Pharmacist Involvement in Preventing Antimicrobial-Associated Diarrhea: Microbial Insights, Clinical Laboratory Interventions, Challenges and Barriers

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Abstracts

Antimicrobial-associated diarrhea is one of the major side effects of antibiotic therapy resulting from disruption of the gut microbiome and the overgrowth of pathogenic bacteria, such as Clostridium difficile. This is not only a danger to patients' health but also to the global challenge of antimicrobial resistance. Pharmacists are therefore placed to minimize risks through their active participation in antimicrobial stewardship programs, education of patients, and clinical intervention. This paper considers the multifaceted roles that pharmacists have, which include optimizing the use of antibiotics, campaigning for probiotics, and counseling on risks and managing AAD. However, there are also several challenges, such as little involvement in stewardship programs, knowledge gaps, and resource constraints. The barriers mentioned above need to be addressed to maximize their contributions. Indeed, application of pharmacogenomics in clinical practice offers an attractive possibility to individualize antibiotic treatment and reduce a risk of AAD by utilizing the skill of pharmacist embracing the revolution in the science of health care to serve better the patients, by making antimicrobial therapy safer and more effective, contributing to the international fight with the spread of antibiotic-resistant flora. This analysis summarises the need for a heightened level of pharmacist involvement in the treatment of AAD and discusses strategies to overcome the challenge so far created.

Keywords: Antimicrobial-associated diarrhea, pharmacists, antimicrobial stewardship, probiotics, gut microbiome, antibiotic resistance, pharmacogenomics, patient education.

1. Introduction

Antimicrobial-associated diarrhea is one of the most significant public health issues for various reasons. For instance, AAD is one of the commonest adverse effects of antibiotic therapy. The incidence of AAD may range between 5% and 25%, depending on the specific type of antibiotic (Xie et al., 2019). The use of broad-spectrum antibiotics like cephalosporins, amoxicillin-clavulanate, and clindamycin has been most commonly associated with a higher risk of AAD (Xie et al., 2019). Another aspect of AAD pertains to the potential for disruption of the gut microbiome. Another feature of AAD relates to how it can disrupt the microbiome of the gut. It can impact the long-term effects. Antibiotics have the ability to destroy beneficial gut bacteria. Then, the opportunistic pathogens can overgrow, such as Clostridium difficile (C. difficile) (Ma et al., 2019; Sun & Hirota, 2015). It can cause severe diarrhea, abdominal pain, and even life-threatening complications (Ma et al., 2019; Sun & Hirota, 2015). The third one is the increase of antibiotic-resistant bacteria, which is a major public health concern. This problem is brought about by the overuse of antibiotics. Research already established that the administration of antimicrobials in the treatment of diarrhea if the actual causative agent is not bacterial causes the onset of antibiotic resistance (Duong et al., 2017; Misau et al., 2018). It promotes this risk of developing antibiotic resistance when antibiotics are inappropriately used in cases of non-bacterial diarrhea (BinKhamis et al., 2012). The clinical and financial burden is also enormous from AAD. This could lead to increased health care cost, inadequate treatment of the causative infection, and increased duration of hospital stay due to having to stop the antibiotics therapy (Gu et al., 2022; Gu et al., 2021). AAD can be severe enough that it may push an individual to withdraw the antibiotics before finishing the course which will undermine the treatment of the main infection (Gu et al., 2022; Gu et al., 2021). Third, and least subtle disadvantage, AAD is associated disproportionately more with vulnerable populations: that means the elderly, immunocompromised, and even hospitalized patients (Szajewska et al., 2016). Such individuals, suffering from severe complications, highlight further the need to tackle AAD as a public health issue. Antibiotics kill the beneficial gut bacteria, allowing opportunistic pathogens to overgrow in the gut. These opportunistic pathogens include Clostridium difficile (C. difficile) (Xie et al., 2019; Ma et al., 2019).

These pathogens may proliferate into severe diarrhea and abdominal pain or even life-threatening complications (Ma et al., 2019). An overuse of antibiotics will treat the diarrhea even when the causative agent may not be a bacterium leads to antibiotic resistance (Duong et al., 2017; Misau et al., 2018). This problem is increased because it uses antibiotics when it is not required for the non-bacterial diarrhea case (BinKhamis et al., 2012). AAD may lead to a delay in discharge from the hospitals, increased cost of healthcare, and a suboptimal treatment of the underlying infection due to discontinuation of antibiotic therapy. This severe AAD leads to premature stoppage of antibiotics, therefore jeopardizing the proper treatment of the pathogen that caused the primary infection (Gu et al., 2022; Gu et al., 2021). AAD highly presents in elderly people and hospitalized patients, especially with poor immunity, and in people who have a predisposing disease, with a larger tendency of major complications (Szajewska et al., 2016). Some antibiotics are more commonly linked with a higher risk of AAD, such as cephalosporins, amoxicillin-clavulanate, and clindamycin (Xie et al., 2019). Other opportunistic pathogens have been linked to AAD, including Clostridium difficile,

Escherichia coli, and Klebsiella species (Ma et al., 2019; Sun & Hirota, 2015). Co-infections will also be expected to aggravate the diarrheal disease condition (Lurchachaiwong et al., 2020).

2. Understanding Antimicrobial-Associated Diarrhea

Common risk factors and causes for AAD are Antibiotics can destroy normal flora in the gut, which allows opportunistic pathogens like Clostridium difficile (C. difficile) to overgrow within it (Xie et al., 2019; Ma et al., 2019). This overgrowth leads to dangerous complications such as diarrheas, abdominal cramps, and even some lethal complications (Ma et al., 2019). One major risk factor that leads to intestinal carriage with resistant bacteria, including drug-resistant E. coli is recent use of antimicrobials within 12 months as a source of risk (Hu et al., 2020). Notably, it has been reported that among antibiotics, cephalosporins, amoxicillin-clavulanate, and clindamycin most confer an increased risk for developing AAD (Xie et al., 2019). It primarily affects the elderly, immunocompromised, and hospitalized patients who are more prone to severe complications (Szajewska et al., 2016). Diarrhea is a risk factor for intestinal carriage of drug-resistant bacteria, including E. coli (Hu et al., 2020). Multiple infections also tend to increase the severity of diarrheal disease (Lurchachaiwong et al., 2020). According to Hu et al. 2020, travel history to India and Southeast Asia are some of the risk factors for intestinal carriage of drug-resistant bacteria such as E. coli. A diet that is vegetarian is another one of the risk factors to intestinal carriage of drug-resistant bacteria such as E. coli, as established by Hu et al. 2020. Beliefs that early institution of antimicrobials leads to a shorter course of diarrhea and perceived delays in culture and sensitivity testing can lead to high rates of empirical antibiotic treatment, even when the diarrhea is self-limiting (Misau et al., 2018). Unwarranted use of antimicrobials can predispose to high levels of resistance at the individual and community level (Misau et al., 2018). Antibiotics, particularly broad-spectrum agents such as cephalosporins, amoxicillin-clavulanate, and clindamycin, can eliminate beneficial gut bacteria, resulting in the overgrowth of opportunistic pathogens, such as Clostridium difficile (C. difficile) (Xie et al., 2019; Ma et al., 2019).

This alteration of the gