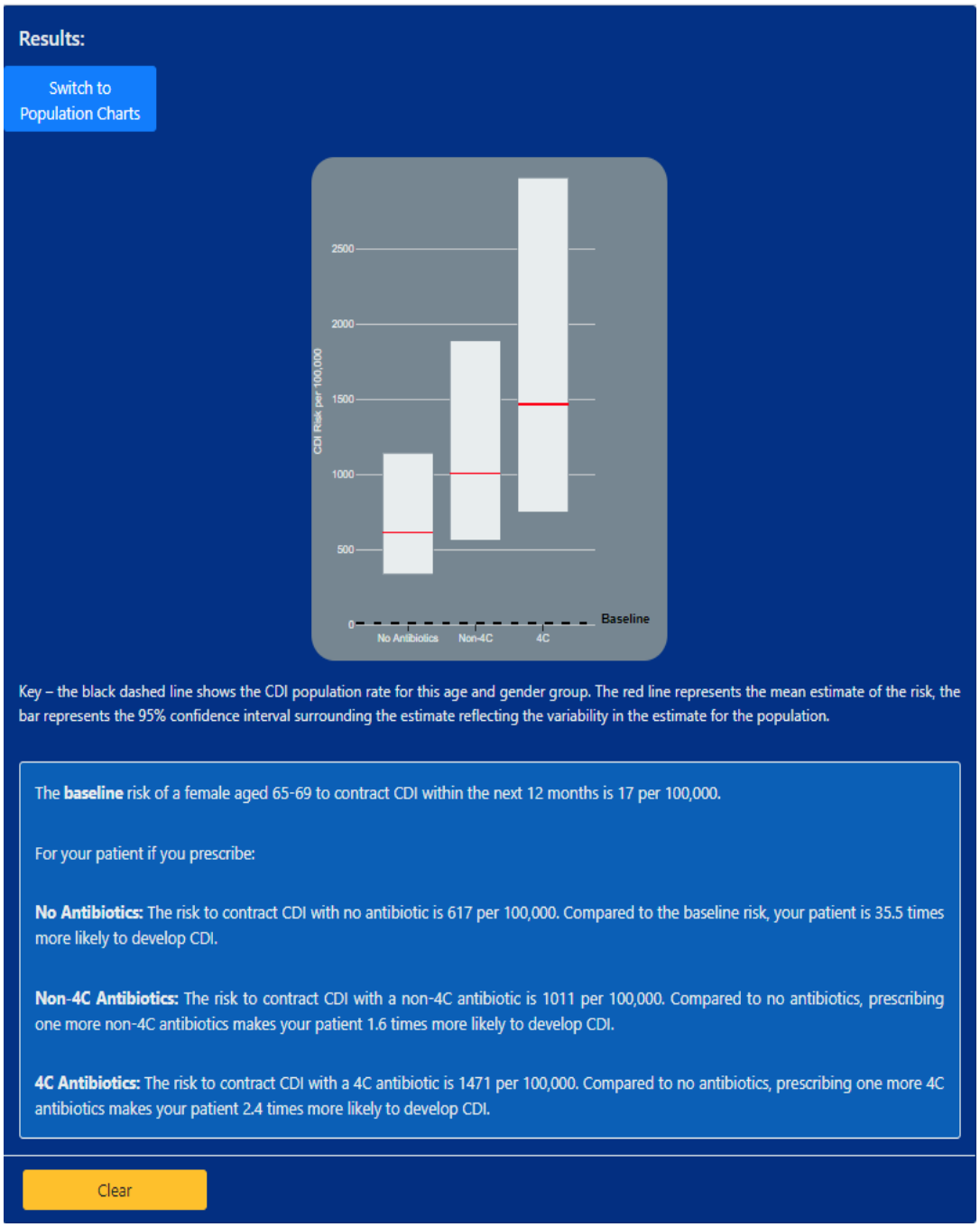


Figure 21. Bar chart results of the example scenario.

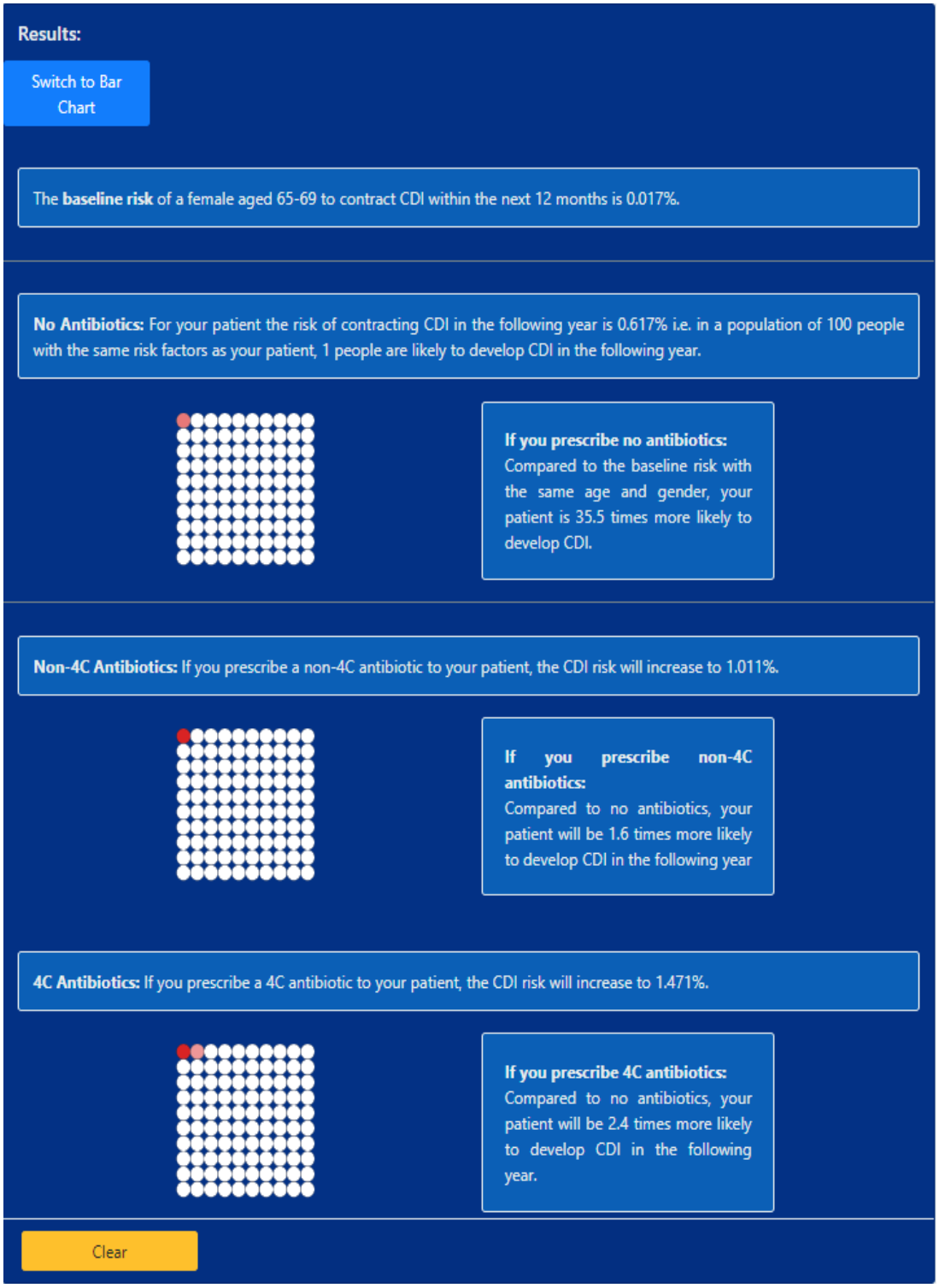


Figure 22. Population diagram result of the example scenario.

The information boxes

The information boxes for the beta version were originally supposed to contain all the ICD-10 codes with their descriptions as seen in table 13, which the developing company inserted as per instructions in the procurement document. Unfortunately, no screenshots were taken to be shown. The first impression of the project team after seeing the information boxes was that there was too much information and that it probably was not necessary to display all the information as seen in table 13. Therefore, the project team decided to simplify the information boxes removing all the ICD-10 codes, and just having conditions summarizing the information that was previously being displayed (See figure 23 – 26). The content of the information boxes will then be reviewed by clinicians during the testing of the beta version.

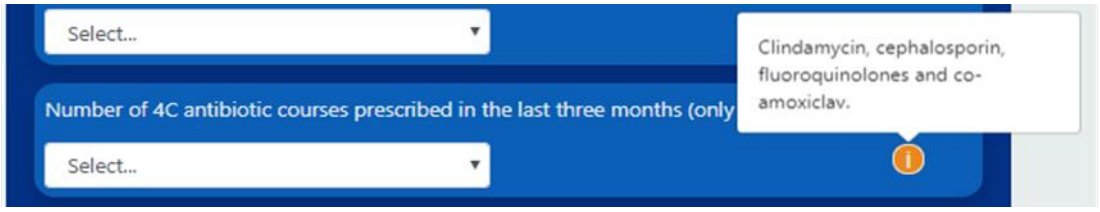


Figure 23. Information box describing what is considered as 4C antibiotics.

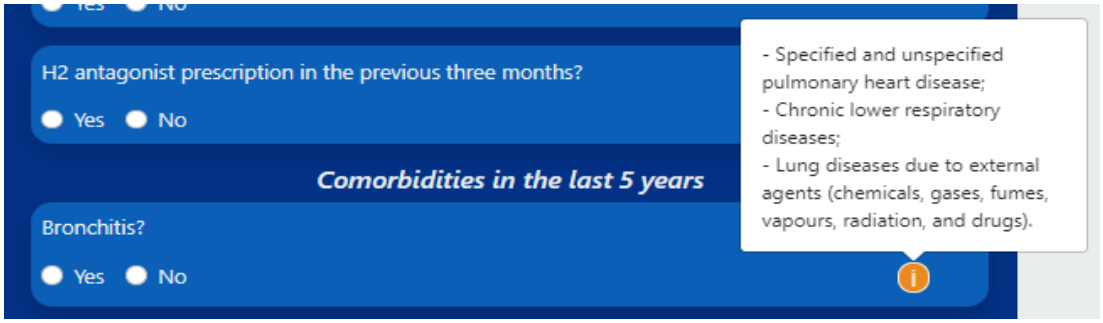


Figure 24. Information box explaining what is considered as bronchitis.

Figure 25. Information box explaining what is considered as Chronic renal problems.

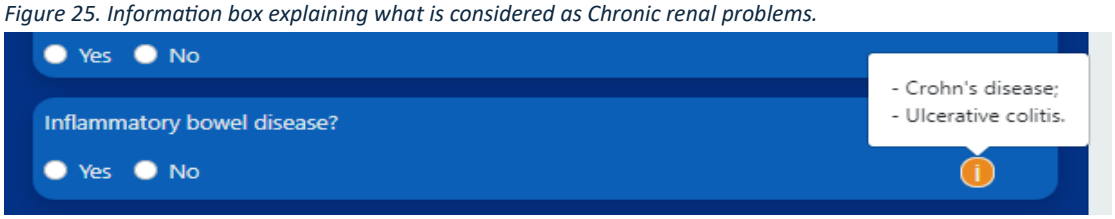


Figure 26. Information box explaining what is considered as Inflammatory bowel disease.

5. Discussion

The development of the beta version of the CDI tool was informed from the findings in chapter 2 and 3. The findings suggested that secondary care clinicians were supportive of having an active digital tool for CDI that would require manual input of patient data, accessing the tool through their phone or their computer. During the last five interviews in chapter 3, clinicians were asked which risk format they preferred to be used in the tool, and since the bar chart and the population diagram were both preferred by the participants, both formats were decided to be incorporated in the beta version of the CDI tool until further investigation.

A digital tool developing company was engaged to develop the beta version using the procurement document, result format document and the mathematical model provided. The initial beta version seen in figure 17 - 19 had minimal information and an error message appeared when selecting the option "Unknown" on the variable "Number of 4C antibiotics courses prescribed in the last three months (only 4C antibiotics)". Therefore, further changes were required to amend v1 of the beta version for CDI. An amendment document was shared with the developers highlighting all the changes in the first and the results pages. The changes made to the beta version for CDI are seen in figure 20 – 16. It is normal for beta versions to go through various stages of amendments when working with digital development companies. This iterative process is essential for refining the tool, as each stage of development brings new insights and opportunities for improvement. As issues are identified and resolved, the tool becomes increasingly robust and user-friendly (Montagni *et al.*, 2017). The collaborative effort between the development company and the project team ensured that the beta version met the required standards and was ready for subsequent testing and validation phases.

In addition, testing with clinicians would not be possible if a beta version was not created. In fact it is crucial when developing a digital tool to conduct user testing as it allows to understand whether the tool is easy to use, useful and what needs to be improved in order to reach user satisfaction (Bai, Mork and Stray, 2017). Some benefits of user testing during the development stage are that it is more cost effective

to make changes to the tool, than after implementation, improved levels of effective use and adoption (Kujala, 2003). Therefore, changes to version two may be required following user testing, however clinicians that will be testing the tool would be able to experience the tool on their phones and computers and provide feedback on its use.

5.1. Strength and limitations

The design of the beta version was meticulously informed by the comprehensive feedback gathered in Chapters 2 and 3. While only three GPs participated in the study outlined in Chapter 2, a total of ten clinicians contributed to Chapter 3, allowing for both validation of initial feedback and the capture of additional insights from a broader group. These chapters documented studies that were structured and analysed using well-established frameworks, including the Consolidated Framework for Implementation Research (CFIR), the GUIDES checklist, and the Technology Acceptance Model (TAM). By employing these frameworks, the studies ensured a rigorous and systematic approach to collecting and interpreting feedback. Consequently, the design of the beta version is grounded in robust, evidence-based insights, reflecting a thorough understanding of user needs, implementation contexts, and technology acceptance factors. This methodical approach not only enhances the reliability of the feedback but also ensures that the design is aligned with best practices and user expectations.

A limitation of this study was the communication gaps that led to misunderstandings of the beta version requirements between the project team and the developers. Despite the creation and sharing of a comprehensive procurement document containing all necessary information, v1 of the beta did not meet the project team's expectations. One possible cause of these misinterpretations could be the timing. Although, the procurement document was shared with the company at the end of June 2019, but due to prior commitments, they were unable to start working on the beta version for CDI until the end of October 2019. The heavy workload and tight project deadlines may have contributed to the developers missing crucial content in v1 of the beta version.

Although v1 of the beta for CDI required some amendments, engaging a digital tool development company brought multiple benefits. Firstly, their extensive experience in developing digital tools for other companies provided valuable insights during the CDI tool's development. They were familiar with the best features to include, such as dropdowns, scrollable lists, and yes/no buttons. Their previous work with the NHS meant they understood the required standards and appropriate colours to use for NHS-related projects. Additionally, no one on the project team had the expertise to develop a beta version capable of displaying the result formats shown in v2 of the beta version for CDI, therefore collaborating with a digital development company was vital for the progression of the study.

5.2. Future work

Having developed the beta version of the digital tool for CDI, it is clear that the next phase would be testing the tool with clinicians to obtain feedback on its usefulness and ease of use. Additionally, feedback on its content such as the information boxes, and the results formats will be key points of investigation. One of the objectives of the testing will be also to include understanding of whether clinicians have a preference on one of the results formats or whether both of them should be included in the final version of the tool.

Following the testing phase, there may be need a to create another amendment document highlighting all the changes that are required to be implemented into the tool that emerged. Upon sharing the document with the developers another round of review by the project team may be needed to ensure all the changes requested have been actioned.

5.3. Conclusion

To conclude using the findings from chapter 2 and 3, a beta version of the digital tool for CDI has been created with a digital development company. In order to inform the developers on the content of the beta version, a procurement document, a results format document and the mathematical model were shared. Upon receiving the first version of the beta version, it was clear that there was need for further changes

before the tool was ready for testing with clinicians. Therefore, an amendment document and a face to face meeting with the developers was undertaken and version two of the beta version created ready for testing.

CHAPTER 5: User testing of the beta version (Stage 4)

1. Introduction

Chapter 4 aimed to develop a beta version of the CDI tool using the findings from chapter 2 and 3. The chapter's primary output was a procurement document detailing the tool's format, content, and functionality. Additionally, documents outlining result formats and the mathematical model were shared with developers. However, despite these efforts, important components were overlooked, and error messages were present. After a face-to-face meeting with the development team and the creation of an amendment document, these issues were addressed, and the tool was deemed ready for testing.

Usability testing allows understanding of whether the digital tool meets the end user's needs and preferences (Bai, Mork and Stray, 2017). Usability tests usually involve a small number of test participants as compared to market research studies and clinical trials (Sandars, 2010). Usability refers to the ease with which a person can use a product in a particular set of circumstances (Sandars, 2010). The focus of usability testing is always the user, and it attempts to systematically identify usability problems at an early stage in the development process so that they can be rectified before the intervention is more widely implemented (Kujala, 2003).

Conducting usability testing of the beta version (version 2) enables refinement of the CDI tool before implementation. Therefore, the aim of this study was to test the beta version created in chapter 4 to understand clinicians' perceptions on the tool's ease of use, usefulness, content and whether there is a preferred result format between the two currently displayed in the tool.

2. Aims and objectives

This chapter (stage 4, figure 27) focused on testing the beta version of the CDI tool (version 2) that was created in chapter 4, with clinicians from primary and secondary care. Through the testing the aim was to gather feedback on the ease of use and usefulness of the CDI tool. Furthermore, to gather feedback on the layout, content and functionality of the tool and make amendments as required.

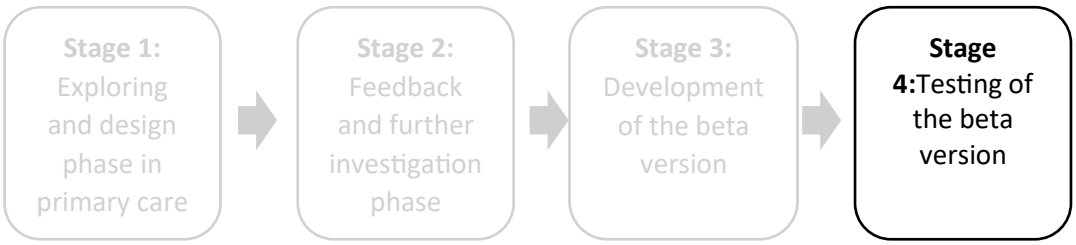


Figure 27. Stages involved in this thesis to develop the CDI risk predictor. Stage 4 discusses the testing of the beta version of the CDI tool.

The stage 4 objectives compromised of:

- Objective 1: Understand whether the CDI tool is easy to use.
- Objective 2: Understand whether the CDI tool is useful during consultation.
- Objective 3: Gather feedback on the layout, content, functionality and understand which result format is preferred among clinicians.
- Objective 4: Amend the CDI tool from the feedback gathered.

3. Method

3.1. Study design and participants

The study involved two focus groups and two one to one interviews that used a mix of open and closed questions, with clinicians from primary and secondary care in Scotland from November 2019 to December 2019. Clinicians were recruited to test and give feedback on the CDI risk prediction tool.

Ethics was obtained through the Strathclyde Institute of Pharmacy and Biomedical Science department, at the University of Strathclyde, aligned to the ethics in chapter 4 (appendix G).

3.2. Participant recruitment strategy

Recruitment for the study was completed through the snowball sampling method where participants were recruited through the support of other participants (Noy, 2008). Three independent connections were contacted to support recruiting participants for the testing of the CDI risk prediction tool. One of the connections offered a time slot to run a focus group with members of the Association of Scottish Antimicrobial Pharmacists (ASAP) during one of their meetings, while another connection gathered together their colleagues for another smaller focus group. Finally, the third connection shared contact details of two participants interested in the testing of the tool and one to one interviews were conducted with the two participants.

The inclusion criteria for participation compromised:

- Clinicians from primary and secondary care across Scotland
- Practitioners prescribing antibiotics

Although practitioners prescribing antibiotics was one of the inclusion criteria, as the recruitment was a snowball sampling method, some participants were not active antibiotic prescribers. However, since their area of work was antimicrobial stewardship and infectious disease, they had good knowledge on the topic and were

able to provide feedback on the content and supporting information displayed in the tool. Reimbursement for participation was not provided in this phase of the study.

3.3. Interview schedule

The interview schedule was comprised of semi-structured questions and closed survey statements. The questions were developed using the Technology Acceptance Model (TAM) (Davis, 1989) as the main objectives of the study were to understand the ease of use and usefulness of the CDI risk prediction tool. The semi-structured questions focused on the content, and layout of the tool while the closed survey statements at the usefulness and ease of use of the tool. The survey compromised of 19 Likert scale questions from totally disagree to totally agree (7 point scale). The statements focused on the importance of reducing CDI and 4C antibiotic prescribing, the usefulness of the tool, the ease of use of the tool in a clinical setting, and whether the result formats of the tool are understandable. A breakdown of the survey statements by the theme is presented in table 16.

The interview schedule (semi structured and closed survey statements) was piloted with clinical researchers from the Pharmacoepidemiology and Health Care research group at the University of Strathclyde, who had clinical practice experience but were not actively prescribing antibiotics. The pilot allowed testing of the flow of questions and the time required for the interviews and took place in a meeting room at the University of Strathclyde. Minor changes to the statements were identified during the pilot which were included in the final interview schedule (appendix O and appendix P).

Table 16. Survey statements broken down by their theme.

Survey statements	Theme
Targeting the reduction of CDI in Scotland is important	General theme
Reduction of 4C antibiotics prescribing in primary care is important	General theme
Reduction of 4C antibiotics prescribing in secondary care is important	General theme
The tool can be useful to support clinicians during antibiotic prescribing	Usefulness
Using the tool can facilitate antibiotic decision making	Usefulness
The tool can be added to the existing workload	Ease of use
The tool can be added to the existing workflow	Ease of use
The patient data required for the tool is easily available	Ease of use
The tool is relevant	Usefulness
The tool's result as a bar chart is understandable	Ease of use
The tool's result as a population diagram is understandable	Ease of use
There will be no difficulties in explaining the results to the patients	Ease of use
The time and tasks required for the tool doesn't seem extensive	Ease of use
The tool doesn't require extensive training	Ease of use
Training could improve the overall interaction with the tool	Ease of use
The tool is easy to use	Ease of use
The tool can be used regularly	Usefulness
I would use the tool	Usefulness
Colleagues could influence my decision to use the tool	General theme

3.4. Data collection

The focus groups and one to one interviews were conducted from November to December 2019 at a convenient time for the clinicians. For one-to-one interviews the option for both face to face and telephone interview was offered. All clinicians opted for face-to-face interviews within their preferred location. On the day of the interview, an information sheet (appendix Q) detailing the aim of the interview and data handling measures was given to the clinicians. Permission for audio-recording, ensuring confidentially and anonymity was sought from each clinician. A consent form (appendix R) was asked to be signed, with the option of withdrawal from the study at any time.

The focus groups and one to one interviews began by formally introducing the researcher, giving a short overview of the project, and outlining the aim of the interview. The link to the tool was shared with the participants who were asked to

access it though their mobile phones or laptops. A case scenario was also shared with participants to test and use the tool. While participants were using the tool they were asked some semi-structured questions allowing the conversation to flow and enable the participant to share any additional views not captured by the posed questions. The activities were concluded by asking participants to complete the survey statements.

The first focus group was conducted during a section of one of the ASAP meetings and due to time limitation, the group was divided into two. All the questions were asked to the first group (focus group 1A) however they were not asked to complete the survey. While the second group (focus group 1B) were asked to complete the survey and were asked the questions around usefulness of the tool to reduce the prescription of 4C antibiotics, the two best things about the tool and two things they would like to change. There was a total of 6 participants in each group. For the one-to-one interviews and second focus group, all participants were asked all the questions and completed the survey.

3.5. Analysis of the data collected

All interviews were recorded using Dictaphones and verbatim transcribed. Each transcript was carefully checked with the recordings to correct any mistakes by AJ. Personal identifiers were removed, and the transcript kept anonymised. Thematic analysis was used to analyse the interviews transcripts including deductive analysis.

The survey data were analysed using Microsoft Excel to calculate the count and percentages of each response.

4. Results

The demographic profiling of the clinicians involved in the research activities are presented in table 17. A total of 17 clinicians participated in this study of which 13 were pharmacists, three were nurses and one was a pharmacy technician. In this study two focus group interviews were conducted, one with 12 clinicians and another with three clinicians. Additionally, two one to one interviews were also conducted with two clinicians.

Table 17. Participant's demographic profile (n=17)

	N (%)		N (%)
Role		**Area of work**	
Pharmacist	13 (76%)	Antimicrobial stewardship and infectious disease	13 (76%)
Nurse	3 (18%)	District nurse	1 (6%)
Pharmacy technician	1 (6%)	Sexual reproductive health	1 (6%)
***Setting**		Veterinary medicine	1 (6%)
Primary care	8 (47%)	*No response*	1 (6%)
Secondary care	14 (82%)	**Years in current role**	
Other (Lecturer)	1 (6%)	1 - 5	4 (23%)
Other (Veterinary pharmacist)	1 (6%)	6 – 10	6 (35%)
Independent prescriber		11 – 15	4 (23%)
Yes	9 (53%)	16 – 20	1 (6%)
No	8 (47%)	20+	2 (12%)
***Participant's patients**		**Place of work**	
Inpatients	13 (76%)	Ninewells Hospital Dundee	4 (23%))
Outpatients	12 (71%	Western General Hospital	2 (12%)
Not applicable	2 (12%)	Glasgow Caledonian University	1 (6%)
Gender		Sandyford Sexual Health	1 (6%)
Female	15 (88%)	NHS Lanarkshire	1 (6%)
Male	2 (12%)	Ayr Hospital	1 (6%)
Age (years)		Hospital for small animals - University of Edinburgh	1 (6%)
30 – 35	3 (18%)	Victoria hospital , Kirkcaldy	1 (6%)
36 – 40	2 (12%)	NHS Borders	1 (6%)
41 – 45	5 (29%)	NHS Greater Glasgow and Clyde	1 (6%)
46 – 50	3 (18%)	Golden Jubilee National Hospital	1 (6%)
51 – 55	3 (18%)	Aberdeen Royal Infirmary	1 (6%)
No response	1 (6%)	Dumfries and Galloway Royal infirmary	1 (6%)

*Participants had the choice to select multiple answers, which means the same person could have selected more than one answer per question. This means the total number of responses to the question could be higher to the number of participants who answered the questions.

4.1. Interviews

This section presents the findings collected through the focus groups and one to one interviews. Each session included use of the beta version, discussion around its content, layout, usefulness and ease of use.

The findings have been presented under clinician's feedback on the content, layout, on the usefulness of the tool to reduce the prescription of 4C antibiotics, the two best things about the tool and two things they would like to change.

As the focus group conducted during the ASAP meeting was split into two groups 1A and 1B, the below interview feedback will indicate which group the feedback was captured from.

Feedback on the content of the tool

This section presents the feedback shared by clinicians on the content of the digital tool for CDI. When asked whether the labelling for the comorbidities is clear, some clinicians had mixed views for the variable 'Bronchitis':

> *"I suppose it could be liable to misinterpretation because people will be coded as having had pneumonia or lower respiratory tract infections. People might get confused as whether that's only to tick the box if they've had bronchitis, but they've not had pneumonia." (P1, 51 – 55 years, primary/secondary care, focus group 1A)*

Another clinician suggested that the labelling bronchitis can lead to further confusion on whether CDI is associated with either chronic or acute issues:

> *"It doesn't, like, specify whether it's an acute or chronic issue. I'm imagining that they might be different, have different risks associated with them." (P2, 41 – 45 years, secondary care, focus group 1A)*

Additionally, clinicians suggested different labelling instead of bronchitis:

> *"I'm not sure people would use the term bronchitis it tends to be lower track infections." (P3, 41 – 45 years, secondary care, focus group 1A)*

> *"instead of bronchitis, [..] similar to what you've got for chronic renal problems, just like chronic respiratory problems, something like that. Bronchitis makes it a bit more specific. If it was just a chronic respiratory disorder, it might make it open up a little bit more." (P4, 30 – 35 years, primary care/lecturer, one to one interviews)*

During the second focus group, similar feedback also emerged around changing the labelling for bronchitis:

> *"Most people, if they were pulling out this tool in secondary care, would recognize chronic renal disease and Chronic pulmonary disease instead." (P5, 41 – 45 years, primary/secondary care, focus group 2)*

When asked whether anything else should be added or removed from the information boxes, a clinician suggested that since transplanted organs was one of the ICD 10 code that the algorithm was created with, it was important to include it in the information box for chronic renal problems:

> *"So, if somebody's had transplant, renal transplant, or if they are undergoing renal dialysis or be specific around renal insufficiency." (P6, 36 – 40 years, secondary care, focus group 2)*

Additionally, another clinician suggested that the variable cancer should also have an information box stating that it includes all cancer type:

> *"I wonder if that might be helpful to say that. Okay. For all cancer types. Yeah. So even the pop-up box just says for all cancer types, just because some clinicians might start to dig a question." (P7, 46 – 50 years, primary care, one to one interviews)*

Finally, it was suggested to make the labels of the variables bolder so that it would be easier to read:

> *"Maybe the bit about last five years needs to be a bit bold. [..] Yeah, just to attract attention. I think you should have to comorbidities as well." (P5, 41 – 45 years, primary/secondary care, focus group 2)*

Feedback on the layout of the tool

This section presents the feedback on the layout of the digital tool for CDI. When asked around the colours used in the tool there were contradicting feedback among clinicians:

> *"I like the layout. I think it's quite clear, the blue is good". (P8, 51 – 55 years, secondary care, focus group 1A)*

> *"I just think the two colours should be more contrasting." (P9, 46 – 50 years, primary/secondary care, focus group 1A)*

When asked if the drop-down option to select the variables was good, a participant responded:

> *"I like the yes and no, and I particularly like the drop down, actually." (P7, 46 – 50 years, primary care, one to one interviews)*

Further discussing on the layout of the tool, another clinician pointed out that the labels in the bar chart should be displayed a little bit clearer as it was difficult to read them on the phone:

> *"I think the three bars could be labelled a bit more clearly because at the bottom, it's all kind of scrunched together on the phone anyway, it doesn't appear as clearly as on the screen." (P1, 51 – 55 years, primary/secondary care, focus group 1A)*

While discussing the result formats, various clinicians suggested they understood better the population diagram and expressed to have the population diagram first in the tool instead of the bar chart:

> *"If people want the technical kind of bar chart, they could switch to that. So have this one first (population diagram) and the other one to the option to go (bar chart). (P8, 51 – 55 years, secondary care, focus group 1A)*

However, a clinician expressed to have the bar chart first and the population diagram second to avoid users bypassing the risk of CDI as the numbers in the population diagram are in a smaller format than the bar chart:

> *"I actually quite like it the way that it is. Even though I prefer the smaller numbers. I quite like that the bigger numbers come first. And I'm not sure why, to be honest, but I quite like that it's giving you, okay, this is the big picture, and then let's break it down again, because I think you're right. I completely understand what you're saying. If there's one person out of 100, you might think that's a really negligible risk or quite a small risk, but if you're looking at, okay, well, maybe 8000 people out of 100,000 that's a high risk." (P4, 30 – 35 years, primary care/lecturer, one to one interviews)*

Additionally, a clinician commented on the usefulness of the population diagram during decision making with patients:

> *"I think if you're counselling a patient, that's easier to visualize 100 people, and that's your risk branding, I think that's easier. I feel like that's almost something you could show a patient if you were to help them make a decision." (P10, 30 – 35 years, primary/secondary care, focus group 2)*

Although, the population diagram was apparent to be the preferred result format among clinicians, various clinician pointed out that the colour grading to indicate the numbers after the decimal point were confusing. Instead, it was suggested to use a half circle or a quarter circle:

"I don't know if I'd have fully understand what the colour the pink meant and particularly as it got darker, I may not have related to that to the point being a higher percentage. So, I just wonder if it needs to be explained. Okay. Or is there a way just to do a half of the circle or a quarter of the circle or I know it gets complicated." (P7, 46 – 50 years, primary care, one to one interviews)

When asked whether there is too much text within the tool, two clinicians responded that:

"I think everything that's there is relevant and concise. I think it's very clear what it is that they're saying. And I personally don't feel like there's too much of it (text)." (P4, 30 – 35 years, primary care/lecturer, one to one interviews)

Feedback on the usefulness of the tool to reduce 4C antibiotic prescribing

This section presents the feedback on the usefulness of the tool to reduce 4C antibiotic prescribing. When asked whether clinicians would use the tool, a clinician stated that the tool could be useful in primary care, while in secondary care they would struggle gathering all the information required to insert in the tool:

"If the clinician has all the data for the patient, they could actually use it. You could sell it through realistic medicine. I mean, this is realistic medicine. This is what we're supposed to be doing, discussing with each individual patient what is important for them and that ticks that. So, for secondary care to have all those things that you need to input, they would struggle, while this could be for GPs maybe." (P1, 51 – 55 years, primary/secondary care, focus group 1A)

The above comment was also echoed by another clinician in another focus group, and highlighted the fact that it could be challenging to gather all the information required to insert in the tool:

"So, I think it's great. my only concern is, but to get all that information is going to be a challenge. And depending on the situation which depends on how easy it is to find a lot of information to populate it. So, I think the tool itself is great,

but I think getting all the necessary, it would be quite difficult because patients don't know how many antibiotics they have had unless you've got an electronic summary of what they've had. A lot of the patients are elderly." (P11, 41 – 45 years, secondary care, focus group 1B)

Differently, other clinicians stated that they would use the tool and encourage other member of staff to use the tool:

"I think the tool would be really useful. [..] I think more and more, particularly in prescribing, In terms of antibiotic resistance and appropriate prescribing, I think tools are really, really useful for practitioners to use." (P7, 46 – 50 years, primary care, one to one interviews)

"I could definitely see myself using it and encouraging other members of staff, maybe less experienced members of staff, who are prescribing to use it more often. Okay. But I think it's definitely useful." (P4, 30 – 35 years, primary care/lecturer, one to one interviews)

Two best things about the tool

This section presents the two best things about the tool that was shared by the clinicians during the study. One clinician stated that the tool can be easily used to back their decision with patients:

"You can share with a patient, but you could use it. So that's backing your decision as well to prescribe it." (P12, 51 – 55 years, secondary care, focus group 1B)

While another clinician highlighted the visuals used for the results formats:

"*So, I really like your visual risk tools. I think they're really useful for staff" (P11, 41 – 45 years, secondary care, focus group 1B)*

Other clinicians highlighted how much they liked the population diagram:

"I love your population diagram." (P7, 46 – 50 years, primary care, one to one interviews)

"It's easy to use, intuitive to use, I like population diagram." (P6, 36 – 40 years, secondary care, focus group 2)

Finally, it was shared that the tool is easy and quick to use:

"I think how easy it was to use, how quick it was to put the information in. And I really like the fact that you had those little information buttons as well to see just if you're not sure." (P4, 30 – 35 years, primary care/lecturer, one to one interviews)

Two things to change about the tool

This section presents what clinicians thought should be changed within the digital tool for CDI. One clinician stated that they would like to see the numbers to be all in percentages as it would be more straight forward to understand:

"Just keep it all percentages like 7.5 times more likely it just confuses. Just keep it all in the same. So, clarify that message and make it a bit more. Hmm. I don't know. Straight forward probably." (P13, No age provided, primary/secondary care, focus group 1B)

While another clinician stated that they don't like the bar chart and didn't understand the colours used for the population diagram to represent the numbers after the decimal point.

"Probably the bar chart, which we've already spoken about. You can't understand it. And the little coloured circles, they're not a full person. I think that would be helpful to change that as well." (P4, 30 – 35 years, primary care/lecturer, one to one interviews)

A similar feedback was also shared by another clinician:

"The pink dot, I wasn't sure what the pink dot is." (P1, 51 – 55 years, primary/secondary care, focus group 1A)

4.2. Survey feedback

This section of the results presents the feedback gathered through the survey. Out of the 17 participants in the study, 11 participants completed the survey. The survey compromised of 19 Likert scale questions, where respondents had to answer from totally disagree to totally agree (7-point scale). The statements focused on the importance of reducing CDI and 4C antibiotic prescribing, the usefulness of the tool, the ease of use of the tool in a clinical setting, and whether the result formats of the tool are understandable. Figure 28 shows an overview of all the responses captured from the survey. All survey respondents stated that they either agree or totally agree that targeting the reduction of CDI in Scotland is important, likewise all respondents either agreed or totally agreed that reduction of 4C antibiotics in primary and secondary care is important. All survey respondents also agreed or totally agreed that the digital tool for CDI can be useful to support clinicians during antibiotic prescribing and decision making. While only 6 (54%) survey respondents stated they agree or totally agree, that the digital tool for CDI can be added to their existing workload and workflow, 10 (90%) of respondents stated they would use the digital tool for CDI. To see in detail the rest of the responses to the survey statements, see figure 28.

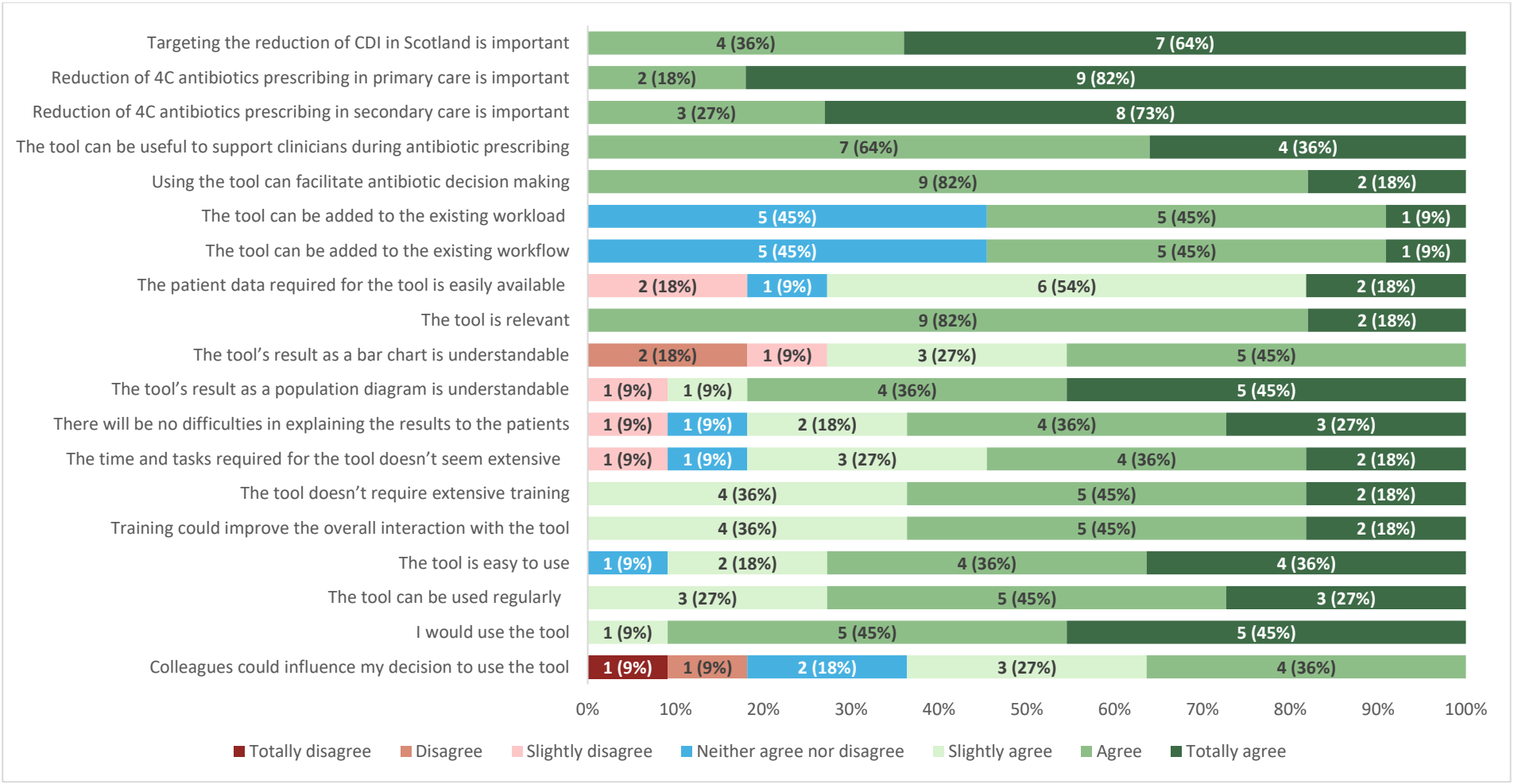


Figure 28. Overview of the survey responses. Total number of participants (n=11)

4.3. Final amendments to the digital tool for CDI

As seen above there were a number of suggestions on the layout and content of the tool. Once the data was collected, the project team made the decision of which amendments to incorporate into the tool. An amendment document was created and shared with the digital solution developing company.

The section below presents the amendments sent to the developers of the digital tool for CDI, following the interviews conducted in this study. The changes requested referred to the first page of the tool which can be seen in table 18, while the changes requested on the results formats can be seen in tables 19 - 21.

A general change that was suggested to the layout of the digital tool for CDI was the use of contrasting colours that can easily be seen by colour blind people.

Changes to the first page (variables page)

Table 18 shows the changes requested to the first page of the digital tool for CDI.

Table 18. Changes to the first page of the digital tool for CDI shared with the developers after the interviews.

Current header	New header (to be actioned)	Programming notes
Bronchitis	Chronic respiratory disease	
Chronic renal problems	Chronic renal disease	
Cancer	N/A	Add an information box with the following text – All cancer type
Comorbidities in the last 5 years	N/A	Move it to the left side of the page instead of the middle.
Chronic renal disease	N/A	Add the following text to the existing info box – Transplanted organ

Changes to the bar chart page

Table 19 shows the changes requested to the bar chart page of the digital tool for CDI.

Table 19. Changes to the bar chart pages of the digital tool for CDI, shared with the developers after the interviews.

Issue	Current text	Programming notes
Bar chart	N/A	Make the x and y-axis font bigger
Vertical (y) axis	N/A	On the vertical axis add a comma on the decimal point: 5,000 or 50,000 or 500,000
The red line on the bars	N/A	Please make the red line on every bar the same thickness
Key - under the chart	The black dashed line shows the CDI population rate for this age and gender group. The red line represents the mean estimate of the risk, the bar represents the 95% confidence interval surrounding the estimate reflecting the variability in the estimate for the population.	**Change text into:** The black dashed line shows the CDI population risk for this age and gender group (without risk factors). The red line represents the mean estimate of the risk, the bar represents the 95% confidence interval surrounding the estimate reflecting the variability in the estimate for the population.
Key - under the chart	N/A	Make it bigger font size

Changes to the population diagram pages

The below changes were requested for the population diagram page of the digital tool for CDI. Table 20 shows the colour grading options suggested for the population diagram.

- Have the population diagram first after clicking “calculate risk factor” and the bar chart as the second option.
- Remove the colour grading, as feedback was too difficult to interpret by clinicians. See the below table to see the 2 options proposed (depending on feasibility):

Table 20. Colour grading options for the population diagram.

Option 1	Circle into 4 quadrants and coloured by rounding up to the nearest 0.25 e.g. 0.1, 0.2 etc would round to 0.25 – one quadrant filled; 0.3, 0.4 rounded up to 0.5 – 2 quadrants filled.			
	0.25	0.5	0.75	1
				
Option 2	Circle into 2 halves and coloured by rounding up to nearest 0.5 e.g. 0.1, 0.3 would round up to one half circle filled; 0.6, 0.7 would round to full coloured circle.			
	0.5		1	
				

Changes for both results pages

Table 21 shows the changes requested to both results pages of the digital tool for CDI.

On both pages in the text boxes, some words have to be changed into bold or italic. Please suggest to us with either bold or italic depending on which format can be perceived better when reading.

Table 21. Changes on both results pages of the digital tool for CDI, shared with developers after the interviews.

Location of the text	Action to be taken	Text in bold or italic
For your patient (second line)	Make text bold or Italics	Your patient
In the “No antibiotic” section, the second sentence starting with (compared to the baseline risk)	Make text bold or Italics	Baseline risk
In the “Non-4C antibiotic” section, the second sentence starting with (compared to no antibiotics)	Make text bold or Italics	No antibiotics
In the “4C antibiotic” section, the second sentence starting with (compared to no antibiotics)	Make text bold or Italics	No antibiotics

4.4. Final format (v3) of the digital tool for CDI (The CDI Risk Predictor)

Figures 29 – 32 show the changes that have been incorporated to the v3 digital tool for CDI, which was informed by the amendment document seen above. The figures compare the digital tool for CDI v2 (old version) with the digital tool for CDI v3 (new version).

Figure 29. Changes to the headers and variable labelling in the first page of the digital tool for CDI.

Figure 30. Changes to the information boxes for the comorbidities.

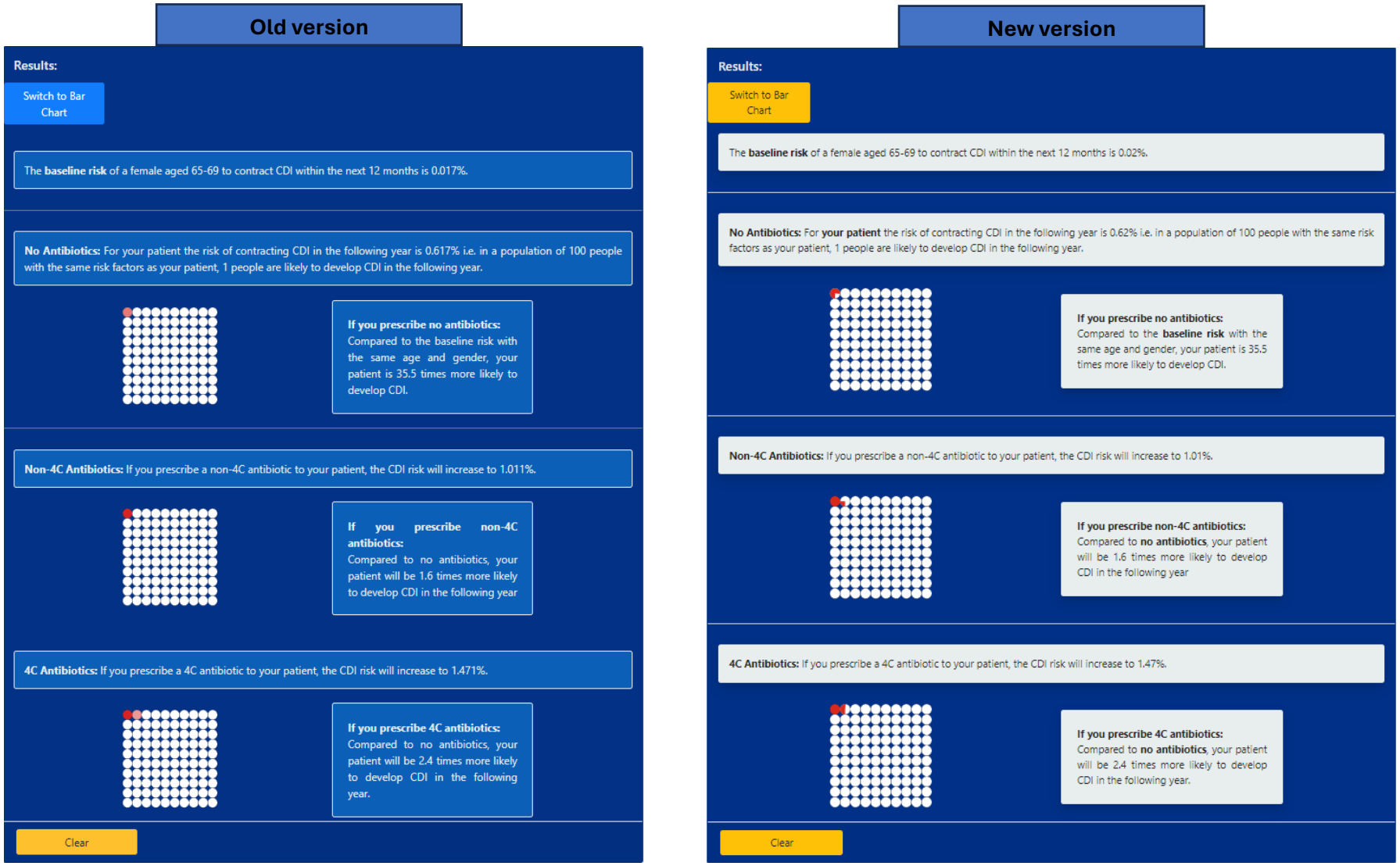


Figure 31. Changes to the population diagram page. The changes made were to the text explaining the risk score and the way the risk was shown in the diagrams.

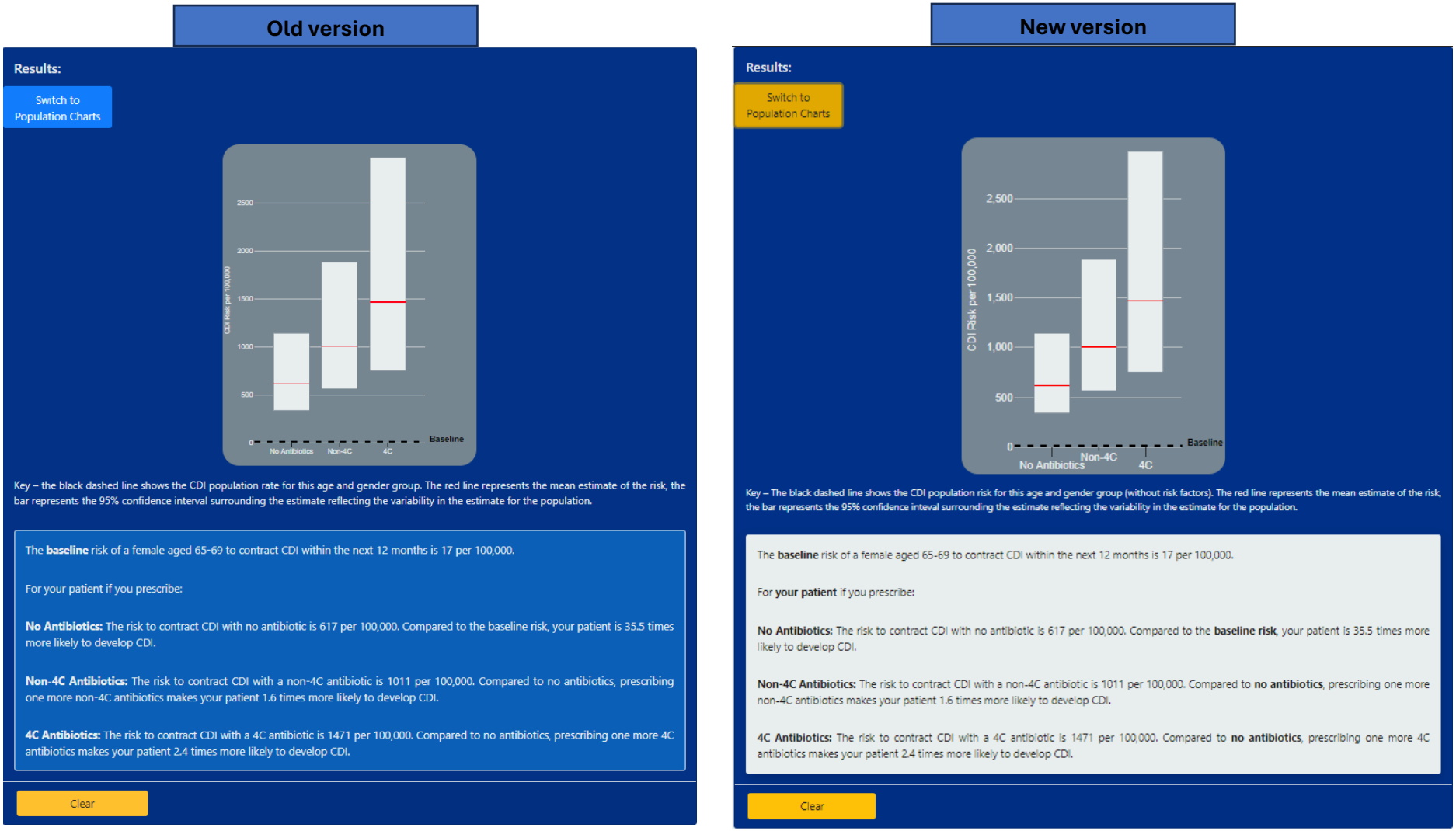


Figure 32. Changes in the bar chart page. The changes were made to the text explaining the patient risk to contract CDI and the size of the graph

5. Discussion

This study aimed at gathering clinician's feedback on the layout, content of the digital tool for CDI, its usefulness and ease of use. A total of 17 clinicians were involved in this study through focus groups, one to one interviews and survey statements. Each session began by asking participants to use and test the digital tool for CDI, this was followed by some questions around the colours used in the tool, the labelling used for the variables, the content in the information boxes and then the result formats. The sessions were followed then by survey statements that gathered participant's feedback on the ease of use of the tool, its usefulness and around the importance of reducing CDI and 4C antibiotic prescribing. The study was concluded by creating an amendment document which was shared with developers and finalising the digital tool for CDI v3 using the findings from this study.

5.1. Main findings of the focus groups and one to one interviews

Usability testing refers to the practice of assessing how easily a digital tool can be used in a particular set of circumstances. The aim of the testing is to understand any usability testing in early development stages before the tool is implemented (Sandars, 2010). Involving users during testing can produce new design ideas, ability to identify issues with the design and suggest improvements (dos Santos *et al.*, 2021). Although the beta version was developed using the feedback gathered in chapter 2 and 3, when the tool was tested among clinicians, there were some minor and major suggestions to the tool.

When clinicians used the digital tool for CDI, they agreed that the labelling used for the comorbidity "bronchitis" wasn't covering all the information that were in the information box and the ICD-10 codes used in the algorithm. In fact, it was suggested to change the labelling from bronchitis to chronic respiratory disease, as it would be more comprehensive for users. Other suggestions included inserting an information box for the comorbidity "cancer" indicating that it refers to all cancers and to make all the label's font bolder. Additionally, other minor changes were also suggested to

improve the content of the digital tool for CDI such as making text bolder, changing of some text in the first page and results pages.

Although some of the suggested changes are minor changes to the tool, it is important to incorporate the changes to avoid high costs for changes once the tool is implemented and to increase the use of the tool (Brunner *et al.*, 2017; dos Santos *et al.*, 2021).

Some major changes that were suggested included to use contrasting colours for the layout of the tool so that colour blind people can better see the digital tool for CDI. Another change suggested was to show the population diagram first instead of the bar chart when calculating the CDI risk score. Concluding, a final major change suggested was to change the colour grading of the population diagram and split the circle into 2 halves or 4 quadrants to give a better perspective of the risk. These changes suggested have given the possibility to improve the digital tool for CDI and have a tool that could meet end user's needs.

One of the major causes to poor uptake of digital tools is the lack of involving end users in the developing stages. A 2018 Canadian study that created a digital tool to improve interprofessional communication and collaboration in a hospital setting showed that involving end users in the developing stages has helped them to create a tool with an improved design, identify software issues, and create a final tool that improved clinicians' workflow (Tang *et al.*, 2018).

Another 2019 American study that aimed at conducting user testing of an interactive surgical dashboard designed to improve the understanding of congenital heart surgical data, shows how crucial end users feedback is to improve digital tools. One major feedback on the tool was around the difficulty of interpretation of the graph in the dashboard and the use of terminology and acronyms to explain the results (Wu *et al.*, 2019). Involving end users at each development stage can avoid implementing difficult results formats and terminology that can lead to misinterpretation and poor adoption of the tool. The interactive surgical dashboard study also highlights that what designers think is a good feature of a digital tool might not be perceived similarly

by the end user, reinforcing again the need for user testing throughout the development stages (Wu *et al.*, 2019).

The findings from the Wu et al study supports the decision taken by the team to incorporate both the population diagram and the bar chart in the final version of the digital tool for CDI. Although there were disagreements on which format was better suited for the CDI digital tool, providing the option to navigate through both formats could potentially reduce misreading or incorrect interpretation of the risk score. This approach also caters to different users' visual preferences. Furthermore, both results formats were chosen after a literature review and feedback from clinicians in chapter 3, and further the formats were improved using the feedback from this chapters participants.

5.2. Findings from the survey

According to the TAM, adoption of a tool is influenced by the end user's perception of its usefulness and ease of use. Therefore, during the development process, it is essential to evaluate a digital tool for both its practical value and its user-friendliness. Testing these aspects ensures that the tool meets user expectations and encourages adoption, ultimately supporting successful implementation and long-term engagement (Davis, 1989).

The survey aimed at understanding the usefulness and ease of use of the tool using statements where respondents had to answer using totally disagree to totally agree. Most of the survey statements were positively rated among respondents, suggesting that the tool is useful and easy to use. A total of 10 (90%) of respondents also indicated they would use the tool during consultation. The only negative response was observed around the ease of understanding the bar chart with 3 (27%) respondents disagreeing with the statement. This finding does not come as a surprise since most interview participants also indicated preference towards the population diagram being shown first in the tool. Measuring end users' perception on usefulness and ease of use of any digital tool is a crucial factor influencing its adoption. A 2016 systematic review that aimed at understanding factors influencing the effective use

of mHealth apps for self-care, discovered that perceived usefulness, perceived ease of use and behavioural intention to use are the top three factors influencing the use of digital tools (Azhar and Dhillon, 2016).

Similar findings were also observed in a 2015 qualitative study that aimed at understanding factors influencing the use of a mobile app for meeting the healthcare needs of persons living with HIV. The study which involved 80 participants found that it is important that end users perceive digital tools as useful, easy to use with little risk associated with its use and have trust in the developers of the tool (Schnall *et al.*, 2015). The findings from the systematic review and Schnall's study both show that perceived usefulness and ease of use can influence the adoption and actual use of the tool. Although at this stage, the adoption and the usage rate of the digital tool for CDI cannot be measured, it is worth investigating in future whether there is correlation between the findings from this survey and the actual use of the tool.

5.3. Strength and limitation

There are many benefits of testing a digital tool with potential end users. Creating the beta version using the feedback from chapter 2 and 3 allowed development of a tool giving clinicians the opportunity to use the tool on their phones. The tool was positively perceived during the testing in this study with some further changes suggested to improve the tool. There were some limitations to this study.

Unlike the studies in previous chapters, this study lacked direct involvement from GPs or physicians, who, as potential end users, could have provided valuable input. However, it included 17 participants—clinicians, pharmacists, and nurses—who are increasingly taking on roles as antibiotic prescribers, making them important prospective users of the CDI tool. The tool was specifically developed to support safe antibiotic prescribing practices, so their feedback remains highly relevant.

Although having GPs participate would have been ideal, findings from Chapter 2 suggest that GPs may be less inclined to adopt the tool, indicating it could be more beneficial for non-medical professionals or junior doctors. Additionally, most participants in this study were experienced clinicians, with over five years in their

roles, and represented various NHS Health Boards across Scotland, which strengthens the reliability and applicability of the feedback collected.

Additionally, not all 17 participants were able to complete the survey, due to limited time running the focus group. However, the survey feedback from the 11 respondents demonstrated agreement with the statements presented in the survey, suggesting a possible consistency of the feedback.

Finally, the tool has not been tested with visually impaired clinicians, where further feedback on the colours of the tool might be lacking. However, the developers of the digital tool have an extensive experience developing digital tools for the healthcare and when requested to use contrasting colours that potential colour blind people could see better, they immediately changed the colours in version 3 (latest version) of the tool.

5.4. Future work

The findings from this study have enabled further improvements to the beta version of the digital tool for CDI. Testing with end users yields numerous benefits, including the identification of design issues, enhancement of design quality, cost reduction for post-implementation amendments, and increased tool adoption (dos Santos *et al.*, 2021). However, a more comprehensive understanding of the tool's usefulness and ease of use can be achieved by testing it in a clinical environment, either through simulated case scenarios or with real patients. Testing the digital tool for CDI in a clinical environment would have been the ideal final step of this PhD. However, due to the COVID-19 pandemic, this was not feasible. As a result, a logical next step would be to test the tool in real-world clinical settings. This would allow for further insights, particularly regarding the availability of data to populate the tool in outpatient settings and its practical use by key antimicrobial prescribers. Such testing would provide valuable feedback on the tool’s effectiveness and usability in clinical practice, helping refine its design for broader adoption. (Svanæs, Alsos and Dahl, 2010; Weichbroth, 2024).

In addition, the study focused on understanding clinicians' perspective on the tool, however, it would be equally important to consider investigating patients' perspective on the tool, specifically their understanding and comprehension of the results pages. This is important particularly for shared decision making where clinician and patient make the decisions around patient's health together. Using the digital tool for CDI during shared decision making, would mean that the patient would require a minimal understanding of what the charts mean when presented to them. Therefore, it would be also interesting to understand patient's perspective on the digital tool for CDI.

5.5. Conclusion

The testing of the digital tool for CDI with the 17 clinicians has enabled further improvement of the tool. Although some of the feedback compromised of minor changes to the text or font of the text of the digital tool, some key changes were suggested resulting in changed layout of the tool. The development process from version 1 (in chapter 4) to the current version 3 of the digital tool for CDI has resulted in some major changes to improve the overall ease and usefulness of the tool. Furthermore, allowing clinicians to use the v2 beta version on their phones allowed a better understanding of how easily they could use the tool. Overall, the feedback from this study suggested that clinicians are finding the tool easy to use and useful, with 10 (90%) of the survey respondents stating that they would use the digital tool for CDI during a consultation.

CHAPTER 6: Final Discussion

1. Thesis background and rationale

Antibiotic prescribing is one of the key contributing factors to CDI. Reduction of broad spectrum antibiotic prescribing and therefore reducing the incidence of CDI has been one of the key aims of the Scottish antimicrobial stewardship programme (Nathwani *et al.*, 2011). As a result of these antibiotic stewardship efforts, incidence of CDI has been reduced significantly (Nathwani *et al.*, 2012). Nonetheless, in 2021 and 2022 there were a total of 1,135 and 1,053 cases of CDI in Scotland of which 859 and 818 cases were HA-CDI and 276 and 235 cases were CA-CDI (NHS National Services Scotland, 2021, 2022), indicating that CDI is still an existing issue, requiring further consideration and antibiotic stewardship's efforts. Consequently, to further support antimicrobial stewardship's efforts around reducing the incidence of CDI, the University of Strathclyde developed a mathematical model using Scottish CA-CDI cases from August 2010 to July 2013 extracted from the Electronic communication of surveillance in Scotland (Kavanagh *et al.*, 2016). The mathematical model was created with the aim of developing a risk predication digital tool in app format, to be used during decision making of prescribing an antibiotic. The model has the ability to generate a risk score to contract CA-CDI in the following 12 months by using multiple patient's data/characteristics (variables). The risk of CDI is predicted for three scenarios: current risk (without antibiotic prescription), for non-4C antibiotics (all antibiotics not marked as high risk for CDI) and for 4C antibiotics (high risk antibiotics for CDI). Therefore, the aim of this thesis is to develop a digital tool for CDI incorporating the mathematical model, a four-stage programme began in 2017.

2. Discussion

The first stage of the programme involved a semi-structured interview with three Scottish primary care GPs and a nurse who were also observed during their patient consultation and engaged in a co-design workshop which produced a low fidelity prototype of the CDI tool. The aim of the study was to understand clinician's perception on CDI and investigate the feasibility of implementing a digital tool for CDI in primary care. The findings from chapter 2 indicated that GPs had their reservations

about having a digital tool for CDI, especially as an app format, due to multiple factors including time limitation, not having patient data up to date due to difficulty accessing hospital data, and low frequency of CDI in primary care.

Clinicians in primary care have a total of 10 minutes during consultations to discuss with the patient their concerns and make a decision on the treatment. Having a digital tool for CDI as an app format would require the clinician to search for the patient data and input it into the tool to calculate the risk score; actions that could be time consuming, unless the tool is integrated into their prescribing system so it can pull the patient data automatically.

Similar findings emerged in a 2018 Australian qualitative study, which aimed at investigating the implementation of a health and lifestyle screening app in a GP practice. One of the key challenges that emerged during the interviews was that clinicians don't have enough time to use the screening app and in order to use the app thoroughly they would require longer consultations or a separate consultation (Webb, Wadley and Sanci, 2018).

Additionally, one of the GPs highlighted that CDI is primarily associated with hospital settings rather than community environments, suggesting implementing the CDI tool within secondary care instead. It's plausible that the perceived low threat of CDI in the community is a result from the relatively small sample size in this study. Involving a larger number of GPs across Scotland may have provided a more comprehensive understanding and highlighted the impact of CDI within community. In a 2022 point prevalence study from July to November 2018 comparing CDI data between hospitals and the community across Europe, it was found that 47% of diarrhoea samples collected in 118 participating community sites were never tested for CDI (Viprey *et al.*, 2022). This suggests that there could be nearly three times as many cases of CDI that go undiagnosed within the community compared to hospitals (Viprey *et al.*, 2022). However, it's important to note that the study does not specify whether this trend occurs in Scotland. Further research specific to Scotland's healthcare system would be beneficial to assess the extent of CDI underdiagnosis in community.

During stage 2 of the programme when engaged with the 10 clinicians from primary and secondary care, the findings revealed wide variations in participants' knowledge and awareness of CDI prevalence and its associated risk factors, including the contentious issue of antibiotics being a significant risk factor for CDI. Suggesting that there might be a need for better education and awareness on the matter.

During stage 1 clinicians initially expressed reservations about a standalone digital tool for CDI, however they were open to the concept of integrating such a tool into their existing prescribing software, such as EMIS® or VISION®. The integration of the digital tool for CDI into their system was seen as a practical solution to streamline their workflow. By automating the extraction of patient data, the integrated tool would save clinicians valuable time, particularly when prescribing 4C antibiotics (high-risk antibiotics associated with CDI). This approach would enhance efficiency and facilitate more informed decision-making during the prescription process.

Insights gathered from interviews with three GPs, coupled with observations of a nurse and a GP, highlighted the potential utility of the digital tool for CDI during treatment decision-making and discussions with patients. This valuable feedback was instrumental in guiding and facilitating the co-design workshop, which aimed to develop a low fidelity prototype of the CDI tool. The resulting prototype adopted the format and layout similar of a familiar software, Script Switch®, known for its functionality in suggesting clinicians with generic medications.

While the low-fidelity prototype was developed following a robust methodology, it's worth noting that the sample size at this stage of the programme was relatively small. Therefore, to validate the findings, gather additional feedback on the prototype, and explore the feasibility of implementing the tool in different settings, would require further investigation. This would involve expanding the sample size and conducting additional research to ensure the reliability and generalisability of the findings.

Feedback on the low-fidelity prototype in stage 2 was largely positive, except for concerns regarding presentation of the risk format, particularly the use of percentages. Clinicians expressed uncertainty about its clinical significance, especially

without a baseline risk reference for the population. This feedback was crucial, as unclear risk communication may prevent clinicians from integrating the tool into their consultations or utilising it for shared decision-making with patients (Fagerlin, Zikmund-Fisher and Ubel, 2011). Once again this highlights the importance of usability testing during the development stages to understand the end user's needs and preferences (Bai, Mork and Stray, 2017).

Although clinicians expressed interest in having a digital tool for CDI to support patient consultations, it became evident that prototype 1 was not viable for implementation in secondary care. In order to successfully implement prototype 1, it would require all the patient data to be located into one prescribing system, which then would allow the tool to automatically extract the needed data to calculate the risk score. The disparate systems used in secondary care, often reliant on paper prescriptions rather than electronic records, posed significant challenges. This would mean implementing a digital tool for CDI such as prototype 1 would not be feasible in secondary care.

Although the implementation of prototype 1 was deemed unfeasible during the interview period, a revised version (prototype 2) was proposed to clinicians in the final five interviews. Differently from prototype 1, prototype 2 was an active format that required clinicians to search for patient data and manually input it into the tool. Additionally, prototype 2 could be accessed through an app or website on clinician's mobile phone or computer. Initially participants were sceptical about prototype 2, due to concerns about time-consuming data searches and input. However, after receiving clarification on how to use the tool and interpret the results, clinicians showed greater interest. They were also keen on using prototype 2 on their mobile phones or computers and show patients their risk to contract CDI using the population diagram as part of the consultation as they thought it can be easily understood by patients. A meta-ethnographic review from 2019 on the perception of mHealth apps revealed that digital tools enhance communication between patients and clinicians, giving patients a sense of inclusion in the decision-making process (Vo, Auroy and Sarradon-Eck, 2019).

Compared to stage 1, in stage 2, interviews revealed a more positive perception towards the adoption of a digital tool for CDI. This shift in attitude could be attributed to several factors. Firstly, a larger pool of clinicians was engaged in the interviews compared to the initial stage, which involved only three GPs. Additionally, the inclusion of allied healthcare professionals from across Scotland may have contributed to a more diverse range of perspectives and insights. Moreover, clinicians in secondary care, where longer consultation times with patients are typically available, exhibited a greater enthusiasm for utilising a digital tool for CDI. This extended consultation duration may be the reason clinicians were keen on the potential benefits of integrating such a tool into their workflow. Overall, these factors may have collectively influenced the positive perception observed towards the adoption of the CDI digital tool during this stage of the programme.

Although there was a positive sense of feedback towards the digital tool for CDI, the interviews concluded with varied feedback on the results format, some clinicians preferring the population diagram while others the bar chart. This suggested that further investigation was needed to determine the preferred format between the population diagram and the bar chart for incorporation in the final version of the digital tool for CDI.

The feedback received in stage 1 and 2 allowed the progression into the third stage of the programme which involved development of the beta version of the digital for CDI by engaging a digital tool development company. A primary objective of this stage was to create a procurement document indicating the layout, content, and results format of the CDI digital tool. This document aimed to ensure that the beta version incorporated all requirements and formats outlined.

Given the varied feedback on the risk formats during stage 2, both the population diagram and the bar chart were requested for incorporation in the beta version, facilitating further feedback during the testing stage.

Despite the sharing of the procurement document with developers, the initial version of the beta version (v1) encountered several issues. Notably, it lacked essential

information explaining the results, and an error message occurred when selecting the "unknown" option for the variable "Number of 4C antibiotics courses prescribed in the last three months (only 4C antibiotics)." Subsequently, a comprehensive document detailing all necessary amendments for the digital tool for CDI was shared with the developers. This led to the creation of v2 of the tool, which was then deemed ready for testing with clinicians. Despite encountering issues with the initial version of the tool, a rigorous examination and ongoing communication with the development team were instrumental in addressing these challenges and ensuring that the tool met the required standards for testing.

Developing the beta version of the CDI tool by incorporating feedback from previous stages and the involvement of a reputable development company with a track record in NHS projects provided valuable expertise in designing user-friendly interfaces and ensuring compliance with relevant standards and regulations. This collaborative approach facilitated the creation of a CDI tool that not only addressed clinical needs but also enhanced user satisfaction and usability. Approaches that are commonly used in beta version development (Montagni *et al.*, 2017; Wiebelitz *et al.*, 2022).

Similar findings were also observed in a 2020 integrative review that aimed at proposing a methodology to create health apps based on successful experiences. The study emphasised the importance of engaging with end users in deciding the content for health apps such as the elements of interface (scroll down feature, buttons, information boxes) (Molina-Recio *et al.*, 2020).

While v2 of the digital tool for CDI adhered to a rigorous methodology, there remained a clear imperative for additional testing and feedback on both the content and layout of the tool to refine its design further. As previously discussed, both result formats (population diagram and bar chart) were incorporated to gather additional feedback and facilitate the decision-making process regarding which format to integrate into the final version of the tool. This iterative approach emphasises the commitment to optimising the tool's usability and effectiveness through ongoing refinement informed by user input and evaluation. Further testing was achieved

during the fourth and last stage of this programme, which focused testing the beta version for CDI developed in stage 3. The study involved focus groups, one to one interviews and completion of survey statements with a total of 17 clinicians from both primary and secondary care settings.

During the interviews, clinicians provided various feedback on the content and layout of the tool. Suggestions ranged from adjusting the labelling of comorbidities to enhancing text visibility by enlarging or boldening it. Specific recommendations included adding an information box for the comorbidity "cancer" to clarify that it includes all cancer types, inserting the population diagram before the bar chart for CDI risk score calculation, and modifying the colour grading of the population diagram. Additionally, clinicians suggested splitting the circle into halves or quadrants to provide a clearer perspective of the risk. Molina-Recio et al highlighted the significance of prioritising usability testing during the development process. The author emphasised the importance of evaluating whether the tool is user-friendly, pinpointing specific usability issues, and promptly addressing them through necessary amendments. These proactive steps, if taken during the early stages of development, can significantly enhance the overall usability of the tool. Not only does this approach streamline the process by reducing the need for extensive amendments in later stages, but it also contributes to cost savings. By investing time and effort upfront to ensure developers can create a more effective and efficient tool that better meets the needs of its users (Molina-Recio *et al.*, 2020).

The survey findings indicated that clinicians generally found the digital CDI tool to be useful and easy to use. Specifically, all respondents expressed positive views regarding the tool's potential to assist in antibiotic prescribing and decision-making processes. Furthermore, majority of respondents expressed willingness to utilise the tool during patient consultations. The only notable concern raised by respondents was around the clarity of the bar chart, a feedback point that was also shared during the interviews.

A 2020 systematic literature review that aimed at understanding factors affecting the adoption of mHealth among clinicians emphasized that both the ease of use of a tool and its perceived usefulness directly impact the intention to use a digital tool. The article further highlighted that clinicians are more inclined to adopt a digital tool when they perceive its benefits and when they find it useful, which subsequently leads to increased frequency of usage. This indicates the critical role of usability and perceived utility in driving adoption and sustained usage of digital tools among healthcare professionals (Jacob, Sanchez-Vazquez and Ivory, 2020). Additionally, ease of use and perceived usefulness can be improved by continuous testing and improvements even post implementation of the tool (Jacob, Sanchez-Vazquez and Ivory, 2020).

The concluding task in this stage involved drafting an amendment document based on the feedback obtained from the interviews. Subsequently, this document was shared with the developers, serving as a blueprint for the creation of V3 of the digital tool for CDI that was named the CDI Risk Predictor.

2.1. Strength and limitations

To our knowledge this is the first programme that attempts to develop a digital tool for CDI for the Scottish health care system.

One notable strength of this thesis lies in its methodological approach, which involved designing and analysing each stage using a diverse range of frameworks such as the CFIR, GUIDES checklist and TAM. Both the CFIR and TAM are well-known and widely used frameworks for informing the development of interventions. Although the GUIDES checklist is a newer and less familiar framework, the methodology used to develop it was rigorous and robust (see section on GUIDES checklist). This meticulous approach was instrumental in ensuring both methodological rigor and validity throughout the research process. Moreover, these frameworks served as invaluable guides in interpreting and synthesizing the research findings, thereby enhancing the overall coherence and robustness of the study.

A limitation of this thesis is the small sample size in some of the studies. During stage 1, only three GPs were involved in the interviews, with only one GP participating in the co-design workshop for the low-fidelity prototype. While stage 2 involved 10 clinicians across four health boards in the interviews, a more extensive representation, particularly from health boards with higher incidences of CDI such as NHS Highlands and NHS Lanarkshire, would have been beneficial. Including more clinicians from these regions could have provided a more comprehensive understanding of the burden of CDI and the prescribing patterns of 4C antibiotics. Nevertheless, a notable strength of this study is the active involvement of end users at various stages. By engaging with end users during the development process, valuable insights were gathered, which have been demonstrated to significantly enhance the implementation and adoption of digital tools (Kerr, 2004). Furthermore, the creation of the beta version of the digital tool for CDI was entrusted to a reputable development company with extensive experience in producing digital solutions for the NHS. This collaboration ensures reliability and draws upon a wealth of expertise, further boosting the credibility of the project.

While a limitation of this thesis is that all research activities concluded by the end of 2019, potentially missing recent developments in the Scottish healthcare system and changes in the perception of technology and CDI post COVID-19 pandemic, a strength lies in the robust methodology used in each stage of this thesis. The comprehensive data collection and analysis conducted throughout the study provide a valuable snapshot of the healthcare landscape at the time of research, offering insights that remain relevant and informative for future investigations.

A final limitation of this thesis is the challenge of generalising its findings beyond the Scottish healthcare system. Scotland's healthcare system has unique governance, policies, and healthcare delivery approaches compared to other regions in the UK, which could impact the direct applicability of findings elsewhere. Therefore, implementing these findings in other UK healthcare systems would require additional research to assess their relevance and effectiveness in different contexts.

In addition to the variability across UK healthcare regions, there are also differences in healthcare infrastructures, technology adoption rates, and regulatory frameworks internationally, which could influence the success of similar digital tools in other countries. Additionally, cultural factors and patient expectations regarding healthcare technology may vary widely, further impacting the potential adoption and usability of the tool.

Despite these limitations, the thesis contributes valuable insights and a strong foundation for future research on digital tools for CDI management. These findings can serve as a comparative baseline, guiding adaptation and implementation efforts across diverse healthcare systems. For instance, future research might focus on customising the tool's features to better align with different clinical workflows, regulatory requirements, and healthcare resources in other settings. Furthermore, continued validation studies could help refine the tool's effectiveness and explore ways to enhance its adaptability to meet the varying needs of healthcare providers across different regions and countries.

2.2. Recommendations

The use of digital tools in healthcare can offer clinicians critical support during patient consultations, streamline workflows, reduce the risk of human error, and improve overall efficiency. While the benefits are clear, barriers like limited clinician involvement in the development process and the demands on clinicians' time have hindered widespread adoption. Key lessons from this program highlight strategies that healthcare systems could adopt to enhance the incorporation and impact of digital tools:

- **Enhance clinical knowledge and awareness:** Equip clinicians with up-to-date knowledge on conditions, diseases, and infections, like CDI, ensuring they can maximize digital tools for effective decision-making.
- **Involve end users in development:** Engage clinicians and other end users at every stage of the development process, incorporating their feedback to create user-friendly, relevant tools that genuinely support clinical work.

- **Incentivise adoption:** Encourage the use of digital tools by providing incentives to clinicians, which can help overcome initial barriers to adoption and demonstrate the organization's commitment to easing clinicians' workloads.
- **Ensure regular monitoring and updates:** Continuously monitor the performance of digital tools and update them based on clinician feedback and evolving medical guidelines. Regular improvements help maintain the tools' relevance and usability over time.
- **Avoid alert fatigue:** Ensure that digital tools only provide essential information, avoiding an overload of irrelevant alerts. This minimizes alert fatigue, ensuring that critical alerts are noticed and acted upon.
- **Provide continuous training:** Regularly train staff on the effective use of digital tools, including updates on new features or tools introduced to enhance workflows. This ensures that clinicians feel confident and supported in using these tools effectively.

By implementing these practices, healthcare systems can more effectively integrate digital tools into everyday clinical workflows, enhancing their impact on patient care and making the tools a reliable asset for clinicians.

2.3. Future research

Future research to further investigate the use of the digital tool for CDI within a clinical context using case scenarios could be beneficial. Case scenario testing is a method used in software development and quality assurance to evaluate how a system behaves in specific, realistic situations that users might encounter. This approach involves creating detailed, narrative descriptions (scenarios) that outline a sequence of events and interactions a user might have with the software. Each scenario is designed to test particular functionalities, workflows, or user interactions within the system (Weichbroth, 2024). Such research could provide insights into the tool's efficacy and user-friendliness, facilitating necessary refinements prior to widespread implementation. Conducting investigations within a clinical setting through case scenarios, requires the involvement of clinicians who can evaluate the

digital tool for CDI through simulated consultations. Their feedback will be instrumental in enhancing the tool's design, optimising functionality, and aligning it with the specific requirements of end users (Weichbroth, 2024).

Additionally, in order to implement the digital tool for CDI it would also be required to be classified as a medical device and provide the UK Conformity Assessed (UKCA) marking. This process involves assessing the tool's conformity with the relevant regulations and standards, ensuring its safety and effectiveness for use in a clinical setting. Obtaining the UKCA marking demonstrates compliance with the applicable requirements and allows the tool to be legally marketed and used as a medical device in the UK (*Medical devices: software applications (apps) - GOV.UK*, 2023). This step is crucial for ensuring patient safety and regulatory compliance, thereby enhancing the credibility and acceptance of the digital tool within the healthcare community.

Subsequently, after obtaining the UKCA marking, several steps are required to ensure continued compliance and readiness for market implementation. Firstly, it's crucial to verify that the digital tool displays the UKCA marking, which indicates compliance with UK regulations and standards. Additionally, compliance with any additional UK market access requirements, such as registration with the MHRA's Devices Online Registration System, is necessary to legally market the device in the UK.

Furthermore, procedures for post-market surveillance must be developed to monitor the performance and safety of the digital tool once it is in use. This includes mechanisms for collecting and analysing feedback from users, reporting adverse events to the MHRA, and implementing corrective actions when necessary. Lastly, staying informed about updates or changes to UK regulations and standards relevant to medical devices is vital. Continuously assessing and adapting the digital tool ensures ongoing compliance with regulatory requirements throughout its lifecycle.

By following these additional steps, the digital tool for CDI can maintain compliance with UK regulations and standards, ensuring its safety and effectiveness while meeting the needs of healthcare professionals and patients in the UK market (*Medical devices: software applications (apps) - GOV.UK*, 2023).

Securing regulatory approval for a digital diagnostic tool as a medical device involves a range of costs, from achieving initial conformity assessment to maintaining ongoing evaluations and improvements. For a low-complexity diagnostic tool, initial approval costs in the UK are estimated between £50,000 and £100,000, covering fees for basic evidence gathering and certification requirements like UKCA marking. However, if more extensive clinical testing or dual approval (UK and EU) is necessary, costs can exceed £200,000. These estimates also account for post-market surveillance and compliance to ensure the tool's efficacy and safety in clinical settings (*Current MHRA fees - GOV.UK*, no date).

In the case of Clostridium difficile infection (CDI) costs, a retrospective study by Robertson et al. showed that each CDI case can cost approximately £5,126 to the Scottish healthcare system (Robertson *et al.*, 2020), with around 1,000 cases occurring annually in Scotland alone (NHS National Services Scotland, 2022). This results in roughly £5 million spent each year on CDI treatments. If a digital tool could reduce even a small portion of CDI cases by supporting more effective antibiotic prescribing, it could help offset the costs associated with regulatory approval, implementation, and ongoing tool management. For instance, a reduction of just 70 cases could potentially recoup the tool's regulatory and implementation costs, while further reductions would result in substantial ongoing savings for the NHS.

2.4. Conclusion

The overarching objective of this thesis was to design and develop a digital tool for *Clostridioides difficile* infection for the Scottish health care system. This was achieved through a comprehensive four-stage programme outlined in this thesis.

The initial two stages explored clinicians' perspective on CDI in primary and secondary care, their perception of using digital tools during consultations with patients and their preferred format for the CDI tool. Stage 1 revealed that while CDI posed minimal concern in primary care settings, clinicians expressed interest in integrating a digital CDI tool into their prescribing systems for enhanced management. A low fidelity prototype (prototype 1) including the features outlined during the interviews and the co-design workshop, was created to obtain further feedback from other clinicians and investigate its possible implementation in secondary care. However, Stage 2 highlighted challenges in implementing prototype 1 in secondary care, primarily due to inconsistencies in patient data across databases. Consequently, prototype 2 was developed as a more versatile, active format of the CDI tool, accessible via mobile devices and computers.

The insights obtained from the initial stages informed the development of a comprehensive procurement document in Stage 3. This document encapsulated all necessary information for the digital tool development company to create the beta version of the CDI tool. Through a close collaboration with the developers, version 2 of digital tool for CDI was created which incorporated all the requirements and features indicated in the procurement document.

The final stage involved rigorous testing of Version 2 of the digital CDI tool with clinicians to gather further insights and identify areas for improvement. The feedback gathered was used to create an amendments document, which was shared with the developers to inform the development of Version 3 of the CDI tool, concluding the four-staged programme.

References

Abraham Goorhuis Dennis Bakker, J. C. S. B. D. C. H. D. W. N. A. A. B. F. W. D. and Kuijper, E. J. (2008) 'Emergence ofClostridium difficileInfection Dueto a New Hypervirulent Strain, Polymerase ChainReaction Ribotype 078'.

Alam, M. J. *et al.* (2017) 'Community Environmental Contamination of Toxigenic Clostridium difficile.', *Open forum infectious diseases*, 4(1), p. ofx018. doi: 10.1093/ofid/ofx018.

Alotaibi, Y. K. and Federico, F. (2017) 'The impact of health information technology on patient safety', *Saudi Medical Journal*. Saudi Arabian Armed Forces Hospital, pp. 1173–1180. doi: 10.15537/smj.2017.12.20631.

Ananthakrishnan, A. N. *et al.* (2013) 'Genetic risk factors for Clostridium difficile infection in ulcerative colitis.', *Alimentary pharmacology & therapeutics*, 38(5), pp. 522–530. doi: 10.1111/apt.12425.

Asempa, T. E. and Nicolau, D. P. (2017) 'Clostridium difficile infection in the elderly: an update on management.', *Clinical interventions in aging*, 12, pp. 1799–1809. doi: 10.2147/CIA.S149089.

Azhar, F. A. Bin and Dhillon, J. S. (2016) 'A systematic review of factors influencing the effective use of mHealth apps for self-care', *2016 3rd International Conference on Computer and Information Sciences, ICCOINS 2016 - Proceedings*, pp. 191–196. doi: 10.1109/ICCOINS.2016.7783213.

Bai, A., Mork, H. C. and Stray, V. (2017) 'A Cost-Benefit Analysis of Accessibility Testing in Agile Software Development: Results from a Multiple Case Study', *1942-2628*, 10(1&2), pp. 96–107. Available at: https://www.duo.uio.no/handle/10852/70786 (Accessed: 4 March 2024).

Balassiano, I. T. *et al.* (2012) 'Clostridium difficile: A problem of concern in developed countries and still a mystery in Latin America', *Journal of Medical Microbiology*, pp. 169–179. doi: 10.1099/jmm.0.037077-0.

Balsells, E. *et al.* (2019) 'Global burden of Clostridium difficile infections: A systematic review and meta-analysis', *Journal of Global Health*, 9(1). doi: 10.7189/jogh.09.010407.

Banks, A. *et al.* (2016) 'Sentinel community Clostridium difficile infection (CDI) surveillance in Scotland, April 2013 to March 2014', *Anaerobe*, 37, pp. 49–53. doi: 10.1016/j.anaerobe.2015.12.008.

Bartlett, J., Chang, T. and Onderdonk, A. (1978) 'WILL THE REAL CLOSTRIDIUM SPECIES RESPONSIBLE FOR ANTIBIOTIC-ASSOCIATED COLITIS PLEASE STEP FORWARD?', *The Lancet*, 311(8059), p. 338. doi: 10.1016/S0140-6736(78)90118-6.

Bartlett, J. G. *et al.* (1977) 'Clindamycin-Associated Colitis Due to a Toxin-Producing Species of Clostridium in Hamsters', *Journal of Infectious Diseases*, 136(5), pp. 701–705. doi: 10.1093/infdis/136.5.701.

Bartlett, J. G. (1994) 'Clostridium difficile: History of Its Role as an Enteric Pathogen and the Current State of Knowledge About the Organism', *Clinical Infectious Diseases*, 18(Supplement_4), pp. S265–S272. doi: 10.1093/clinids/18.Supplement_4.S265.

Bartlett, J. G. (2008) 'Historical Perspectives on Studies of iClostridium difficile/i and iC.

difficile/i Infection', *Clinical Infectious Diseases*, 46(s1), pp. S4–S11. doi: 10.1086/521865.

Bauer, M. S. *et al.* (2015) 'An introduction to implementation science for the non-specialist.', *BMC psychology*, 3(1), p. 32. doi: 10.1186/s40359-015-0089-9.

Beaulieu, M. *et al.* (2007) ' Risk of Clostridium difficile -Associated Disease Among Patients Receiving Proton-Pump Inhibitors in a Quebec Medical Intensive Care Unit ', *Infection Control & Hospital Epidemiology*, 28(11), pp. 1305–1307. doi: 10.1086/521664.

Berenson, C. S. *et al.* (2023) 'Prevalence of Comorbid Factors in Patients With Recurrent Clostridioides difficile Infection in ECOSPOR III, a Randomized Trial of an Oral Microbiota–Based Therapeutic', *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 77(11), p. 1504. doi: 10.1093/CID/CIAD448.

de Beurs, D. *et al.* (2017) 'Active involvement of end users when developing web-based mental health interventions', *Frontiers in Psychiatry*, 8(MAY), p. 72. doi: 10.3389/fpsyt.2017.00072.

Bignardi, G. E. (1998) 'Risk factors for Clostridium difficile infection', *Journal of Hospital Infection*, 40(1), pp. 1–15. doi: 10.1016/S0195-6701(98)90019-6.

Billheimer, D. *et al.* (2014) 'Combined Benefit of Prediction and Treatment: A Criterion for Evaluating Clinical Prediction Models', *Cancer Informatics*, 13(Suppl 2), p. 93. doi: 10.4137/CIN.S13780.

Birken, S. A. *et al.* (2017) 'Criteria for selecting implementation science theories and frameworks: Results from an international survey', *Implementation Science*, 12(1), pp. 1–9. doi: 10.1186/s13012-017-0656-y.

Boiko, O. *et al.* (2020) 'Risks of use and non-use of antibiotics in primary care: Qualitative study of prescribers' views', *BMJ Open*, 10(10), pp. 1–9. doi: 10.1136/bmjopen-2020-038851.

Bond, S. E. *et al.* (2017) 'Outcomes of multisite antimicrobial stewardship programme implementation with a shared clinical decision support system', *Journal of Antimicrobial Chemotherapy*, 72(7), pp. 2110–2118. doi: 10.1093/JAC/DKX080.

Borren, N. Z. *et al.* (2017) 'The emergence of Clostridium difficile infection in Asia: A systematic review and meta-analysis of incidence and impact', *PLOS ONE*. Edited by A. Deshpande, 12(5), p. e0176797. doi: 10.1371/journal.pone.0176797.

Boven, A. *et al.* (2023) 'Clostridioides difficile infection-associated cause-specific and all-cause mortality: a population-based cohort study', *Clinical Microbiology and Infection*, 29(11), pp. 1424–1430. doi: 10.1016/J.CMI.2023.07.008.

Brunner, J. *et al.* (2017) 'User-centered design to improve clinical decision support in primary care', *International Journal of Medical Informatics*, 104, pp. 56–64. doi: 10.1016/J.IJMEDINF.2017.05.004.

Carter, G. P., Rood, J. I. and Lyras, D. (2010) 'The role of toxin A and toxin B in Clostridium difficile-associated disease: Past and present perspectives.', *Gut microbes*, 1(1), pp. 58–64. doi: 10.4161/gmic.1.1.10768.

Castro, I. *et al.* (2019) 'Doctor, my patient has CDI and should continue to receive antibiotics. The (unresolved) risk of recurrent CDI.', *Revista espanola de quimioterapia :*

publicacion oficial de la Sociedad Espanola de Quimioterapia, 32 Suppl 2, pp. 47–54. Available at: http://www.ncbi.nlm.nih.gov/pubmed/31475811.

Chang, T. W. *et al.* (1978) 'Clindamycin-induced enterocolitis in hamsters as a model of pseudomembranous colitis in patients.', *Infection and immunity*, 20(2), pp. 526–529. Available at: http://www.ncbi.nlm.nih.gov/pubmed/669810.

Ciaran P. Kelly M.B., C. P. M. D. and J. Thomas LaMont, M. D. (1991) 'Clostridium difficile colitis', *The New England Journal of Medicine*, 325. doi: 10.1056/NEJM199112053252301.

Ciarán P. Kelly MD and J. Thomas LaMont, M. D. (2005) 'Clostridium difficile infection', *annual review of Medicine*, 102(4), pp. 484–485. Available at: http://search.jamas.or.jp/link/ui/2005190803.

Current MHRA fees - GOV.UK (no date). Available at: https://www.gov.uk/government/publications/mhra-fees/current-mhra-fees (Accessed: 13 November 2024).

Dabbs, A. D. V. *et al.* (2009) 'User-centered design and interactive health technologies for patientsi', *CIN - Computers Informatics Nursing*, 27(3), pp. 175–183. doi: 10.1097/NCN.0b013e31819f7c7c.

Dagliati, A. *et al.* (2018) 'Big Data as a Driver for Clinical Decision Support Systems: A Learning Health Systems Perspective', *Frontiers in Digital Humanities*, 5. doi: 10.3389/fdigh.2018.00008.

Damschroder, L. J. *et al.* (2009) 'Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science', *Implementation Science*, 4(1), p. 50. doi: 10.1186/1748-5908-4-50.

Davis, F. D. (1989) 'Perceived Usefulness, Perceived Ease of Use, and User Acceptance of Information Technology', *MIS Quarterly*, 13(3), p. 319. doi: 10.2307/249008.

Dell'Era, C. and Landoni, P. (2014) 'Living Lab: A Methodology between User-Centred Design and Participatory Design', *Creativity and Innovation Management*, 23(2), pp. 137–154. doi: 10.1111/caim.12061.

Dent, T. H. S. *et al.* (2012) 'Risk Prediction Models: A Framework for Assessment', *Public Health Genomics*, 15(2), pp. 98–105. doi: 10.1159/000334436.

Depestel, D. D. and Aronoff, D. M. (2013) 'Epidemiology of Clostridium difficile infection.', *Journal of pharmacy practice*, 26(5), pp. 464–475. doi: 10.1177/0897190013499521.

Deshpande, A. *et al.* (2013) 'Community-associated Clostridium difficile infection and antibiotics: a meta-analysis', *Journal of Antimicrobial Chemotherapy*, 68(9), pp. 1951–1961. doi: 10.1093/jac/dkt129.

Dial, S. *et al.* (2008) 'Patterns of antibiotic use and risk of hospital admission because of Clostridium difficile infection.', *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, 179(8), pp. 767–772. doi: 10.1503/cmaj.071812.

Dickman, J. *et al.* (2019) 'Using the Technology Acceptance Model to Explore User Experience, Intent to Use, and Use Behavior of a Patient Portal Among Older Adults With Multiple Chronic Conditions: Descriptive Qualitative Study', *J Med Internet Res 2019;21(4):e11604 https://www.jmir.org/2019/4/e11604*, 21(4), p. e11604. doi:

10.2196/11604.

Dolan, J. G. and Iadarola, S. (2008) 'Risk communication formats for low probability events: an exploratory study of patient preferences.', *BMC medical informatics and decision making*, 8, p. 14. doi: 10.1186/1472-6947-8-14.

Donskey, C. J. (2010) 'Preventing Transmission of iClostridium difficile/i : Is the Answer Blowing in the Wind?', *Clinical Infectious Diseases*, 50(11), pp. 1458–1461. doi: 10.1086/652649.

Durham, D. P. *et al.* (2016) 'Quantifying transmission of Clostridium difficile within and outside healthcare settings', *Emerging Infectious Diseases*, 22(4), pp. 608–616. doi: 10.3201/eid2204.150455.

Durovic, A., Widmer, A. F. and Tschudin-Sutter, S. (2018) 'New insights into transmission of Clostridium difficile infection—narrative review', *Clinical Microbiology and Infection*. Elsevier B.V., pp. 483–492. doi: 10.1016/j.cmi.2018.01.027.

Everett M Rogers (2013) 'Diffusion of Innovations, 4th Edition - Everett M. Rogers'. Edited by 4th Edition, p. 2013. Available at: https://books.google.co.uk/books?hl=en&lr=&id=v1ii4QsB7jIC&oi=fnd&pg=PR15&ots=DLZxtNZl7T&sig=5zOml_c9dTnV2l49p6j3jTv65is&redir_esc=y#v=onepage&q&f=false.

Eze, P. *et al.* (2017) 'Risk factors for Clostridium difficile infections - an overview of the evidence base and challenges in data synthesis.', *Journal of global health*, 7(1), p. 10417. doi: 10.7189/jogh.07.010417.

Fagerlin, A., Zikmund-Fisher, B. J. and Ubel, P. A. (2011) 'Helping Patients Decide: Ten Steps to Better Risk Communication', *JNCI: Journal of the National Cancer Institute*, 103(19), pp. 1436–1443. doi: 10.1093/JNCI/DJR318.

Fahy, N. *et al.* (2021) 'Use of digital health tools in Europe', *Use of digital health tools in Europe: Before, during and after COVID-19*. Available at: https://www.ncbi.nlm.nih.gov/books/NBK576970/ (Accessed: 13 November 2024).

Farooq, P. D. *et al.* (2015) 'Pseudomembranous colitis.', *Disease-a-month : DM*, 61(5), pp. 181–206. doi: 10.1016/j.disamonth.2015.01.006.

Feldman-Stewart, D. *et al.* (2000) 'Perception of Quantitative Information for Treatment Decisions', *Medical Decision Making*, 20(2), pp. 228–238. doi: 10.1177/0272989X0002000208.

Fellmeth, G., Yarlagadda, S. and Iyer, S. (2010) 'Epidemiology of community-onset Clostridium difficile infection in a community in the South of England', *Journal of Infection and Public Health*, 3(3), pp. 118–123. doi: 10.1016/j.jiph.2010.07.002.

Fernandez, M. E. *et al.* (2018) 'Developing measures to assess constructs from the Inner Setting domain of the Consolidated Framework for Implementation Research', *Implementation Science*, 13(1), p. 52. doi: 10.1186/s13012-018-0736-7.

Forster, A. J. *et al.* (2012) 'The effect of hospital-acquired infection with Clostridium difficile on length of stay in hospital.', *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, 184(1), pp. 37–42. doi: 10.1503/cmaj.110543.

Furuya-Kanamori, L. *et al.* (2015) 'Comorbidities, exposure to medications, and the risk of

community-acquired clostridium difficile infection: A systematic review and meta-analysis', *Infection Control and Hospital Epidemiology*, 36(2), pp. 132–141. doi: 10.1017/ice.2014.39.

Furuya-Kanamori, L. *et al.* (2017) '25-Hydroxyvitamin D Concentrations and iClostridium difficile/i Infection: A Meta-Analysis', *Journal of Parenteral and Enteral Nutrition*, 41(5), pp. 890–895. doi: 10.1177/0148607115623457.

Garavand, A. *et al.* (2016) 'Factors influencing the adoption of health information technologies: a systematic review', *Electronic physician*, 8(8), pp. 2713–2718. doi: 10.19082/2713.

Garg, A. X. *et al.* (2005) 'Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: A systematic review', *Journal of the American Medical Association*, pp. 1223–1238. doi: 10.1001/jama.293.10.1223.

Getachew, E. *et al.* (2023) 'Digital health in the era of COVID-19: Reshaping the next generation of healthcare', *Frontiers in Public Health*, 11, p. 942703. doi: 10.3389/FPUBH.2023.942703.

Glasgow, R. E., Vogt, T. M. and Boles, S. M. (1999) 'Evaluating the public health impact of health promotion interventions: The RE-AIM framework', *American Journal of Public Health*. American Public Health Association Inc., pp. 1322–1327. doi: 10.2105/AJPH.89.9.1322.

Godoe, P. and Johansen, T. S. (2012) 'Understanding adoption of new technologies : Technology readiness and technology acceptance as an integrated concept', 3, pp. 38–53.

Goudarzi, M. *et al.* (2014) 'Clostridium difficile Infection: Epidemiology, Pathogenesis, Risk Factors, and Therapeutic Options', *Scientifica*, 2014, pp. 1–9. doi: 10.1155/2014/916826.

Guerrero, D. M. *et al.* (2013) 'Asymptomatic carriage of toxigenic Clostridium difficile by hospitalized patients', *Journal of Hospital Infection*, 85(2), pp. 155–158. doi: 10.1016/J.JHIN.2013.07.002.

Health Protection of Scotland (2013) *Healthcare Associated Infection Annual Report 2013*, *Healthcare Associated Infection Annual Report 2013*.

Health Protection of Scotland (2018) *Scottish one health antimicrobial use and antimicrobial resistance in 2018 annual report*. Available at: https://hpspubsrepo.blob.core.windows.net/hps-website/nss/2894/documents/2_2019-11-12-SONAAR-2018-Report.pdf.

Health Protection of Scotland (2020) *Healthcare - Associated Infections Surveillance : Annual Report*.

Heinlen, L. and Ballard, J. D. (2010) 'Clostridium difficile infection', in *American Journal of the Medical Sciences*. Lippincott Williams and Wilkins, pp. 247–252. doi: 10.1097/MAJ.0b013e3181e939d8.

ISO (2019) *Ergonomics of human-system interaction — Part 210: Human-centred design for interactive systems*, *International Standard*. Available at: https://www.iso.org/obp/ui/#iso:std:iso:9241:-210:ed-2:v1:en.

Jacob, C., Sanchez-Vazquez, A. and Ivory, C. (2020) 'Social, organizational, and technological factors impacting clinicians' adoption of mobile health tools: Systematic literature review', *JMIR mHealth and uHealth*. JMIR Publications, p. e15935. doi: 10.2196/15935.

Kaltsas, A. *et al.* (2012) 'Clinical and laboratory characteristics of Clostridium difficile infection in patients with discordant diagnostic test results', *Journal of Clinical Microbiology*, 50(4), pp. 1303–1307. doi: 10.1128/JCM.05711-11.

Karen C., C. and John G., B. (2011) 'Biology of iClostridium difficile/i : Implications for Epidemiology and Diagnosis', *Annual Review of Microbiology*, 65(1), pp. 501–521. doi: 10.1146/annurev-micro-090110-102824.

Kavanagh, K. *et al.* (2016) 'Cumulative and temporal associations between antimicrobial prescribing and community-associated iClostridium difficile/i infection: population-based case–control study using administrative data', *Journal of Antimicrobial Chemotherapy*, p. dkw528. doi: 10.1093/jac/dkw528.

Keith, R. E. *et al.* (2017) 'Using the Consolidated Framework for Implementation Research (CFIR) to produce actionable findings: a rapid-cycle evaluation approach to improving implementation', *Implementation Science*, 12(1), p. 15. doi: 10.1186/s13012-017-0550-7.

Kerr, D. (2004) 'Factors influencing the development and adoption of knowledge based decision support systems for small, owner-operated rural businesses', *Artificial Intelligence Review*, 22(2), pp. 127–147. doi: 10.1023/B:AIRE.0000045503.74951.7a.

Kesselheim, A. S. *et al.* (2011) 'Analysis & commentary: Clinical decision support systems could be modified to reduce "alert fatigue" while still minimizing the risk of litigation', *Health Affairs*, 30(12), pp. 2310–2317. doi: 10.1377/hlthaff.2010.1111.

Khanna, S. *et al.* (2012) 'The epidemiology of community-acquired clostridium difficile infection: A population-based study', *American Journal of Gastroenterology*, 107(1), pp. 89–95. doi: 10.1038/ajg.2011.398.

Kilsdonk, E., Peute, L. W. and Jaspers, M. W. M. (2017) 'Factors influencing implementation success of guideline-based clinical decision support systems: A systematic review and gaps analysis', *International Journal of Medical Informatics*. Elsevier Ireland Ltd, pp. 56–64. doi: 10.1016/j.ijmedinf.2016.12.001.

King, A. *et al.* (2017) 'Comparative epidemiology of Clostridium difficile infection: England and the USA', *International Journal for Quality in Health Care*, 29(6), pp. 785–791. doi: 10.1093/intqhc/mzx120.

Kirk, M. A. *et al.* (2015) 'A systematic review of the use of the Consolidated Framework for Implementation Research', *Implementation Science*, 11(1), p. 72. doi: 10.1186/s13012-016-0437-z.

Kotila, S. M. *et al.* (2013) 'Clostridium difficile contamination of public tap water distribution system during a waterborne outbreak in Finland', *Scandinavian Journal of Public Health*, 41(5), pp. 541–545. doi: 10.1177/1403494813481648.

Kuipers, E. J. and Surawicz, C. M. (2008) 'Clostridium difficile infection.', *Lancet (London, England)*, 371(9623), pp. 1486–1488. doi: 10.1016/S0140-6736(08)60635-2.

Kujala, S. (2003) 'User involvement: A review of the benefits and challenges', *Behaviour & Information Technology*, 22(1), pp. 1–16. doi: 10.1080/01449290301782.

Kumar, A. and Abraham, A. (2017) 'Opinion Mining to Assist User Acceptance Testing for Open-Beta Versions', *Journal of Information Assurance and Security*, 12, pp. 146–153. Available at: www.mirlabs.net/jias/index.html.

Kurniabudi, K., Sharipuddin, S. and Assegaff, S. (2014) 'A Literature Review: Acceptance Models for e-learning Implementation in Higher Institution', in *Proceedings of the 2014 International Conference on Advances in Education Technology*. Paris, France: Atlantis Press. doi: 10.2991/icaet-14.2014.20.

Kux, B. R. *et al.* (2017) 'Factors Influencing the Implementation and Distribution of Clinical Decision Support Systems (CDSS).', *Studies in health technology and informatics*, 243, pp. 127–131. Available at: http://www.ncbi.nlm.nih.gov/pubmed/28883185.

Kwok, C. S. *et al.* (2012) 'Risk of clostridium difficile infection with acid suppressing drugs and antibiotics: Meta-analysis', *American Journal of Gastroenterology*, 107(7), pp. 1011–1019. doi: 10.1038/ajg.2012.108.

Laka, M., Milazzo, A. and Merlin, T. (2020) 'Factors that impact the adoption of clinical decision support systems (CDSS) in healthcare settings for evidence-based decision making'. doi: 10.21203/rs.3.rs-34358/v1.

Lam, H. *et al.* (2021) 'Identifying actionable strategies: using Consolidated Framework for Implementation Research (CFIR)-informed interviews to evaluate the implementation of a multilevel intervention to improve colorectal cancer screening', *Implementation Science Communications*, 2(1). doi: 10.1186/S43058-021-00150-9.

Larson, H. E. *et al.* (1977) 'Undescribed toxin in pseudomembranous colitis.', *British medical journal*, 1(6071), pp. 1246–1248. doi: 10.1136/bmj.1.6071.1246.

Lawes, T. *et al.* (2017) 'Effect of a national 4C antibiotic stewardship intervention on the clinical and molecular epidemiology of Clostridium difficile infections in a region of Scotland: a non-linear time-series analysis', *The Lancet Infectious Diseases*, 17(2), pp. 194–206. doi: 10.1016/S1473-3099(16)30397-8.

Lees, E. A. *et al.* (2016) 'The role of Clostridium difficile in the paediatric and neonatal gut - a narrative review.', *European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology*, 35(7), pp. 1047–1057. doi: 10.1007/s10096-016-2639-3.

Legenza, L. *et al.* (2018) 'Epidemiology and outcomes of Clostridium difficile infection among hospitalised patients: Results of a multicentre retrospective study in South Africa', *BMJ Global Health*, 3(4). doi: 10.1136/bmjgh-2018-000889.

Leonard, J., Marshall, J. K. and Moayyedi, P. (2007) 'Systematic review of the risk of enteric infection in patients taking acid suppression', *American Journal of Gastroenterology*, pp. 2047–2056. doi: 10.1111/j.1572-0241.2007.01275.x.

Lessa, F. C. *et al.* (2014) 'Determinants of Clostridium difficile infection incidence across diverse United States geographic locations', *Open Forum Infectious Diseases*, 1(2). doi: 10.1093/ofid/ofu048.

Leung, J. *et al.* (2013) 'Possible association between obesity and Clostridium difficile infection.', *Emerging infectious diseases*, 19(11), pp. 1791–1798. doi: 10.3201/eid1911.130618.

Levinson, W. (2012) *Review of medical microbiology and immunology*. McGraw-Hill Medical. Available at: http://www.langetextbooks.com/0071774343.php?c=home.

Liberati, E. G. *et al.* (2017) 'What hinders the uptake of computerized decision support

systems in hospitals? A qualitative study and framework for implementation', *Implementation Science*, 12(1), p. 113. doi: 10.1186/s13012-017-0644-2.

Liubakka, A. and Vaughn, B. P. (2016) 'Clostridium difficile Infection and Fecal Microbiota Transplant.', *AACN advanced critical care*, 27(3), pp. 324–337. doi: 10.4037/aacnacc2016703.

Lomotan, E. A. *et al.* (2012) 'Evaluating the use of a computerized clinical decision support system for asthma by pediatric pulmonologists', *International Journal of Medical Informatics*, 81(3), pp. 157–165. doi: 10.1016/j.ijmedinf.2011.11.004.

Loo, V. G. *et al.* (2011) 'Host and Pathogen Factors for iClostridium difficile/i Infection and Colonization', *New England Journal of Medicine*, 365(18), pp. 1693–1703. doi: 10.1056/NEJMoa1012413.

MacLean, Lord and Chairman (2014) 'The Vale of Leven Hospital Inquiry Report'. Available at: www.valeoflevenhospitalinquiry.org (Accessed: 18 September 2024).

Maisa A, R. G. (2019) 'Comparing the epidemiology of community-and hospital-associatedClostridium difficileinfections in Northern Ireland, 2012–2016: apopulation data linkage and case–case study', *Epidemiology and Infection*.

Martinez, F. (2012) 'Clostridium difficile outbreaks: prevention and treatment strategies', *Risk Management and Healthcare Policy*, p. 55. doi: 10.2147/rmhp.s13053.

Maunder, A. *et al.* (2007) 'Designing interactive systems for the developing world - Reflections on user-centred design', in *2007 International Conference on Information and Communication Technologies and Development, ICTD 2007*. doi: 10.1109/ICTD.2007.4937419.

May, C. and Finch, T. (2009) 'Implementing, Embedding, and Integrating Practices: An Outline of Normalization Process Theory', *Sociology*, 43(3), pp. 535–554. doi: 10.1177/0038038509103208.

McDermott, L. *et al.* (2010) 'Developing a computer delivered, theory based intervention for guideline implementation in general practice', *BMC Family Practice*, 11, p. 90. doi: 10.1186/1471-2296-11-90.

Medical devices: software applications (apps) - GOV.UK (2023). Available at: https://www.gov.uk/government/publications/medical-devices-software-applications-apps (Accessed: 1 May 2024).

Miller, A. C. *et al.* (2020) 'Risk for Clostridioides difficile Infection Among Hospitalized Patients Associated With Multiple Healthcare Exposures Prior to Admission', *The Journal of Infectious Diseases*, 224(4), p. 684. doi: 10.1093/INFDIS/JIAA773.

Miller, A. C. *et al.* (2023) 'Comparison of Different Antibiotics and the Risk for Community-Associated Clostridioides difficile Infection: A Case-Control Study', *Open forum infectious diseases*, 10(8). doi: 10.1093/OFID/OFAD413.

Mobasheri, M. H. *et al.* (2015) 'The ownership and clinical use of smartphones by doctors and nurses in the UK: A multicentre survey study', *BMJ Innovations*, 1(4), pp. 174–181. doi: 10.1136/bmjinnov-2015-000062.

Moir, T. (2018) 'Why Is Implementation Science Important for Intervention Design and

Evaluation Within Educational Settings?', *Frontiers in Education*, 3. doi: 10.3389/feduc.2018.00061.

Molina-Recio, G. *et al.* (2020) 'Proposal for the user-centered design approach for health apps based on successful experiences: Integrative review', *JMIR mHealth and uHealth*, 8(4), p. e14376. doi: 10.2196/14376.

Montagni, I. *et al.* (2017) 'Co-creating and Evaluating a Web-app Mapping Real-World Health Care Services for Students: The servi-Share Protocol.', *JMIR research protocols*, 6(2), p. e24. doi: 10.2196/resprot.6801.

Mullish, B. H. and Williams, H. R. T. (2018) 'Clostridium diffi cile infection and antibiotic-associated diarrhoea', *Clinical Medicine, Journal of the Royal College of Physicians of London*, 18(3), pp. 237–241. doi: 10.7861/clinmedicine.18-3-237.

Natarajan, M. *et al.* (2015) 'Gender Differences in Non-Toxigenic Clostridium difficile Colonization and Risk of Subsequent C. difficile Infection.', *Clinical research in infectious diseases*, 2(2). Available at: http://www.ncbi.nlm.nih.gov/pubmed/28713874.

Nathwani, D. *et al.* (2011) 'Scottish Antimicrobial Prescribing Group (SAPG): development and impact of the Scottish National Antimicrobial Stewardship Programme', *International Journal of Antimicrobial Agents*, 38(1), pp. 16–26. doi: 10.1016/J.IJANTIMICAG.2011.02.005.

Nathwani, D. *et al.* (2012) 'Antimicrobial stewardship in Scotland: impact of a national programme', *Antimicrobial Resistance and Infection Control*, 1(1), p. 7. doi: 10.1186/2047-2994-1-7.

NHS National Services Scotland (2020) 'Antimicrobial Resistance and Healthcare Associated Infections Scotland. 2020 Annual Report', (September). Available at: https://www.nss.nhs.scot/media/2256/hai-annual-report-2020.pdf.

NHS National Services Scotland (2021) 'ARHAI Scotland 2021 Annual Report', (September).

NHS National Services Scotland (2022) 'ARHAI Scotland 2022 Annual Report', (September).

Nilsen, P. (2015) 'Making sense of implementation theories, models and frameworks', *Implementation Science*, 10(1), pp. 1–13. doi: 10.1186/s13012-015-0242-0.

Nowell, L. S. *et al.* (2017) 'Thematic Analysis', *International Journal of Qualitative Methods*, 16(1), p. 160940691773384. doi: 10.1177/1609406917733847.

Noy, C. (2008) 'Sampling Knowledge: The Hermeneutics of Snowball Sampling in Qualitative Research', *https://doi.org/10.1080/13645570701401305*, 11(4), pp. 327–344. doi: 10.1080/13645570701401305.

Oka, K. *et al.* (2012) 'Molecular and microbiological characterization of Clostridium difficile isolates from single, relapse, and reinfection cases', *Journal of Clinical Microbiology*, 50(3), pp. 915–921. doi: 10.1128/JCM.05588-11.

Olakotan, O. O. and Mohd Yusof, M. (2021) 'The appropriateness of clinical decision support systems alerts in supporting clinical workflows: A systematic review', *Health Informatics Journal*, 27(2). doi: 10.1177/14604582211007536/ASSET/IMAGES/LARGE/10.1177_14604582211007536-FIG2.JPEG.

Olsen, M. A. *et al.* (2018) 'Increasing age has limited impact on risk of Clostridium difficile

infection in an elderly population', *Open Forum Infectious Diseases*, 5(7). doi: 10.1093/ofid/ofy160.

Oren, A. and Rupnik, M. (2018) 'Clostridium difficile and Clostridioides difficile: Two validly published and correct names', *Anaerobe*, 52, pp. 125–126. doi: 10.1016/J.ANAEROBE.2018.07.005.

Permpalung, N. *et al.* (2016) 'Association between NSAIDs and Clostridium difficile-Associated Diarrhea: A Systematic Review and Meta-Analysis.', *Canadian journal of gastroenterology & hepatology*, 2016, p. 7431838. doi: 10.1155/2016/7431838.

Pick, R. A. (2008) 'Benefits of Decision Support Systems', in *Handbook on Decision Support Systems 1*. Berlin, Heidelberg: Springer Berlin Heidelberg, pp. 719–730. doi: 10.1007/978-3-540-48713-5_32.

Public Health England (2020) 'Annual epidemiological commentary: bacteraemia, MSSA bacteraemia and C . difficile infections, up to and including financial year April 2018 to March 2019', (March), pp. 1–88. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/843870/Annual_epidemiological_commentary_April_2018-March_2019.pdf.

Rineh, A. *et al.* (2014) 'Clostridium difficile infection: molecular pathogenesis and novel therapeutics', *Expert review of anti-infective therapy*, 12(1), p. 131. doi: 10.1586/14787210.2014.866515.

Rittmann, B. and Stevens, M. P. (2019) 'Clinical Decision Support Systems and Their Role in Antibiotic Stewardship: a Systematic Review', *Current Infectious Disease Reports 2019 21:8*, 21(8), pp. 1–12. doi: 10.1007/S11908-019-0683-8.

Roberts, K., Dowell, A. and Nie, J. B. (2019) 'Attempting rigour and replicability in thematic analysis of qualitative research data; A case study of codebook development', *BMC Medical Research Methodology*, 19(1), p. 66. doi: 10.1186/s12874-019-0707-y.

Robertson, C. *et al.* (2020) 'Cost burden of Clostridioides difficile infection to the health service: A retrospective cohort study in Scotland', *Journal of Hospital Infection*, 106(3), pp. 554–561. doi: 10.1016/j.jhin.2020.07.019.

Ross, J. *et al.* (2016) 'Factors that influence the implementation of e-health: a systematic review of systematic reviews (an update)', *Implementation Science*, 11(1), p. 146. doi: 10.1186/s13012-016-0510-7.

Rossello, X. *et al.* (2019) 'Risk prediction tools in cardiovascular disease prevention: A report from the ESC Prevention of CVD Programme led by the European Association of Preventive Cardiology (EAPC) in collaboration with the Acute Cardiovascular Care Association (ACCA) and the Association of Cardiovascular Nursing and Allied Professions (ACNAP).', *European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology*, 18(7), pp. 534–544. doi: 10.1177/1474515119856207.

Al Saif, N. and Brazier, J. S. (1996) 'The distribution of Clostridium difficile in the environment of South Wales', *Journal of Medical Microbiology*, 45(2), pp. 133–137. doi: 10.1099/00222615-45-2-133.

Sandars, J. (2010) 'The importance of usability testing to allow e-learning to reach its

potential for medical education', *Education for Primary Care*, 21(1), pp. 6–8. doi: 10.1080/14739879.2010.11493869/ASSET//CMS/ASSET/2F5D2ADE-9BAA-446F-AA69-4E7BBD746FEB/14739879.2010.11493869.FP.PNG.

dos Santos, T. B. *et al.* (2021) 'Prototyping for user involvement activities: How to achieve major benefits', *CIRP Journal of Manufacturing Science and Technology*, 33, pp. 465–472. doi: 10.1016/J.CIRPJ.2021.04.013.

Sartelli, M. *et al.* (2019) '2019 update of the WSES guidelines for management of Clostridioides (Clostridium) difficile infection in surgical patients', *World Journal of Emergency Surgery*, 14(1), p. 8. doi: 10.1186/s13017-019-0228-3.

Sayedy, L., Kothari, D. and Richards, R. J. (2010) 'Toxic megacolon associated Clostridium difficile colitis', *World Journal of Gastrointestinal Endoscopy*, 2(8), p. 293. doi: 10.4253/WJGE.V2.I8.293.

Schäffler, H. and Breitrück, A. (2018) 'Clostridium difficile - From colonization to infection', *Frontiers in Microbiology*. Frontiers Media S.A. doi: 10.3389/fmicb.2018.00646.

Schmidt, A. *et al.* (2023) 'Patients' perspectives on a patient-oriented electronic decision support tool to reduce overuse of proton pump inhibitors (arriba-PPI): a qualitative study in primary care', *BMC Primary Care*, 24(1), pp. 1–6. doi: 10.1186/S12875-023-01991-0/PEER-REVIEW.

Schnall, R. *et al.* (2015) 'Trust, Perceived Risk, Perceived Ease of Use and Perceived Usefulness as Factors Related to mHealth Technology Use', *Studies in health technology and informatics*, 216, p. 467. doi: 10.3233/978-1-61499-564-7-467.

ScotGov (2024) 'ARHAI Scotland 2023 Annual Report', (October).

Seekatz, A. M. and Young, V. B. (2014) 'Clostridium difficile and the microbiota', *Journal of Clinical Investigation*. American Society for Clinical Investigation, pp. 4182–4189. doi: 10.1172/JCI72336.

Seltman, A. (2012) 'Surgical management of clostridium difficile colitis', *Clinics in Colon and Rectal Surgery*, 25(4), pp. 204–209. doi: 10.1055/s-0032-1329390.

Senbekov, M. *et al.* (2020) 'The Recent Progress and Applications of Digital Technologies in Healthcare: A Review', *International Journal of Telemedicine and Applications*, 2020(1), p. 8830200. doi: 10.1155/2020/8830200.

Shibl, R., Lawley, M. and Debuse, J. (2013) 'Factors influencing decision support system acceptance', *Decision Support Systems*, 54(2), pp. 953–961. doi: 10.1016/J.DSS.2012.09.018.

Shim, J. O. (2014) 'Clostridium difficile in Children: To Treat or Not to Treat?', *Pediatric gastroenterology, hepatology & nutrition*, 17(2), pp. 80–84. doi: 10.5223/pghn.2014.17.2.80.

Simango, C. (2006) 'Prevalence of Clostridium difficile in the environment in a rural community in Zimbabwe', *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 100(12), pp. 1146–1150. doi: 10.1016/j.trstmh.2006.01.009.

Slater, H. *et al.* (2017) 'End User and Implementer Experiences of mHealth Technologies for Noncommunicable Chronic Disease Management in Young Adults: Systematic Review', *J*

Med Internet Res 2017;19(12):e406 https://www.jmir.org/2017/12/e406, 19(12), p. e8888. doi: 10.2196/JMIR.8888.

Spigaglia, P. (2016) ' Recent advances in the understanding of antibiotic resistance in Clostridium difficile infection ', *Therapeutic Advances in Infectious Disease*, 3(1), pp. 23–42. doi: 10.1177/2049936115622891.

Stivers, T. (2021) 'Managing Patient Pressure to Prescribe Antibiotics in the Clinic', *Pediatric Drugs*, 23(5), pp. 437–443. doi: 10.1007/S40272-021-00466-Y/TABLES/8.

Sutton, R. T. (2020) 'An overview of clinical decision support systems : bene fi ts , risks , and strategies for success', *npj Digital Medicine*, pp. 1–10. doi: 10.1038/s41746-020-0221-y.

Svanæs, D., Alsos, O. A. and Dahl, Y. (2010) 'Usability testing of mobile ICT for clinical settings: Methodological and practical challenges', *International Journal of Medical Informatics*, 79(4), pp. e24–e34. doi: 10.1016/J.IJMEDINF.2008.06.014.

Tang, T. *et al.* (2018) 'Clinician user involvement in the real world: Designing an electronic tool to improve interprofessional communication and collaboration in a hospital setting', *International Journal of Medical Informatics*, 110, pp. 90–97. doi: 10.1016/J.IJMEDINF.2017.11.011.

Tedesco, F. J., Barton, R. W. and Alpers, D. H. (1974) 'Clindamycin associated colitis. A prospective study', *Annals of Internal Medicine*, 81(4), pp. 429–433. doi: 10.7326/0003-4819-81-4-429.

Thomson, R., Edwards, A. and Grey, J. (2005) 'Risk communication in the clinical consultation.', *Clinical medicine (London, England)*, 5(5), pp. 465–469. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16268328.

Tian, L. *et al.* (2023) 'Proton pump inhibitors may enhance the risk of digestive diseases by regulating intestinal microbiota', *Frontiers in Pharmacology*, 14, p. 1217306. doi: 10.3389/FPHAR.2023.1217306.

Ticinesi, A. *et al.* (2015) 'Multimorbidity in elderly hospitalised patients and risk of Clostridium difficile infection: a retrospective study with the Cumulative Illness Rating Scale (CIRS).', *BMJ open*, 5(10), p. e009316. doi: 10.1136/bmjopen-2015-009316.

Tydeman, F. *et al.* (2021) 'Incidence of Clostridioides difficile infection (CDI) related to antibiotic prescribing by GP surgeries in Wales', *Journal of Antimicrobial Chemotherapy*, 76(9), p. 2437. doi: 10.1093/JAC/DKAB204.

Usher-Smith, J. *et al.* (2015) 'Risk prediction tools for cancer in primary care', *British Journal of Cancer*, 113(12), p. 1645. doi: 10.1038/BJC.2015.409.

Vaismoradi, M., Turunen, H. and Bondas, T. (2013) 'Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study', *Nursing and Health Sciences*, 15(3), pp. 398–405. doi: 10.1111/nhs.12048.

Varonen, H., Kortteisto, T. and Kaila, M. (2008) 'What may help or hinder the implementation of computerized decision support systems (CDSSs): A focus group study with physicians', *Family Practice*, 25(3), pp. 162–167. doi: 10.1093/fampra/cmn020.

Vasilescu, I. M. *et al.* (2021) 'Gut Dysbiosis and Clostridioides difficile Infection in Neonates and Adults', *Frontiers in Microbiology*, 12. doi: 10.3389/FMICB.2021.651081.

Van de Velde, S. *et al.* (2016) 'Tailoring implementation strategies for evidence-based recommendations using computerised clinical decision support systems: Protocol for the development of the GUIDES tools', *Implementation Science*, 11(1). doi: 10.1186/s13012-016-0393-7.

de Velde, S. Van (2017) 'GUIDES CHECKLIST'.

Van de Velde, S., Heselmans, A., *et al.* (2018) 'A systematic review of trials evaluating success factors of interventions with computerised clinical decision support', *Implementation Science*. BioMed Central Ltd. doi: 10.1186/s13012-018-0790-1.

Van de Velde, S., Kunnamo, I., *et al.* (2018) 'The GUIDES checklist: development of a tool to improve the successful use of guideline-based computerised clinical decision support.', *Implementation science : IS*, 13(1), p. 86. doi: 10.1186/s13012-018-0772-3.

Vermeir, P. *et al.* (2015) 'Communication in healthcare: a narrative review of the literature and practical recommendations', *International Journal of Clinical Practice*, 69(11), pp. 1257–1267. doi: 10.1111/IJCP.12686.

Viprey, V. F. *et al.* (2022) 'A point-prevalence study on community and inpatient Clostridioides difficile infections (CDI): Results from Combatting Bacterial Resistance in Europe CDI (COMBACTE-CDI), July to November 2018', *Eurosurveillance*, 27(26), p. 2100704. doi: 10.2807/1560-7917.ES.2022.27.26.2100704/CITE/REFWORKS.

Vo, V., Auroy, L. and Sarradon-Eck, A. (2019) 'Patients' Perceptions of mHealth Apps: Meta-Ethnographic Review of Qualitative Studies.', *JMIR mHealth and uHealth*, 7(7), p. e13817. doi: 10.2196/13817.

Vogel, C. *et al.* (2023) 'In vitro evaluation of a computer-assisted decision support system for the primary care of polytrauma patients', *European Journal of Trauma and Emergency Surgery*, pp. 1–6. doi: 10.1007/S00068-023-02295-9/FIGURES/3.

Voth, D. E. and Ballard, J. D. (2005) 'Clostridium difficile Toxins: Mechanism of Action and Role in Disease', *Clinical Microbiology Reviews*, 18(2), p. 247. doi: 10.1128/CMR.18.2.247-263.2005.

Wadhwa, R. *et al.* (2008) 'Analysis of a failed clinical decision support system for management of congestive heart failure.', *AMIA ... Annual Symposium proceedings. AMIA Symposium*, 2008, pp. 773–777. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18999183.

Warner, G. *et al.* (2018) 'Applying the consolidated framework for implementation research to identify barriers affecting implementation of an online frailty tool into primary health care: a qualitative study', *BMC Health Services Research*, 18(1). doi: 10.1186/S12913-018-3163-1.

Wasylewicz, A. T. M. and Scheepers-Hoeks, A. M. J. W. (2019) 'Clinical Decision Support Systems', in *Fundamentals of Clinical Data Science*. Cham: Springer International Publishing, pp. 153–169. doi: 10.1007/978-3-319-99713-1_11.

Webb, M. J., Wadley, G. and Sanci, L. A. (2018) 'Experiences of General Practitioners and Practice Support Staff Using a Health and Lifestyle Screening App in Primary Health Care: Implementation Case Study.', *JMIR mHealth and uHealth*, 6(4), p. e105. doi: 10.2196/mhealth.8778.

Weber, D. J. *et al.* (2013) 'Role of the environment in the transmission of Clostridium difficile in health care facilities', *American Journal of Infection Control*, 41(5 SUPPL.). doi: 10.1016/j.ajic.2012.12.009.

Weichbroth, P. (2024) 'Usability Testing of Mobile Applications: A Methodological Framework', *Applied Sciences 2024, Vol. 14, Page 1792*, 14(5), p. 1792. doi: 10.3390/APP14051792.

Weiss, K. *et al.* (2015) 'Effects of proton pump inhibitors and histamine-2 receptor antagonists on response to fidaxomicin or vancomycin in patients with Clostridium difficile-associated diarrhoea', *BMJ Open Gastroenterology*, 2(1), p. e000028. doi: 10.1136/BMJGAST-2014-000028.

Wever, R., van Kuijk, J. and Boks, C. (2008) 'User-centred design for sustainable behaviour', *International Journal of Sustainable Engineering*, 1(1), pp. 9–20. doi: 10.1080/19397030802166205.

Wiebelitz, L. *et al.* (2022) 'Designing User-friendly Medical AI Applications - Methodical Development of User-centered Design Guidelines', *Proceedings - 2022 IEEE International Conference on Digital Health, ICDH 2022*, pp. 23–28. doi: 10.1109/ICDH55609.2022.00011.

Wienert, J. (2019) 'Understanding Health Information Technologies as Complex Interventions With the Need for Thorough Implementation and Monitoring to Sustain Patient Safety', *Frontiers in ICT*, 6(APR), p. 9. doi: 10.3389/fict.2019.00009.

Wilcox, M. H. *et al.* (2017) 'Role of cephalosporins in the era of Clostridium difficile infection', *Journal of Antimicrobial Chemotherapy*, 72(1), pp. 1–18. doi: 10.1093/jac/dkw385.

Wilkinson, C. R. and De Angeli, A. (2014a) 'Applying user centred and participatory design approaches to commercial product development', *Design Studies*, 35(6), pp. 614–631. doi: 10.1016/j.destud.2014.06.001.

Wilkinson, C. R. and De Angeli, A. (2014b) 'Applying user centred and participatory design approaches to commercial product development', *Design Studies*, 35(6), pp. 614–631. doi: 10.1016/j.destud.2014.06.001.

Williams, G. A. *et al.* (2022) 'COVID-19 and the use of digital health tools: opportunity amid crisis that could transform health care delivery'.

Wilson, K. M. *et al.* (2011) 'An organizing framework for translation in public health: The knowledge to action framework', *Preventing Chronic Disease*, 8(2).

Wiuff, C. *et al.* (2011) 'The epidemiology of Clostridium difficile in Scotland', *Journal of Infection*, 62(4), pp. 271–279. doi: 10.1016/J.JINF.2011.01.015.

Wu, D. T. Y. *et al.* (2019) 'Usability Testing of an Interactive Dashboard for Surgical Quality Improvement in a Large Congenital Heart Center', *Applied Clinical Informatics*, 10(5), pp. 859–869. doi: 10.1055/S-0039-1698466/ID/JR190090RA-38/BIB.

Yoon, M. Y. and Yoon, S. S. (2018) 'Disruption of the Gut Ecosystem by Antibiotics.', *Yonsei medical journal*, 59(1), pp. 4–12. doi: 10.3349/ymj.2018.59.1.4.

Zhang, S. *et al.* (2016) 'Cost of hospital management of Clostridium difficile infection in United States-a meta-analysis and modelling study', *BMC Infectious Diseases*, 16(1). doi:

10.1186/s12879-016-1786-6.

Zheng, K. *et al.* (2005) 'Understanding technology adoption in clinical care: Clinician adoption behavior of a point-of-care reminder system', *International Journal of Medical Informatics*, 74(7–8), pp. 535–543. doi: 10.1016/j.ijmedinf.2005.03.007.

Appendices

Appendix A

Scottish Healthcare Associated Infection Prevention Institute (SHAIPI)

Thank you for stating your interest in participating in our project about the development of a tool to improve antibiotic prescribing.

This letter is to confirm your participation in the project, provide a brief overview of the project and what your participation will involve.

The project

This project aims to create a digital tool to help GPs identify those at high risk of Clostridium difficile (CA-CDI) accompanied with estimates of how this risk could be modified by their prescribing decision helping them deliver patient-centred, safe and effective antibiotic stewardship.

The Mathematics & Statistics department of the University of Strathclyde has developed a prediction algorithm that can estimate the risk of a patient getting CA-CDI. We are currently working on the development of a software tool that would incorporate this algorithm in a way to suit the GPs needs when prescribing antibiotics.

Your Role

Your role in this project would be to help inform the user-experience research team at University of Strathclyde on the needs and requirements of GPs and also to help give feedback on the initial designs of the tool via face to face or phone interviews and consultations and/or short half day workshops or group discussions with a members of the research team. You are expected to participate in at least 2 half-day sessions between now and the end of March 2018. The first session would be on a one to one basis where a researcher would interview you. The second session would be a group session where you, along with the other two GPs involved and a researcher would work together to produce ideas about the design and functionality of the tool. *There is no requirement for you to have any technical knowledge or skills related to design and software in order to participate in the workshop*. Finally depending on your availability and willing to continue with this project, we may arrange an observation of your regular practice (researcher observing your work practice and taking notes) and one or two more sessions about the evaluation of the first workshop's outcomes (an initial prototype).

The process and your involvement is depicted in Figure A.

The next steps of the project and your potential further involvement is depicted in Figure B.

Your main contact for this project would be Charalampos (**Babis**) Kyfonidis, who is the research assistant responsible for the design of the tool.

His contact details are:
Charalampos (**Babis**) Kyfonidis
email: Charalampos.kyfonidis@strath.ac.uk
tel: 07922096576

NHS ISD will reimburse £210 for each half day (4 hour) GP session and receipted travel expenses. Your GP practice can claim back the money for these sessions from ISD. The first stage is to provide practice info to be set up as a customer, please contact Marion Bennie's secretary Sue Hewitt, email: suehewitt@nhs.net , tel: 0131 275 6388, project ref: SHAIP

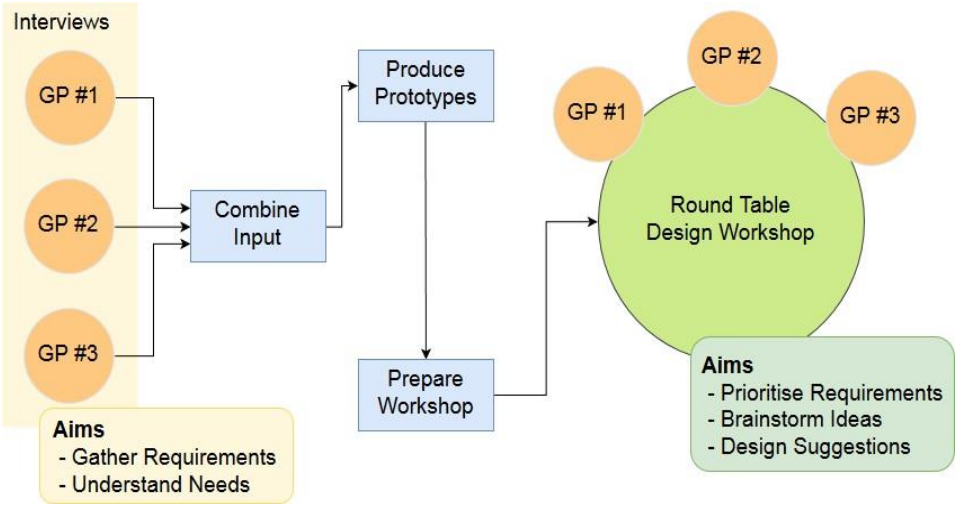


Figure A: Project Phases and GPs' Involvement

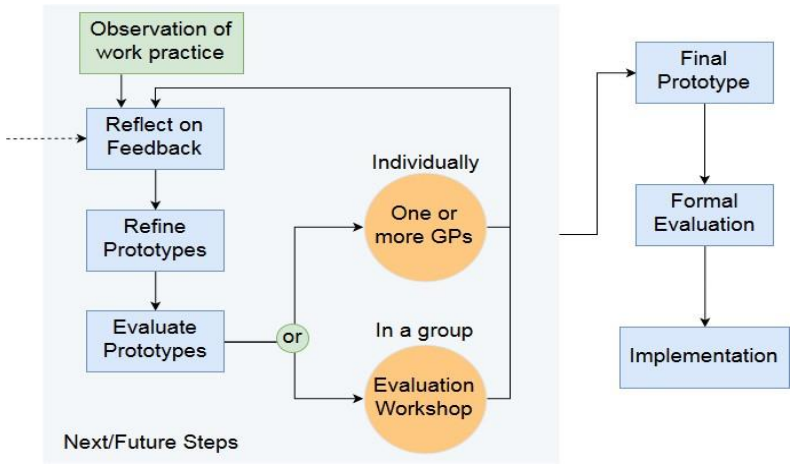


Figure B: Next/Future Phases and Potential Involvement

Primary Investigators for this project are:

Prof Marion Bennie
Strathclyde Institute of Pharmacy and Biomedical Sciences – University of Strathclyde
Information Services Division, NHS National Services Scotland
+44 (0)141 548 2113
marion.bennie@strath.ac.uk

Prof Chris Robertson
Department of Mathematics and Statistics – University of Strathclyde
Health Protection Scotland, NHS National Services Scotland
+44 (0)141 548 3215
chris.robertson@strath.ac.uk

Appendix B

GP Champions meeting

Date:

Participants:

Purpose: Requirements Gathering with 3 GP champions in Feb 2018 to understand their requirements, needs, perceptions about C.Diff and Clinical Decision Support tools.

Procedure

Introduction

Hi, my name is Babis. I am a research assistant from University of Strathclyde. I am working on the design of a clinical decision support tool for antibiotic prescription. The tool informs prescribers on the patient's risk of getting Clostridium Difficile.

This is Ansu, a PhD student from University of Strathclyde. Ansu is looking at the potential implementation and diffusion of such a tool in everyday practice of GPs and other potential prescribers in the future.

Goals of the interview

This interview is about

1. Meeting you in person
2. Understand the current prescription process in relation to antibiotic prescribing
3. Understand your needs, requirements and thoughts of a potential CDI risk assessment tool (clinical decision support tool)

It is a semi-structured interview, meaning that I have a set of questions to start from, but we are free to elaborate on whatever we think it is important.

The interview will take approximately 90 mins.

It will be recorded for the purposes of looking back at the notes to make sure we have captured everything you say during the interviews. Any data that is used or presented will always be anonymous and we will not quote you directly unless we ask explicitly for this.

Questions

Prescription process

1. What is your role and how long have you been in this role? **(CFIR: characteristics of the individual)**
2. How much time is there available for each patient appointment? **(CFIR: Patient needs and resources)**
    a. Is it enough for anti-biotic prescribing?
3. Can you describe the prescription process for antibiotics – from the moment a patient comes to the appointment. **(CFIR: Patient needs and resources)**

    a. In your opinion, are there any things that need improvement in the prescription process (prompts if needed – more time, better systems, and more information available to you or patient)?
    b. Do you always have the patient's record available when you are prescribing?

Dynamics

4. In your opinion, what do patients expect when they come to clinic with a suspected infection? **(CFIR: Patient needs and resources)**
5. How do patients influence your choice to prescribe antibiotics? **(CFIR: Patient needs and resources)**
    a. According to your experience and understanding; to what extend are patients able to understand the risks of antibiotics for their health? **(CFIR: Patient needs and resources)**
        i. Do patients care about the risks of antibiotics in your opinion? **(CFIR: Patient needs and resources)**
6. In your opinion, how can a GP balance between patient expectations and patient actual needs? **(CFIR: Patient needs and resources)**
7. In your opinion, do you think the unnecessary antibiotic prescription in Scotland is high? **(CFIR: Culture)**
    a. Are we in a good way?
    b. What needs to be done?

C.Diff awareness

8. To what extend do you believe C.Diff is a public health issue for Scotland? **(CFIR: Culture)**
    a. In your opinion, what can be done to reduce C.Diff cases?
9. Are you aware of any knowledge exchange channels on antibiotic prescribing (portals, forums, seminars)? **(CFIR: External policies and incentives)**

Prescribing antibiotics and C.Diff

10. Do you think prescribers need help or support when prescribing antibiotics? **(CFIR: Knowledge and beliefs about the intervention)**

11. Are there tools to guide your decision on anti-biotic prescription? **(CFIR: External policies and incentives)**
    a. Do the tools include C.Diff?
    b. Do the tools include 4Cs?
    c. Is the tool effective/useful?
12. How often do GPs in your practice prescribe 4Cs?
13. How often do you think about C.Diff when you have a patient with a possible infection? **(CFIR: Patient needs and resources)**
    d. At what stage of the decision process you think about C.Diff?
    e. Can you remember an example?
    f. Have you ever chose different anti-biotics because of high risk for C.Diff?

14. How do you identify a patient in high risk of getting C.Diff? **(CFIR: Patient needs and resources)**
    g. What are the things you have to consider for C.Diff when you are prescribing antibiotics?
    h. Can you decide with confidence about risky cases?
    i. What would you consider a difficult or "grey" case for deciding if someone is at risk for C.Diff?
        i. Can you give examples?

15. Are there cases where a GP would prescribe 4Cs even if a patient is in high risk for C.Diff?

Technology in workplace

16. How would you describe your current relationship with technology in general? **(CFIR: self-efficacy)**
17. What do you think about technology when it comes to supporting your general practice? **(CFIR: self-efficacy)**
    a. Can you provide any good or bad experiences with technology use in your general practice?
18. Which system are you using for prescribing?
    a. Does it provide any suggestions or alerts for patients? (**GUIDES checklist = DOMAIN 3 The CDS context)**

        i. Eg for allergies

Decision Support

19. What do you think makes a medical app / website successful or unsuccessful? (**GUIDES checklist =DOMAIN 2 The CDS context)**
    b. What would make you trust a medical apps/websites?

c. How do you learn about new medical apps/websites? **(CFIR: external policies and incentives)**
d. Do the GPs in your practice share medical apps / websites or persuade others use medical apps? **(CFIR: individual identification with organization)**
e. Is it easy or difficult for an app/website to be adopted by the GPs? (**GUIDES checklist = DOMAIN 1 The CDS context)**
f. What would make you adopt a medical app / website? (**GUIDES checklist = DOMAIN 1 The CDS context)**

ii. Apart from the board imposing you to.
iii. What is the most important aspect of these?

20. How much time from your appointments would you devote to use a decision support tool? (**GUIDES checklist = DOMAIN 3 The CDS context)**

21. How do you think the patients would react to the use of a decision support tool? (**GUIDES checklist = DOMAIN 1 The CDS context)**

22. Do you believe that such a tool would impact the prescriber-patient relationship? (**GUIDES checklist = DOMAIN 2 The CDS context)**
    a.
23. When or how do you think a decision support tool would be most **useful**? (**GUIDES checklist = DOMAIN 3 The CDS context)**

    a. Which context?
        i. What about when record is not available (at care home)?

    b. In the case of a "succesfull" decision support tool, do you think that some GPs would adopt it and others not? (**GUIDES checklist = DOMAIN 4 The CDS context)**

        i. Why?

C.Diff Tool

24. What would you like a C.Diff decision support tool to inform you about? (**GUIDES checklist = DOMAIN 2 The CDS context)**

f. Would it be helpful if a tool could quantify a patient's risk of getting C.Diff?

25. Which platform (eg. phone, computer or other) would be most suitable for a decision support tool? (**GUIDES checklist = DOMAIN 3 The CDS context)**

26. How would you expect a C.Diff decision support tool to look like? (**GUIDES checklist = DOMAIN 2 The CDS context)**

    g. Would you prefer a passive interaction (alert, message before you finalise the prescription, red sign), or an active interaction (like an app or a website)?
    h. How many patient attributes would you be willing to insert to generate a risk score for C.Diff?

27. How easily do you think such a tool can be added to the existing workflow? (**GUIDES checklist = DOMAIN 1The CDS context)**
    i. What are the barriers?
    j. What would make it work?
    k. Is your current patient data quality are good enough to support such tool? (**GUIDES checklist =DOMAIN 1 The CDS context)**

Debrief

Thank you for your participation and for sharing your insights and experiences with us. All the opinions we collect will be used to prepare a co-design workshop. In this workshop researchers and GPs will produce ideas and designs for a tool that identifies patients with high risk of getting CDiff.

We will invite you in this workshop and we will of course share the findings with you. Moreover, will be in touch to ask you for your reaction to any prototypes based on the designs we come up with during the workshop. Your opinions as practitioners are important to us as we are aiming to develop something truly useful that could be integrated into routine practice.

Do you have anything else you would like to add or comment on – or anything you would like to ask us about the project?

Stop recording

Outcomes

Factors that explain the current GP's behaviour and perceptions towards prescribing, technology, CDS tools, the prescriber-patient dynamics and C.Diff. Moreover, understand their needs, concerns and the local prescribing context.

Appendix C

Developing a toolkit to identify those at high risk of getting Clostridium Difficle (CDI)

Participants Information Sheet for Interviews

Invitation

My name is Charalampos (Babis) Kyfonidis and I am Research assistant at the University of Strathclyde.

This interview is about understanding the needs, perceptions and requirements when it comes to digital prescribing and clinical decision support tools.

Taking part in the interview is entirely up to you. Before you decide, please take a moment to read this document. I am happy to go through the information sheet with you and explain it. Please ask if anything is unclear.

Summary

Healthcare associated infections (HAI) are a significant burden to both patients and costs within the NHS in Scotland (estimated 2013 inpatient cost £137 million) despite considerable progress in the implementation of infection control precautions and transmission based precautions. The HAI Clostridium difficle infection (CDI) is associated with significant morbidity and mortality (hospitalised patients with CDI, 2x length of stay and risk of death than matched controls) and increased healthcare costs. A sizeable proportion (~27%) of CDI cases in Scotland are associated with acquisition in the community (CA-CDI) with the majority (83%) occurring outwith a care home setting. For these patients, antibiotic prescribing in the community is a major modifiable risk factor.

This project aims to create a digital tool (e.g. desktop, web based or mobile application) to help GPs identify those at high risk of CA-CDI accompanied with estimates of how this risk could be modified by their prescribing decision helping them deliver patient-centred, safe and effective antibiotic stewardship.

Our research team has developed a risk prediction model, using a range of statistical and machine learning techniques creating algorithms to identify those at highest risk. To date we have achieved a model with 70% sensitivity and 81% specificity.

Our key objectives are now to (1) to design a digital tool to help identify those at high risk of CA-CDI and (2) test the acceptability and usefulness of the tool to inform prescribing decisions in practice.

What would taking part involve?

You will be interviewed by a trained researcher and audio recorded. The interview is going to be a semi-structured interview, where the researcher will have a set of open-ended questions to lead the discussion and you can add your professional experiences and opinions to influence the design of the tool. The questions will be about the current prescription process, your perceptions about technology and its use in your working environment in general, and about the potential of the proposed CDI clinical decision support tool being developed as part of this project.

Do I have to take part?

No. Taking part in the study is entirely up to you. If you agree to be interviewed I will ask you to sign a consent form.

What are the possible benefits of taking part?

The outcomes of the interview will help us understand the prescribing process, the strengths and weaknesses of the current practices but also your requirements and needs from a clinical decision support tool for CDI. This way we can effectively design the tool to be usable and acceptable.

What are the possible disadvantages and risks of taking part?

There are no disadvantages of you taking part other than offering a small amount of your time to contribute to the research.

What happens if I wish to withdraw from the study?

You are free to withdraw at any time without being penalised or disadvantaged in any way and you can still claim the hours you have had been involved in the project.

How and why are we collecting information?

Audio recordings of the interview: It is crucial for me to be able to go back and listen in detail what was discussed in the interview. I want to be able to understand your responses and plan the next phases based on your requirements. The interview will be transcribed and analysed for emerging themes and then the audio discarded.

Will my participation be kept confidential?

Yes. The consent form will be stored in a locked file cabinet in a locked office or on a password protected computer. In the consent form, you will be assigned an identifier and all your data stored will be related to this identifier. Hence, all data would be pseudo-anonymised and only I would have access to your name and preferred contact method (email or postal address, facebook page etc). We will store all the pseudo-anonymised data on password secured university's drives. Any recordings will be deleted from the audio recorder after they are copied to the university's drive. All the pseudo-anonymised data will be deleted 5 years after the end of the study. Any pseudo-anonymised data cannot be withdrawn once they have been included in the study. Pseudo-anonymised data will be used to support other research in the future, and may be shared anonymously with other researchers. All data stored will be stored in accordance with the Data Protection Act (1998).

What if there is a problem?

If you have a problem about any aspect of this study, you should speak to the academic in charge, Dr Marilyn Lennon, who will do her best to answer your questions [0141 548 3098]. If you remain unhappy and wish to complain formally, you can do this by speaking to the ethics chair of Computer and Information Sciences department, Dr Marc Roper [01415482956 - marc.roper@strath.ac.uk].

Who is organising and funding the project?

This project is funded by The Medical Research Council's Confidence in Concept Programme.

Full contact details of the researchers:

For more information about the study or feedback please contact:

Researcher contact details:
Name: Charalampos Kyfonidis
Address: 16 Richmond Street,
Glasgow G1 1XQ. Scotland, United Kingdom
Telephone: 0141 548-4101
Email: charalampos.kyfonidis@strath.ac.uk

Academic Supervisor details:
Name: Dr Marilyn Lennon
Address: 16 Richmond Street,
Glasgow G1 1XQ. Scotland, United Kingdom
Telephone: 0141 548-3098
Email: marilyn.lennon@strath.ac.uk

Thank you for taking the time to read this Information Sheet.

Appendix D

Participant Identification Number for this study:

CONSENT FORM

Title of Project: Developing a toolkit to identify those at high risk of getting Clostridium Difficile (CDI)

Name of Researcher: Charalampos (Babis) Kyfonidis

		Please initial box
1	I confirm that I have verbally informed about the purpose of the study and the audio recording of my interview. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason.	
3	I understand I can withdraw from the study any personal data (i.e. data which identify me or my child personally) at any time.	
4	I understand that anonymised data will be used to support other research in the future, and may be shared anonymously with other researchers.	
5	I understand that the results of this study might be published, without exposing me or my personal data.	
6	I understand that anonymised data cannot be withdrawn once they have been included in the study.	
7	I understand that my personal data and my personal data will remain confidential and will not be made publicly available.	
8	I consent to being participant in this study.	
11	I consent to being audio recorded during the interview.	

Name of Participant Date

Signature

Name of Person Date

Signature taking consent

Appendix E

GP Co-design workshop for designing a C. diff tool.

11th of October from 11:00-13:00.

Introduction: (5-10 minutes)

1. Sign the ethical forms
2. Introduction

Outcomes of the precious phases:

- *C.diff* is not considered a threat
- *C.diff* in primary care is rare
- GPs tend to ignore EMIS®/InPS VISION® alerts
- GPs don't want an app to inform about *C.diff* only
- The tool should be implemented into the GP's system (within EMIS®/InPS VISION®)
- Script-Switch® is the good option
- GPs like the printout's idea

Need for the tool:

C.diff is influenced by primary care prescribing, even when non 4Cs are prescribed.

The tool:

We have an algorithm that can calculate the risk of a patient getting *C.diff*, if they are prescribed a 4C and a non-4C.

Limitations:

- The patient data need to be accurate.
- Alternatives cannot be provided

Based on the model, its limitations and the requirements from the GPs, we recognized the following aim for a risk predictive *C.diff* tool.

3. Aim of the tool (5 minutes)

- **Overall**: Reduce unnecessary prescription of 4C antibiotics for high-risk patients.

- **By**: Recognise high-risk patients for *C.diff* when they are about to be prescribed 4C antibiotics.
-

4. Aim of the workshop (5 minutes)
    - Find out the platform (passive or active)
    - Only GPs or Patients as well (Patient's responsibility)
    - The message that will be shown
    - Aesthetics of the tool (created as a wireframe, rough pen and paper prototypes)
    - Find out at which consultation phase will the tool be used
    - Design something that will be used and adopted

Icebreaker: (5-10 minutes)

- Let us do a small exercise to show you what we mean by.
- Can you please draw:
    -A stickman
    -A rectangle
    -A circle
    -A rounded rectangle
    -An arrow

- We asked you to draw these shapes as they will be the main tools for expressing and concretising ideas about the look and the functionality of the tool we are designing.

Let me show you an example we created for you to use these and other similar shapes or symbols for concretising your ideas about the tool.

- We use such simple tools because we are not expecting anything professional but only something that can capture your ideas and can be easily amended.

Choose a platform

Communicate the possible platform options for the tool and card sorting

- Show the options
    - Mobile app

- Website
- Script-Switch®
- Leaflet
- Combination → Script-Switch® + Website
  → Leaflet + Mobile app or Website or Script-Switch®
- Other

- Ask to card sort these options
- Ask them why
- Patient involvement and responsibility?
- Speak about the passive and active system and their limitations
- Ask when it will be used

ACTIVE SYSTEM

→Cons:

- Mobile phone is not preferred to be used in front of patients
- If GPs do not find C. diff an issue they wouldn't willingly go and look for the score in an active system
- Might take some time to find and input the data and therefore slow down the consultation
- GP might not recognize/miss a high-risk patient

→ Pros:

- The data will be accurate since the GP will be putting in the data
- Can be used for house calls

PASSIVE SYTEM

→ Cons:

- Some data might be missing due to hospital and out of hour data
- No Alternatives
- If too frequent alerts, might ignore them
- Can only be used when connected to the GP system (not good for house calls)

→ Pros:

- It won't miss high-risk patients/ the GPs don't have to remember to go and check
- It will save time

- Ask to card resort them again
- Ask at which stage they think the tool will be used

Design the outline

Script-Switch®:

- **Current template**

→ Pros

- GPs are familiar with it
- it might be easily adopted

→ Cons

- not all sections may be relevant for the *C.diff* tool
- no accept alternatives button

- **Custom C. diff template**

→ Pros

- customise the layout to what we need and to fit better to the *C.diff* tool requirement

→ Cons

- might confuse GPs and they might find a way to ignore or block the message

Design the specific feature

Script- Switch®:

- "Accept replacement" button options

→ Pros

→ Cons

- no accept button for alternative
- might annoy and confuse GPs if the button is replaced

Generally:

- The message (wording)
  - Should talk about benefit?
- The risk-score

Discuss about the different options

- 4 times VS 10 times (increase of the risk)
- Percentage (out of the general population)
- Low-high risk
- Graph

Conclusion: (10 minutes)

- After you choose to prescribe a 4C for a high-risk patient, would you like to have a section where it asks why you prescribed a 4C? yes/no? why?
- What do you this about the workshop?
- Which part did you like the most?
- Anything to be improved?
- How should the outcome of the project be communicated to the GPs?
- Would you recommend this tool for other prescribers?

Thank you!

Appendix F

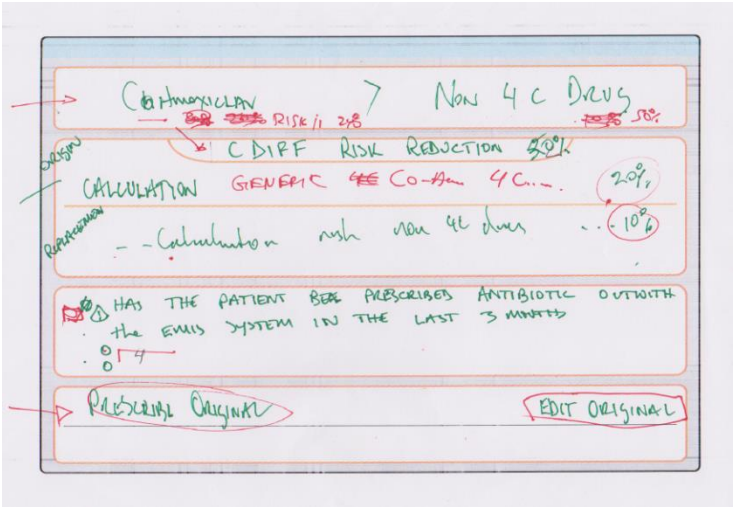


Figure C. Sketch of the CDI tool layout created by the GP during the co-design workshop

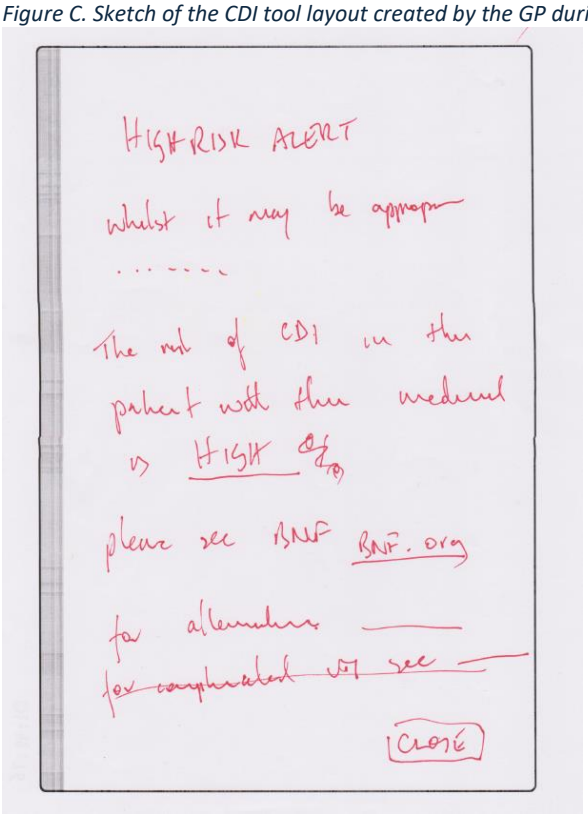


Figure D. Sketch of the high-risk alert pop up for the CDI tool, created by the GP during the co-design workshop

Appendix G

University of Strathclyde Science

STRATHCLYDE INSTITUTE OF PHARMACY & BIOMEDICAL SCIENCES

Ansu Joseph
Strathclyde Institute of Pharmacy and Biomedical Sciences
University of Strathclyde
Glasgow

3rd April 2019

Dear Ansu,

Ethical review of reseach project "development of a risk predictive tool for *Clostridium difficile*"

The above ethical review has been evaluated by the Departmental Ethics Committee and no concerning issues have been identified. Ethical approval is therefore confirmed.

Regards,

Dr Christopher Prior
Convenor, Departmental Ethics Committee
Strathclyde Institute of Pharmacy and Biomedical Sciences
University of Strathclyde
116 Cathedral Street
Glasgow
G4 0NR

(44) 141 548 2459
c.b.prior@strath.ac.uk

THE LEADERSHIP & MANAGEMENT AWARDS 2017 | Winner
THE AWARDS 2016 | WINNER
THE

Appendix H

Project title: Development of a risk predictive tool for *Clostridium difficile*

Project description:

The health-care-associated Clostridium difficile infection (CDI) is associated with significant morbidity and mortality and increased healthcare costs. One of the major factors associated with CDI is antibiotic prescribing, especially 4C antibiotics (e.g co-amoxiclav, clindamycin...).

In order to assist prescribers during antibiotic prescription, a risk prediction model has been developed to calculate patient's risk of CDI (based on some patient's demographic and clinical characteristics); hence identify patients at high risk of CDI.

So far, a website prototype of this risk predictive model has been created for secondary care and we would be seeking feedback on the tool's layout, ease of use, usability and preferences on the risk formats. Therefore we require volunteers to participate in a 30-45 minutes face to face interview to provide feedback on the generated prototype. The interviews can be conducted as one to one or as a focus group discussion.

Volunteers can be: Physicians and allied health professionals, who prescribe antibiotics.

Setting: Primary and secondary care.

If you would like to volunteer to participate in this study, please contact Ansu Joseph directly using the contact details below.

The volunteers will then be provided with an Information Sheet about the study and will be contacted by the researcher from the University of Strathclyde to arrange a suitable venue and time for the interview.

This programme is in collaboration with the Scottish Antimicrobial Prescribing Group (SAPG).

For more information about the study please contact:

Researcher Contact details:
Name: Ansu Joseph A.

Address: 27 Taylor Street,
Glasgow G4 0NR, Scotland.

Telephone: 07449825971
Email: ansu.joseph@strath.ac.uk

Academic supervisor details:
Name: Dr. Amanj Kurdi

Address: 27 Taylor Street,
Glasgow G4 0NR, Scotland.

Telephone: 141 548 2181
Email: amanj.baker@strath.ac.uk

Appendix I

Participant Information Sheet for Clinicians

Name of department: Strathclyde Institute of Pharmacy and Biomedical Sciences (SIPBS)
Title of the study: Development of a risk predictive tool for *Clostridium difficile*

Introduction: Who are we?

Researcher contact details:

Name: Ansu Joseph A.
Address: 27 Taylor Street, Glasgow G4 0NR, Scotland.
Telephone: 01415482367
Email: ansu.joseph@strath.ac.uk

Chief Investigator details:

Name: Dr. Amanj Kurdi
Address: 27 Taylor Street, Glasgow G4 0NR, Scotland.
Telephone: 0141 548 2181
Email: amanj.baker@strath.ac.uk

What is the purpose of this research?
Clostridium difficile infection (CDI) is associated with significant morbidity, mortality and increased healthcare costs. One of the major factor associated with CDI is antibiotic prescribing, especially 4C antibiotics (e.g. co-amoxiclav, clindamycin…).
In order to assist prescribers during antibiotic prescription, a risk prediction model has been developed to calculate the patient's risk of CDI. The model calculates the risk based on the patient's risk factor variables that can be extracted from the GPs patient data. Currently, a low fidelity prototype of this risk predictive model has been created through the engagement of 3 GP champions. This tool will allow prescribers, to identify high-risk patients to contract CDI and potentially reduce the incidence of CDI in Scotland.

The aim of this interview is to evaluate and obtain feedback on the prototype from clinicians and their general perception of the study. Feedback from end users is crucial to amend and improve the prototype in order to develop and implement a tool that can be easily adopted.

Do you have to take part?
Taking part in the study is entirely voluntary. If you agree to be interviewed I will ask you to sign a consent form and your participation will be anonymous. Refusing or withdrawing participation will not affect you or any aspects of your work.

What will you do in the project?
You will be interviewed by a trained researcher and audio recorded for analysis purposes. You will be presented with the low fidelity prototype and asked your views on it. This will be combined with semi-structured interview questions, where the researcher will have a set of open-ended questions to lead the discussion and you can add your professional experiences and opinions to influence the development of the tool. The questions will be about your general perception on CDI, the use of technology in your practice, your prescription process, feedback on the risk predictive prototype for

CDI and general perception of the CDI tool. The interview will take approximately 45 minutes (can be flexible based on your availability).

Why have you been invited to take part?
The risk predictive prototype was created with the participation of 3 GP champions. However, in order to create a digital tool that can be successfully adopted and implemented by prescribers, it is crucial to involve all potential end users, including other antibiotic prescribers such as physicians but also allied health professionals.

Although for the first stage of the project we focused on primary care, we are interested in exploring the potential implementation and feasibility of the tool in secondary care setting as the patient's first point of entry.

What information is being collected in the project?
In addition to the recordings made during the research activity, you will be asked to provide your demographic information for example your age, job role your location and your name as part of the consent process.

Who will have access to the information?
Data collected will be transcribed and the recordings will be anonymised.

Where will the information be stored and how long will it be kept for?
All data will be collected and stored on a remote (secure) University server in accordance with the provisions of the Data Protection Act 1998. The University of Strathclyde is registered with the Information Commissioner's Office who implements the Data Protection Act 1998. All personal data on participants will be processed in accordance with the provisions of the Data Protection Act 1998.

Thank you for reading this information – please ask any questions if you are unsure about what is written here.

Please also read our Privacy Notice for Research Participants

What happens next?
If you would like to find out more about the project please contact Ansu Joseph A. directly. If you decide to participate in an interview, you will be asked to sign a consent form. You're free to withdraw from the study at any moment without being disadvantaged in any way.
At the completion of the project if you wish to receive feedback on the outcomes, please talk with the researcher.

If you have any questions/concerns, during or after the research, or wish to contact an independent person to whom any questions may be directed or further information may be sought from, please contact:

Secretary to the University Ethics Committee, Research & Knowledge Exchange Services
University of Strathclyde, Graham Hills Building
50 George Street
Glasgow G1 1QE

Telephone: 0141 548 3707 / Email: ethics@strath.ac.uk

Appendix J

Consent Form for Clinicians

Name of department: Strathclyde Institute of Pharmacy & Biomedical Sciences (SIPBS)
Title of the study: Development of a risk predictive tool for *Clostridium difficile*

- I confirm that I have read and understood the Participant Information Sheet for the above project and the researcher has answered any queries to my satisfaction.
- I confirm that I have read and understood the Privacy Notice for Participants in Research Projects and understand how my personal information will be used and what will happen to it (i.e. how it will be stored and for how long).
- I understand that my participation is voluntary and that I am free to withdraw from the project at any time, up to the point of completion, without having to give a reason and without any consequences.
- I understand that I can request the withdrawal from the study of some personal information and that whenever possible researchers will comply with my request. This includes the following personal data:
    - audio recordings of interviews that identify me;
    - My personal information from transcripts.
- I understand that anonymised data (i.e. data that do not identify me personally) cannot be withdrawn once they have been included in the study.
- I understand that any information recorded in the research will remain confidential and no information that identifies me will be made publicly available.
- I consent to being a participant in the project.
- I consent to being audio recorded as part of the study.

(PRINT NAME)	
Signature of Participant:	Date:

Appendix K

Table A. comparison of interview questions from chapter 3 and first section of chapter 4

Introductory questions for chapter 4	Interview questions for chapter 3
1. Have you ever used a **risk predictive tool** in your practice?	Are there tools to guide your decision on anti-biotic prescription?
a. Do you **use** or find them **useful**?	Is the tool effective/useful?
b. On **which platform** are your current risk predictive tools? (mobile, computer etc..)	
2. Is C.diff a health care **burden** to you?	To what extend do you believe C.Diff is a public health issue for Scotland?
a. Can you **identify** a patient that might get C.diff with confidence?	How do you identify a patient in high risk of getting C.Diff?
b. Do you see **a lot of cases** of C.diff?	
c. When was the **last time** you saw a patient with C.diff?	
3. What's your perception on the **relationship between 4C antibiotics and C.diff?**	How often do you think about C.Diff when you have a patient with a possible infection?
a. Do all of them **result equally** towards contracting C.diff?	
b. Do you think the prescription of 4C antibiotics **is high in Scotland?**	In your opinion, do you think the unnecessary antibiotic prescription in Scotland is high?
c. Do you think **your prescribing does contribute** to an impact to C.diff?	Are there cases where a GP would prescribe 4Cs even if a patient is in high risk for C.Diff?
d. Do you think **primary care and secondary care**	

antibiotic prescribing has the same impact on C.diff?	
4. Would you like to have a tool that helps you **identify patients** that are at high risk to contract C.diff?	Would it be helpful if a tool could quantify a patient's risk of getting C.Diff?
a. What should the **tool inform** you?	What would you like a C.Diff decision support tool to inform you about?
b. Is the **patient data** in your system **accurate**?	Is your current patient data quality are good enough to support such tool?

Appendix L

CDI prototype CLINICIANS INTERVIEW SCHEDULE

Give introduction

INTRODUCTORY QUESTIONS

5. Have you ever used a **risk predictive tool** in your practice?
    a. Do you **use** or find them **useful**?
    b. On **which platform** are your current risk predictive tools? (mobile, computer etc..)

6. Is C.diff a health care **burden** to you?
    a. Can you **identify** a patient that might get C.diff with confidence?
    b. Do you see **a lot of cases** of C.diff?
    c. When was the **last time** you saw a patient with C.diff?

7. What's your perception on the **relationship between 4C antibiotics and C.diff**
    a. Do all of them **result equally** towards contracting C.diff?
    b. Do you think the prescription of 4C antibiotics **is high in Scotland**?
    c. Do you think **your prescribing does contribute** to an impact to C.diff?
    d. Do you think **primary care and secondary care** antibiotic prescribing has the same impact on C.diff?

8. Would you like to have a tool that helps you **identify patients** that are at high risk to contract C.diff?
    a. What should the **tool inform** you?
    b. Is the **patient data** in your system **accurate**?

Show the prototype

EASE OF USE

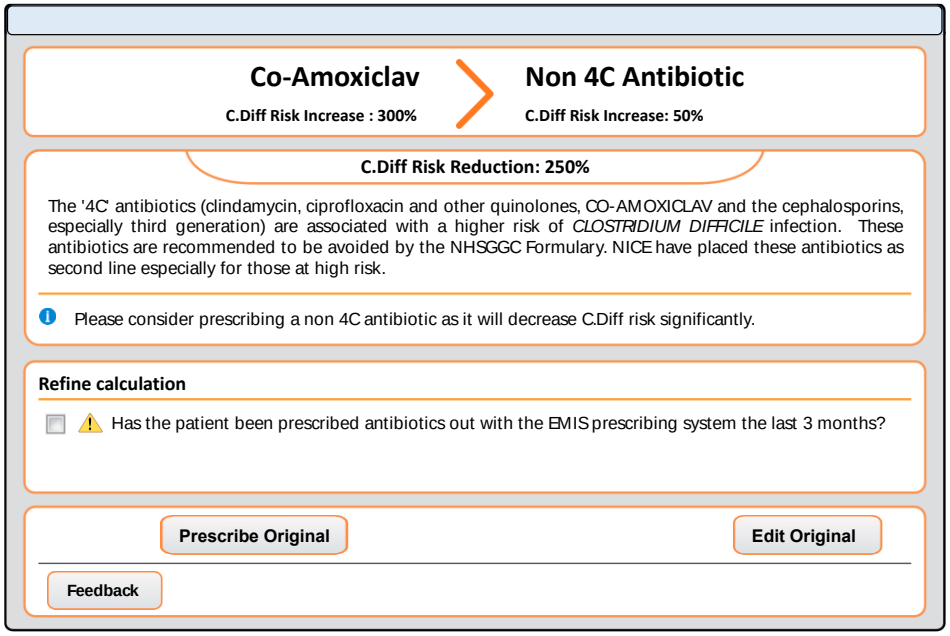
9. Do you think the tool showed to you could be **implemented** into your prescribing system?
    a. Would you prefer an active system in your setting?
10. Do you think it would be **easy for users to interact** with the tool? Especially the **refining calculation button**?
11. What **challenges** do you think there would be for you or other clinicians **to use** such a tool?

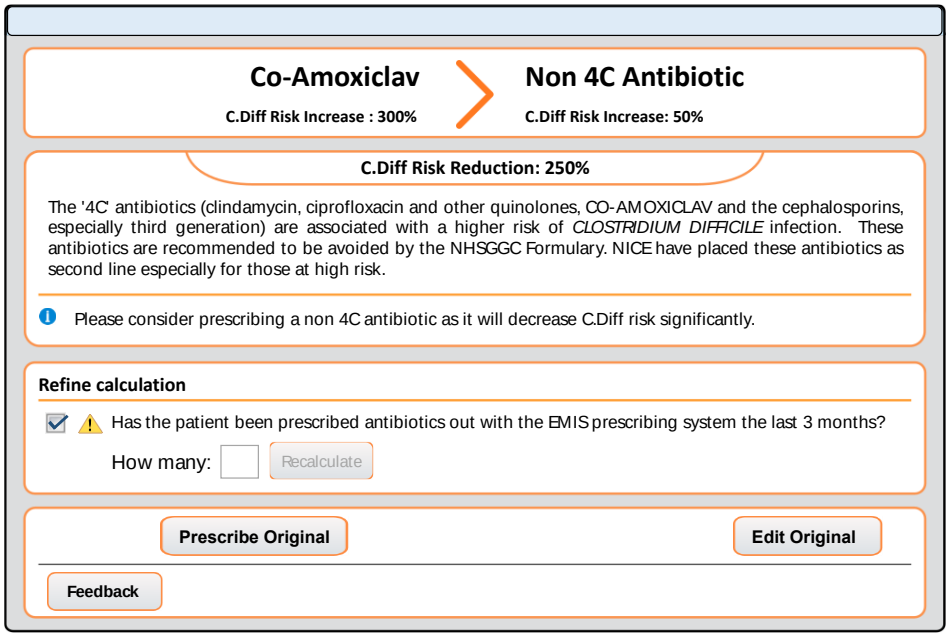
USEFULNESS

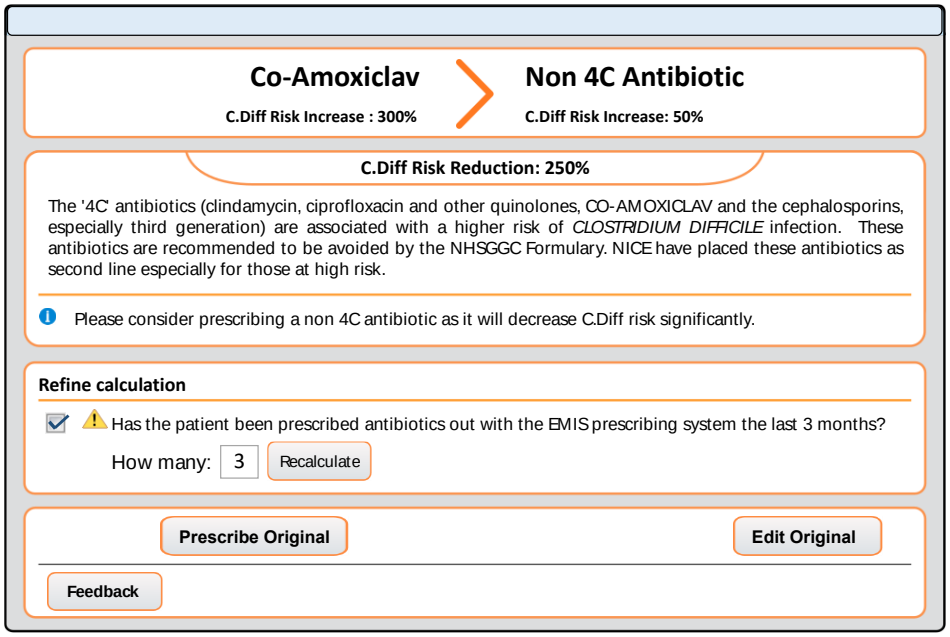
12. Is there a clear **benefit** in using the tool?
    a. Do you think the **message** provided through you is it **enough** for decision making?
    b. Is it **clear** to you why the tool provides the information for a **given patient**?
13. Do you think **everyone** in your department/setting would find this tool **useful**?
14. Is the **risk-score** delivered in an appropriate **mode**?
    a. If not, how would you like the **result** to be **displayed**? (Percentage, compared to baseline, high/medium etc..)
    b. Do you like the **layout** of the tool you just saw?
    c. Is it **appropriate** to use the **high risk pop-up** for prioritizing high risk patients?
    d. Is there **any part of the layout** that you would change?

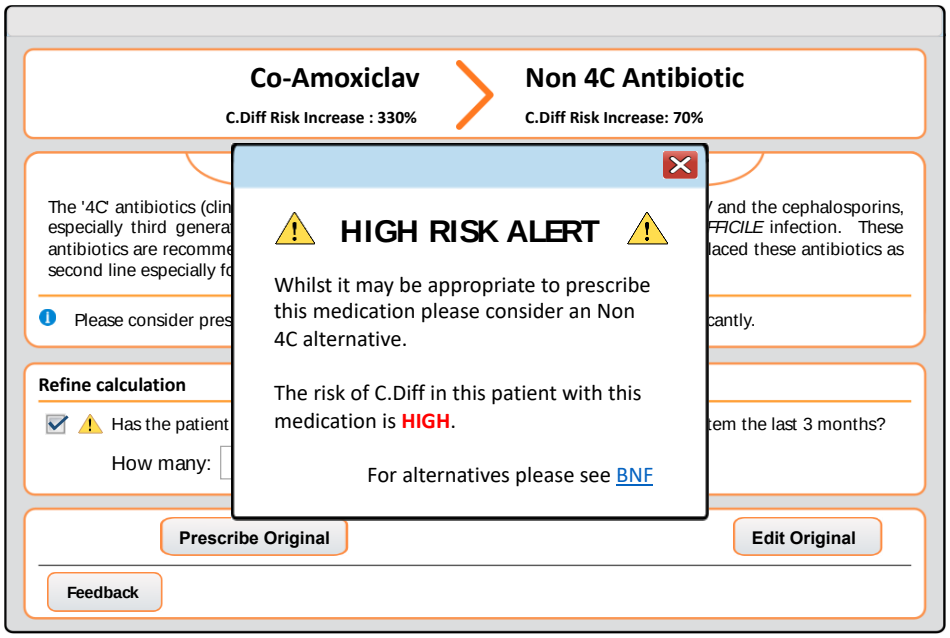
Appendix M

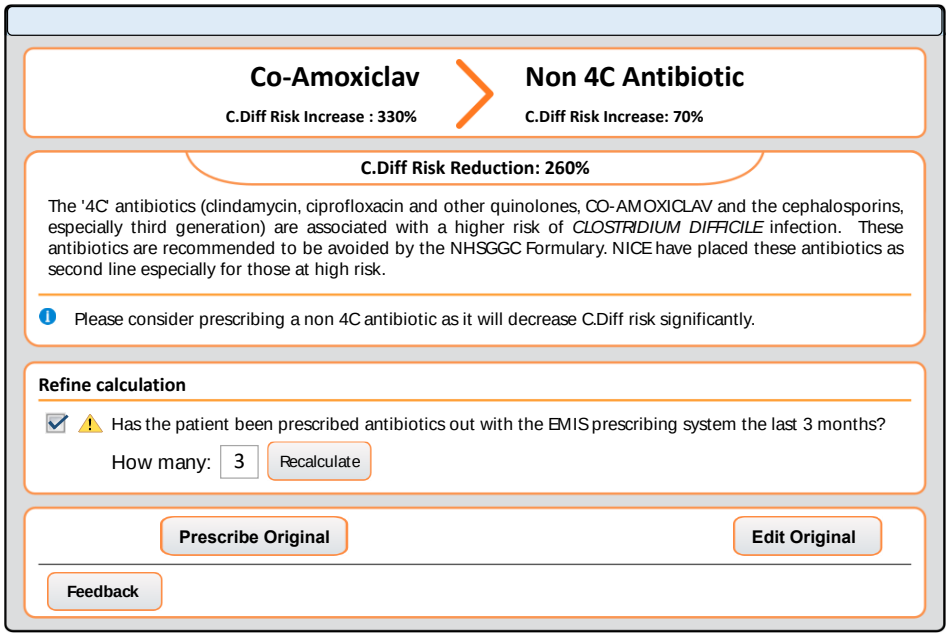
Prototype 1



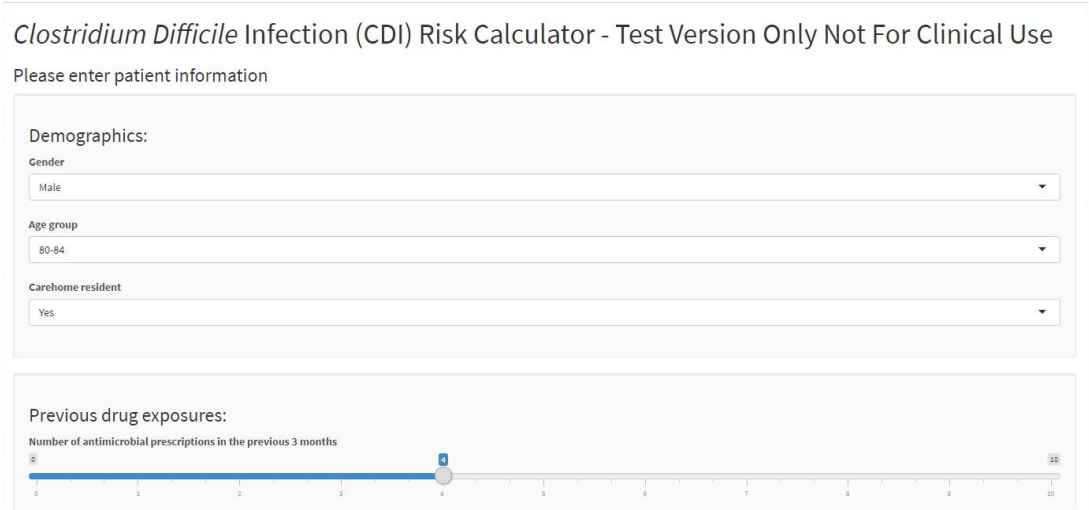



Co-Amoxiclav
C.Diff Risk Increase : 300%
Non 4C Antibiotic
C.Diff Risk Increase: 50%
C.Diff Risk Reduction: 250%
The '4C' antibiotics (clindamycin, ciprofloxacin and other quinolones, CO-AMOXICLAV and the cephalosporins, especially third generation) are associated with a higher risk of CLOSTRIDIUM DIFFICILE infection. These antibiotics are recommended to be avoided by the NHSGGC Formulary. NICE have placed these antibiotics as second line especially for those at high risk.
Please consider prescribing a non 4C antibiotic as it will decrease C.Diff risk significantly.
Refine calculation
Has the patient been prescribed antibiotics out with the EMIS prescribing system the last 3 months?
How many: 3
Recalculate
Prescribe Original
Edit Original
Feedback

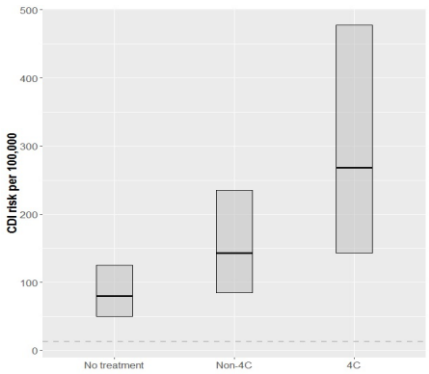

Co-Amoxiclav
C.Diff Risk Increase : 330%
Non 4C Antibiotic
C.Diff Risk Increase: 70%
HIGH RISK ALERT
Whilst it may be appropriate to prescribe this medication please consider an Non 4C alternative.
The risk of C.Diff in this patient with this medication is HIGH.
For alternatives please see BNF
Refine calculation
How many:
Prescribe Original
Edit Original
Feedback


Co-Amoxiclav
C.Diff Risk Increase : 330%
Non 4C Antibiotic
C.Diff Risk Increase: 70%
C.Diff Risk Reduction: 260%
The '4C' antibiotics (clindamycin, ciprofloxacin and other quinolones, CO-AMOXICLAV and the cephalosporins, especially third generation) are associated with a higher risk of CLOSTRIDIUM DIFFICILE infection. These antibiotics are recommended to be avoided by the NHSGGC Formulary. NICE have placed these antibiotics as second line especially for those at high risk.
Please consider prescribing a non 4C antibiotic as it will decrease C.Diff risk significantly.
Refine calculation
Has the patient been prescribed antibiotics out with the EMIS prescribing system the last 3 months?
How many: 3
Recalculate
Prescribe Original
Edit Original
Feedback

Prototype 2


Clostridium Difficile Infection (CDI) Risk Calculator - Test Version Only Not For Clinical Use
Please enter patient information
Demographics:
Gender
Male
Age group
80-84
Carehome resident
Yes
Previous drug exposures:
Number of antimicrobial prescriptions in the previous 3 months

Bar chart with Confidence intervals:



*Grey dashed line shows the CDI population rate for this age and gender group

CDI risk for this patient in the following one year is 7119 per 100,000 (95% confidence interval (CI): 3238-14604 per 100,000). Compared to the CDI risk of the general population with same age and gender of 41 per 100,000, this patient 175.1 times more likely to develop CDI in the following year. (Risk ratio = 175.1, 95% CI: 79.6-359.1)

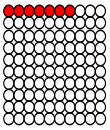
Prescribing one course of non-4C antibiotics to this patient will increase the CDI risk in the following year to 12338 per 100,000 (95% CI: 5404-25604 per 100,000). Compared to no antibiotic, prescribing one more course of non-4c antibiotics makes this patient 1.7 times more likely to develop CDI in the following year. (Risk ratio = 1.7, 95% CI: 1.6-1.9)

Prescribing one course of 4C antibiotics to this patient will increase the CDI risk in the following year to 21894 per 100,000 with (95% CI: 9140-44573 per 100,000). Compared to no antibiotic, prescribing one course of 4c antibiotics makes this patient 3.1 times more likely to develop CDI in the following year. (Risk ratio = 3.1, 95% CI: 2.6-3.5)

Population diagram:

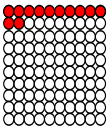
No antibiotic (Baseline): The risk of contracting CDI in the following year is **7%**
In other words, in a population of 100 people with the same risk factors as this patient, 7 people are likely to develop CDI in the following year. The average risk of a male aged 80-84 years is 0.041%

What does this mean?



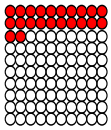
If you prescribe no antibiotics:
Compared to the general population with the same age and gender, this patient is 175.1 times more likely to develop CDI.

Non-4C antibiotics: If you prescribe a non-4C antibiotic to this patient, the CDI risk will increase to 12% making the patient 1.7 times more likely to develop CDI compared to no antibiotic prescribing.



If you prescribe non-4C antibiotics:
Compared to the baseline, this patient will be 1.7 times more likely to develop CDI in the following year

4C antibiotics: If you prescribe a 4c antibiotic to this patient, the CDI risk will increase to 22% making the patient 3.1 times more likely to develop CDI compared to no antibiotic presc



If you prescribe 4C antibiotics:
Compared to the baseline, this patient will be 3.1 times more likely to develop CDI in the following year.

Appendix N

Risk prediction tool's outcome communication

Risk prediction tools have been introduced into the health care system in order to enhance and improve the patient care delivery. The use of risk prediction tool for a different range of diseases have been highly used for the prevention, diagnosis or for treatment. There are two main types of risk prediction tools, for the screening of future disease development of asymptomatic and symptomatic people (Usher-Smith et al., 2015). These prediction tools are created through the incorporation of multifactorial models or algorithms that incorporate the relevant risk factors or variables (Dent et al., 2012). These risk factors can be carrying from age to genetic biomarkers (Dent et al., 2012) in order to provide with a risk score for the development of a certain disease. The use of risk prediction tools can be beneficial for the patient treatments choice since different risks and benefit are associated with different treatments (Thomson et al., 2005) but also reduce unnecessary health costs (Dent et al., 2012). Through the use of risk tools, shared decision making has become more popular, where the patient and the consultant, discuss the treatment choice's risk and benefit to choose the most appropriate therapy (Feldman-Stewart et al., 2000; Thomson et al., 2005). There is currently a different range of risk communication, however clinicians often find many not reliable or not informative enough for decision making. Also many studies have reported the difficulties patients face to understand and read the risk estimates during shared decision consultations (Feldman-Stewart et al., 2000; Waters et al., 2006). Since a great number of risk prediction tools have been developed and are available to be used, the tools utility and ease of risk estimation has to be considered during the development of the tool. Therefore the aim of this paper is to assess the currently available risk score communications and discuss the advantage and disadvantage of each approach, and also determine the suitable ones for the CDI risk prediction tool.

Numerical risk estimation

Risk prediction tool can estimate the risk in different formats such as percentage, frequency, risk labels, or through graphs. Depending on the purpose of the tool, different risk estimation is used. Controversies arise when the reliability and comprehensiveness of the risk estimation is doubted.

Studies have suggested the use of percentage as the most comprehensive format (Sinayev et al., 2015), however its appropriate risk perception was also discussed (Thomson et al., 2005). In a study Hoffrage et al. conducted, where he assessed the risk compression of physicians using probabilities and frequencies, only 10% of the physicians were able to provide the right answer using probability, while 46% of the physicians were able to provide the correct answer using frequency. Also it was noted that 25% of more time was required to answer the problem using probability (Hoffrage & Gigerenzer, 1998). The use of probabilities and percentage is very common in health counselling sessions however percentage can be misleading (Hoffrage et al., 2000). Contrary natural frequencies have been shown to be less misleading and more comprehensive. In 1995, a report stating that women who took a particular contraceptive pill had 100% chance to form thromboembolism, which stopped many women to stop taking the

pill causing several unwanted pregnancies that lead to abortion. What the report meant was that among 14,000 women who didn't take the pill, 1 had the thromboembolism, while out of 14,000 women who took the pill, the diseases increased from 1 person to two people, causing the relative increase of 100% (Kurz-Milcke, Gigerenzer, and Martignon 2008). This suggests in order to avoid misinterpretation, messages showing relative risk should be avoided. For instance the risk communication using " 5 out of 100 or out of 100 people like you 5 will have a stroke in 12 months" is less prone for misinterpretation than "you have 5% of risk to get a stroke in 12 months"(Thomson et al., 2005).

For the use of verbal risk estimates, there is very little evidence and there is concern for different interpretation from person to person. The use of verbal risk estimates such as "high, medium and low", can cause struggle in understanding the true risk, since in different risk predictions it can portray different value and risk. Therefore the use of verbal risk estimates is not recommended, hence, it won't be suggested to be used for this study. (Edwards et al., 1996; Thomson et al., 2005)

Graphical risk estimation

Graphical risk estimation, is the representation of risk using bar charts, pie charts, population diagrams or other forms of visual image. The use of graphical representation of risk, was highly appreciated and suggested that it helps to communicate the risk better than numerical formats (Waters et al., 2006). Risk bars charts can be used to highlight and compare the risk a patient has following the use of different treatments correlated to the current risk. Figure 1, illustrates the risk a patient has, in cases where, no antibiotic, non-4C antibiotic and 4C antibiotic is prescribed. The bar chart suggests which treatment causes the patient to be at high risk to contract *Clostridium difficile* infection (CDI), which can be used as an aid during the treatment choice. Although, graphical risk estimation is been generally appreciated and can be easily compered (Thomson et al., 2005), it has been criticised as well, stating that if not presented in the correct format, they can be as misleading as the numerical risk estimation (Kurz-Milcke et al., 2008).

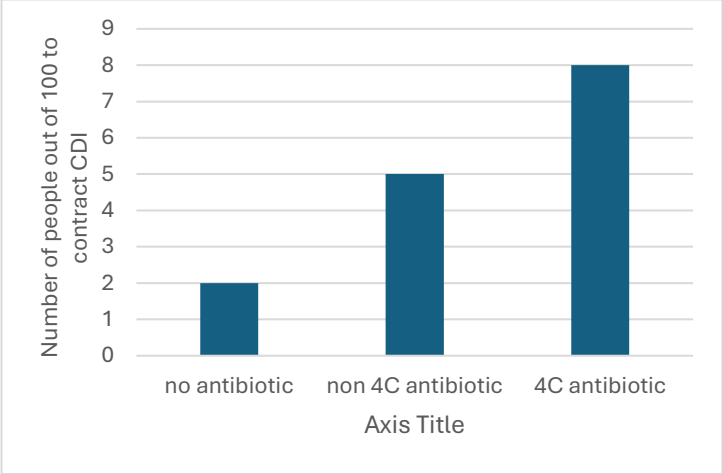


Figure E. Risk for the patient to contract CDI, if no antibiotic, non-4C antibiotic and 4C antibiotics consumed. Risk represented in bar chart.

Population diagrams represents the risk using the population as an analogue, where each circle performs as an individual. Population diagrams can show the risk a person has compared with a set number of the population (e.g 100, 1000, 10000) that have similar risk factors. This type of diagrams are used mostly to predict the event of risk in the nearer or further future (e.g in 12 months, 15 years). As it can be seen in Figure F, it illustrates, the risk a woman to have breast cancer in 15 years compared to the baseline population of 100 people with similar risk factors. The black circles in the graph on the right show, the number of women that will form cancer in 15 years compared to the healthy women (white circles). This diagram is also the visual representation of natural frequency discussed earlier "5 women in 100 will have breast cancer in the next 15 years". The use of population diagrams has shown to communicate risk in greater manner than bar charts or other forms (Dolan & Iadarola, 2008; Kurz-Milcke et al., 2008). However, through a single population diagram it is not possible to compare the risk a patient has using different treatments, like it can be seen in the bar chart. In order to demonstrate the risk different treatments have, different population diagrams have to be displayed, which can lead the risk comprehension to take longer.

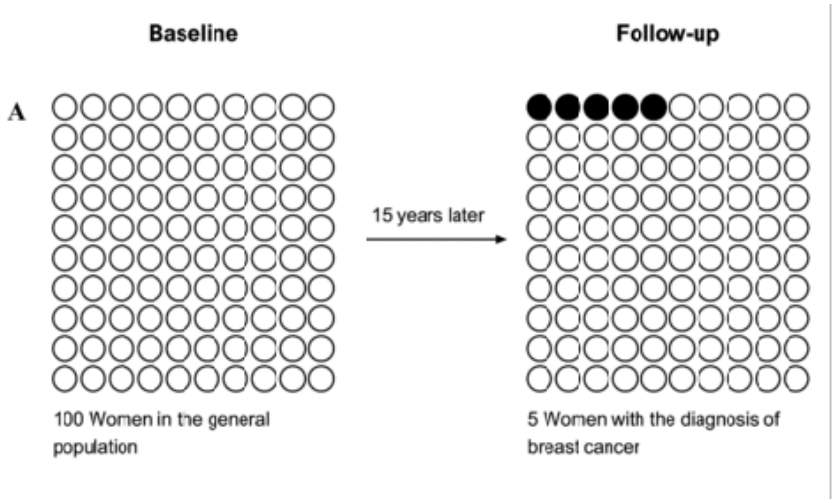


Figure F. Population diagram representing, the risk to have breast cancer in 15 years in a population of 100 women. (Kurz-Milcke et al., 2008)

The risk ladder has been used to inform the risk or diagnose a person for a certain disease using estimates such as low at the bottom and high the top of a risk ladder. People that have less numerical literacy find such a ladder useful and compressive to understand the risk for a given disease (Keller et al., 2009). However, it can be less informative than the population diagram, since a natural frequency for a disease cannot be assessed. Clinicians might not find such method reliable since it doesn't provide enough information to diagnose a person with a disease or help with the choice of treatment with certainty. Also, in order to use the risk ladder numerical risk cut offs have to be determined, which can differ from tool to tool, leading confusion and not preferred by clinicians. The combination of numerical format with the risk ladder can be seen as more informative, however as for the population diagram, the risk ladder will not provide risk a patient has for different treatment choices.

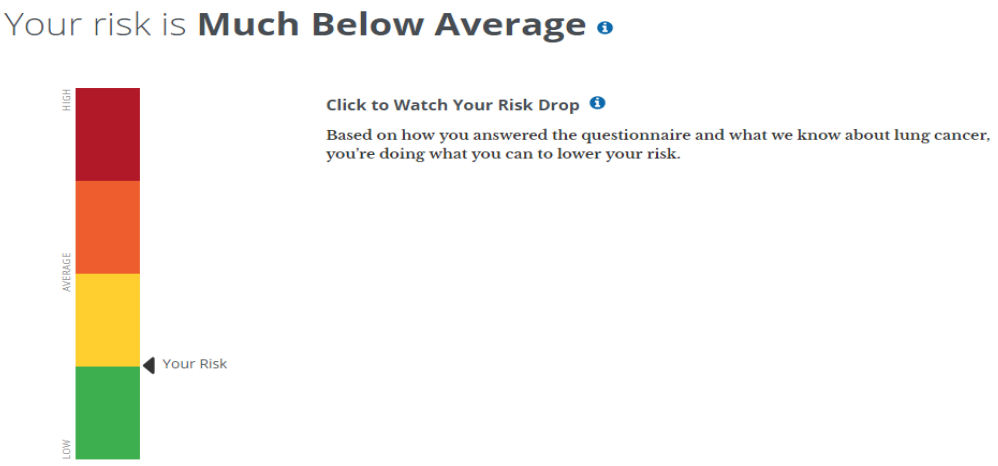


Figure G. Risk ladder, for lung cancer (*Your Disease Risk - Prevention - Siteman Cancer Center*, n.d.)

Risk estimation options for the CDI tool

Risk prediction can be a great aid to use for treatment choice, disease diagnosis or for prevention of a future disease. During the development of a risk prediction tool, the target of use and potential end users profile has to be taken into consideration. One of the major advantage of using a risk prediction is the shared decision taking between the consultant and the patients, which provides the patient to have a better understanding of the treatment choice, its risks and benefits. Depending on the risk prediction target and end users profile, the tool has to be designed in a manner that it accomplishes its purpose and is comprehensive.

The risk prediction tool for *Clostridium difficile* aims to provide the risk a given person has, depending on the choice of antibiotic. The mathematical model has been designed to provide a risk for the following cases: risk score when no antibiotic has been prescribed, non-4C antibiotic and 4C antibiotic has been prescribed. The tool aims to alert clinicians that are considering the prescription of 4C antibiotic, which leads the risk increase to contract CDI following the prescription. Therefore, using such a tool could help clinicians during the treatment choice.

From the analysis of the above described risk estimates, it seems that, natural frequencies are preferred over the risk estimation as percentage, since it provide a more transparent risk estimation. From the literature it was also seen that, the use of graphical risk estimation was preferred since it can be more comprehensive for patients that are part of shared decision making. Although different types of graphical presentations are available, not all of them can be used for this risk prediction tool. In order to compare the risk a patient has with the use of different treatment choice, the most illustrative graph is the bar chart. The population diagram, can also be used, however in order to demonstrate the risk a patient has for three different treatment choices, three population diagrams have to be used and displayed. Also several studies have demonstrated the risk communication using combined estimates with greater comprehension and reliability to the risk (Dolan & Iadarola, 2008; Janssen et al., 2018; Waters et al., 2006). Therefore for the *Clostridium difficile* tool the use of numerical and graphical combination is suggested. The suggested formats are using the natural frequency in combination of bar chart or population diagrams.

Example of natural frequency and bar chart:

The risk a 70 year old patient to contract CDI within the next 12 months is:
With no treatment 2 out of 100
With non-4C antibiotic 5 out of 100
With 4C antibiotic 8 out of 100

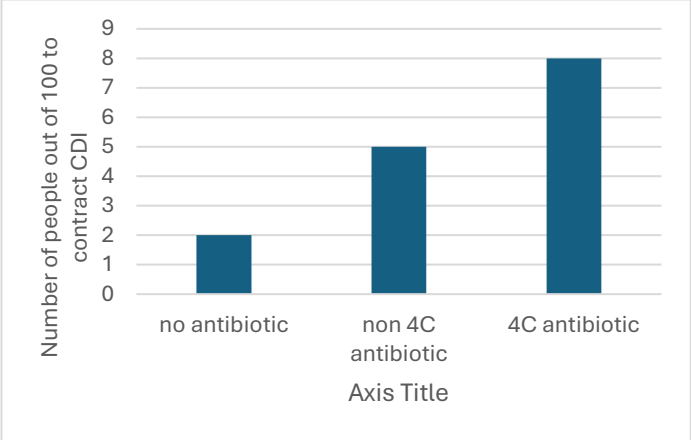
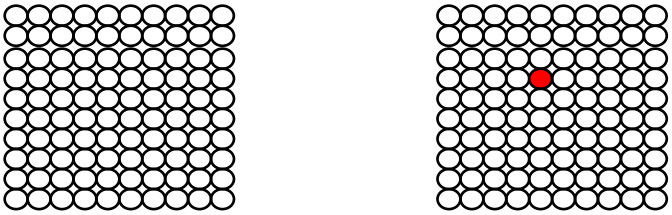


Figure H. Example of combination of natural frequency and bar chart for the CDI tool

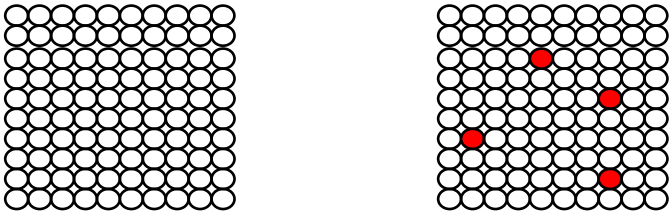
Example of natural frequency and population diagram:

The risk a 70 year old patient to contract CDI within the next 12 months is:

With no treatment 1 out of 100



With non-4C antibiotic 4 out of 100



With 4C antibiotic 12 out of 100

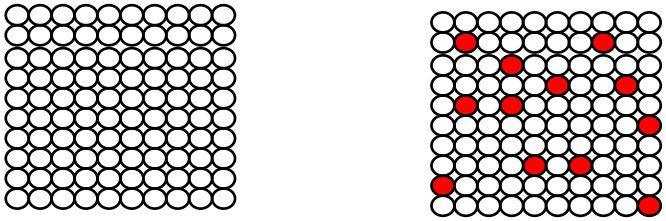


Figure J. Example of combination of natural frequency and population diagram for the CDI tool

Appendix O

CDI risk predictor focus group discussion schedule

10 minutes

Note: To the entire group of participants

1. Give introduction about the project, give information sheet and consent forms
2. Show the prototype on a PowerPoint presentation
3. Split the group into two (7-9 people each)
4. Provide the link of the tool to all the participants
5. Provide a case scenario and ask the participants to use the tool on their phone (in pairs if no phone) and ask to insert the provided variables and calculate the risk for CDI.

Group 1

20 minutes

On PPT show the labelling of the comorbidities and ask the following questions to the group

1. Is the labelling for the comorbidities clear?

   PROMT: When you see the label, which diseases do you think it includes?

Show the information/ definition section of each comorbidities (Show as PPT)

PROMT: When you saw the comorbidities labelling earlier did you think it would include these diseases?

PROMT: is there anything else you would add or remove in the definition/ information section to explain better the comorbidities?

Show the longer list of descriptions by ICD code)

PROMT: Which listing do you think better describes the comorbidities labelling

2. Is there anything about the layout you would change?

   PROMT: colour?

   PROMT: variable selection format (drop down, tapping yes/no)

   PROMT: Result format?

   PROMT: is the graph understandable?

   PROMT: Is there too much text?

   PROMT: Do you like the numeric presentation?

PROMT: would you change anything about the numeric presentation? Or is there another format you prefer?

PROMT: could you tell me what you understand from these graphs and text for this particular patient?

PROMT: do you have a preference on the result format?

PROMT: do you prefer the bar chart or the population chart?

PROMT: do you think both format should be included or neither of them? Why?

3. Do you think introducing this tool can be useful to have an impact in reducing 4C antibiotics or unnecessary antibiotic prescribing? Why? Why not?

4. What are the two things you most like about the tool?
5. What are the two things you would most like to change about the tool?
6. Is there any other comment you would like to add?

Group 2

20 minutes

Circulate the questionnaire (Attached as Ansu CDI questionnaire) and ask the participants to complete it.

Once completed collect the questionnaire and ask the following questions.

1. Do you think introducing this tool can be useful to have an impact in reducing 4C antibiotics or unnecessary antibiotic prescribing? Why? Why not?

2. What are the two things you most like about the tool?
3. What are the two things you would most like to change about the tool?
4. Is there any other comment you would like to add?

Note: To all participants of both groups

Ask if they would be interested in participating in further testing of the tool and if yes collect their contact details

Appendix P

Survey statements on the CDI risk predictor

Date: _____
Name: _____
Role: _____

	Totally disagree	Disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Agree	Totally agree
Targeting the reduction of CDI in Scotland is important	☐	☐	☐	☐	☐	☐	☐
Reduction of 4C antibiotics prescribing in primary care is important	☐	☐	☐	☐	☐	☐	☐
Reduction of 4C antibiotics prescribing in secondary care is important	☐	☐	☐	☐	☐	☐	☐
The tool can be useful to support clinicians during antibiotic prescribing	☐	☐	☐	☐	☐	☐	☐
Using the tool can facilitate antibiotic decision making	☐	☐	☐	☐	☐	☐	☐
The tool can be added to the existing workload	☐	☐	☐	☐	☐	☐	☐
The tool can be added to the existing workflow	☐	☐	☐	☐	☐	☐	☐
The patient data required for the tool is easily available	☐	☐	☐	☐	☐	☐	☐
The tool is relevant	☐	☐	☐	☐	☐	☐	☐
The tool's result as a bar chart is understandable	☐	☐	☐	☐	☐	☐	☐

	Totally disagree	Disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Agree	Totally agree
The tool's result as a population chart is understandable	☐	☐	☐	☐	☐	☐	☐
There will be no difficulties in explaining the results to the patients	☐	☐	☐	☐	☐	☐	☐
The time and tasks required for the tool doesn't seem extensive	☐	☐	☐	☐	☐	☐	☐
The tool doesn't require extensive training	☐	☐	☐	☐	☐	☐	☐
Training could improve the overall interaction with the tool	☐	☐	☐	☐	☐	☐	☐
The tool is easy to use	☐	☐	☐	☐	☐	☐	☐
The tool can be used regularly	☐	☐	☐	☐	☐	☐	☐
I would use the tool	☐	☐	☐	☐	☐	☐	☐
Colleagues could influence my decision to use the tool	☐	☐	☐	☐	☐	☐	☐

Appendix Q

Participant Information Sheet for Clinicians

Name of department: Strathclyde Institute of Pharmacy and Biomedical Sciences (SIPBS)
Title of the study: Development of a risk predictive tool for *Clostridium difficile*

Introduction: Who are we?

Researcher contact details:

Name: Ansu Joseph A.
Address: 27 Taylor Street, Glasgow G4 0NR, Scotland.
Telephone: 01415482367
Email: ansu.joseph@strath.ac.uk

Chief Investigator details:

Name: Dr. Amanj Kurdi
Address: 27 Taylor Street, Glasgow G4 0NR, Scotland.
Telephone: 0141 548 2181
Email: amanj.baker@strath.ac.uk

What is the purpose of this research?
Clostridium difficile infection (CDI) is associated with significant morbidity, mortality and increased healthcare costs. One of the major factor associated with CDI is antibiotic prescribing, especially 4C antibiotics (e.g. co-amoxiclav, clindamycin…).
In order to assist prescribers during antibiotic prescribing, a risk prediction model has been developed to calculate the patient's risk of CDI. The model calculates the risk based on the patient's risk factor variables that can be extracted from the patient data. Currently, a simulation version of this risk predictive model has been created through the engagement of clinicians. This tool will allow prescribers, to identify high-risk patients to contract CDI and potentially reduce the incidence of CDI in Scotland.

The aim of this focus group is to evaluate and obtain feedback on the prototype from clinicians and their general perception of the study. Feedback from end users is crucial to amend and improve the prototype in order to develop and implement a tool that can be easily adopted.

Do you have to take part?
Taking part in the study is entirely voluntary. If you agree to be of the focus group I will ask you to sign a consent form and your participation will be anonymous. Refusing or withdrawing participation will not affect you or any aspects of your work.

What will you do in the project?
You will be part of a focus group with other health professionals. The study will be guided by a trained researcher and audio recorded for analysis purpose. You will be presented with the simulation version and asked your view on it. The purpose of the focus group is to share your opinion and discuss with the other participants the topics presented by the researcher. This will be combined with semi-structured interview questions and a questionnaire where the researcher will have a set of open-ended questions to lead the discussion and you can add your professional experiences and opinions to influence the development of the tool. The questions will be about your general perception on CDI, the use of technology in your practice, your prescription process, and feedback on the risk predictive prototype for CDI. The focus group will take approximately 45 minutes.

Why have you been invited to take part?
The risk predictive prototype was created with the participation of 3 GP champions. However, in order to create a digital tool that can be successfully adopted and implemented by prescribers, it is crucial to involve all potential end users, including other antibiotic prescribers such as more physicians and allied health professionals.

Although for the first stage of the project we focused on primary care, we are interested in exploring the potential implementation and feasibility of the tool in secondary care setting as the patient's first point of entry.

What information is being collected in the project?
In addition to the recordings made during the research activity, you will be asked to provide your demographic information for example your age, job role your location and your name as part of the consent process.

Who will have access to the information?
Only Ansu Joseph A. and her supervisor Dr. Amanj Kurdi will have access to the data. For transcribing and validation reasons the researchers might ask other researchers to go through the interview recordings and transcription, however everything will be completely anonymised.

Where will the information be stored and how long will it be kept for?
All data will be collected and stored on a remote (secure) University server in accordance with the provisions of the Data Protection Act 1998. The University of Strathclyde is registered with the Information Commissioner's Office who implements the Data Protection Act 1998. All personal data on participants will be processed in accordance with the provisions of the Data Protection Act 1998.

Thank you for reading this information – please ask any questions if you are unsure about what is written here.

Please also read our Privacy Notice for Research Participants (See next page)

What happens next?
If you would like to find out more about the project please contact Ansu Joseph A. directly. If you decide to participate in a focus group, you will be asked to sign a consent form. You're free to withdraw from the study at any moment without being disadvantaged in any way.
At the completion of the project if you wish to receive feedback on the outcomes, please talk with the researcher.

If you have any questions/concerns, during or after the research, or wish to contact an independent person to whom any questions may be directed or further information may be sought from, please contact:

Secretary to the University Ethics Committee, Research & Knowledge Exchange Services
University of Strathclyde, Graham Hills Building
50 George Street
Glasgow G1 1QE

Telephone: 0141 548 3707 / Email: ethics@strath.ac.uk

Privacy Notice for Participants in Research Projects

Introduction
The University of Strathclyde is committed to transparency and to complying with its responsibilities under data protection legislation. This privacy notice sets out important information regarding how we use your information and your rights under the legislation. This privacy notice relates to individuals participating in research projects led by the University of Strathclyde. Please note that this standard information should be considered alongside information provided by the researcher for each project, which is usually in the form of a Participant Information Sheet (PIS). The PIS will include further details about how personal information is processed in the particular project, including: what data is being processed; how it is being stored; how long it will be retained for, and any other recipients of the personal information. It is usually given to participants before they decide whether or not they want to participate in the research.
Data controller and the data protection officer
The University of Strathclyde is the data controller under data protection legislation. This means that the University is responsible for how your personal data is used and for responding to any requests from you in relation to your personal data. Any enquiries regarding data protection should be made to the University's Data Protection Officer at dataprotection@strath.ac.uk.
Legal basis for processing your personal information
If you are participating in a research project, we may collect your personal information. The type of information that we collect will vary depending on the project. Our basis for collecting this information is outlined below:

Type of information	**Basis for processing**
Personal information and associated research data collected for the purposes of conducting research.	It is necessary for the performance of a task carried out in the public interest.
Certain types of personal information such as information about an individual's race, ethnic origin, politics, religion, trade union membership, genetics, biometrics (where used for ID purposes), health, sex life, or sexual orientation are defined as 'Special Category' data under the legislation.	It is necessary for the performance of a task carried out in the public interest and It is necessary for scientific or historical research purposes in accordance with the relevant legislation (Data Protection Act 2018, Schedule 1, Part 1, Para 4).

Criminal conviction / offence data	It is necessary for the performance of a task carried out in the public interest and is processed in accordance with Article 10 of the General Data Protection Regulation and the Data Protection Act 2018, Schedule 1, Part 1, Para 4.

Details of transfers to third countries and safeguards

For some projects, personal information may be processed outside the EU. This will normally only be done when research is taking place in locations outside the EU. If this happens, the University will ensure that appropriate safeguards are in place. You will be fully informed about any transferring of data outside the EU and associated safeguards, usually in the Participant Information Sheet.

Sharing data

If data will be shared with other individuals or organizations, you will be advised of this in the PIS.

Retention of consent forms

If you participate in a research project, you may be asked to sign a participant consent form. Consent forms will typically be retained by the University for at least as long as the identifiable research data are retained. In most cases they will be retained for longer, the exact time frame will be determined by the need for access to this information in the unfortunate case of an unanticipated problem or a complaint. 5 years after the research is completed will be suitable for many projects, but beyond 20 years will be considered for any longitudinal or 'high risk' studies involving children, adults without capacity or a contentious research outcome.

Data subject rights

You have the right to: be informed about the collection and use of your personal data; to request access to the personal data we hold about you; you are entitled to request to have personal data rectified if it is inaccurate or incomplete; you have the right to request to object to your data being processed and you can request to restrict the processing of your personal information. To exercise these rights please contact dataprotection@strath.ac.uk.

However, please note - in some research projects, it may **not be** possible to provide these rights because doing so would prevent or seriously impair the achievement of the research purpose. For instance, if you are participating in a focus group with multiple participants, if the research has progressed to a later stage of analysis, or findings have been published, it may not be possible to remove any one individual's personal data without having an adverse effect on the entire dataset.

Right to complain to supervisory authority

If you have any concerns/issues with the way the University has processed your personal data, you can contact the Data Protection Officer at dataprotection@strath.ac.uk. You also have the right to lodge a complaint against the University regarding data protection issues with the Information Commissioner's Office (https://ico.org.uk/concerns/).

Appendix R

Consent Form for Clinicians

Name of department: Strathclyde Institute of Pharmacy & Biomedical Sciences (SIPBS)
Title of the study: Development of a risk predictive tool for *Clostridium difficile*

- I confirm that I have read and understood the Participant Information Sheet for the above project and the researcher has answered any queries to my satisfaction.
- I confirm that I have read and understood the Privacy Notice for Participants in Research Projects and understand how my personal information will be used and what will happen to it (i.e. how it will be stored and for how long).
- I understand that my participation is voluntary and that I am free to withdraw from the project at any time, up to the point of completion, without having to give a reason and without any consequences.
- I understand that I can request the withdrawal from the study of some personal information and that whenever possible researchers will comply with my request. This includes the following personal data:
    - audio recordings of interviews that identify me;
    - My personal information from transcripts.
- I understand that anonymised data (i.e. data that do not identify me personally) cannot be withdrawn once they have been included in the study.
- I understand that any information recorded in the research will remain confidential and no information that identifies me will be made publicly available.
- I consent to being a participant in the project.
- I consent to being audio recorded as part of the study.

(PRINT NAME)	
Signature of Participant:	Date:

Clinician Demographic Information

What is your job role? (Select one):

- ☐ Physician
- ☐ Pharmacist
- ☐ Nurse
- ☐ Other: _____

In which setting do you work?

- ☐ Primary care
- ☐ Secondary care
- ☐ Other:_____

Are you an independent prescriber?

- ☐ Yes
- ☐ No

Are your patients:

- ☐ Inpatients
- ☐ Outpatients
- ☐ Not applicable

In what area do you work?

_____

What is your age? _____

What is your gender?

- ☐ Male
- ☐ Female
- ☐ Other
- ☐ Prefer not to say

How many years have you been in your current job role? _____

Where is your main place of work? (Please enter the name of the hospital / clinic you mainly work from)

_____

The End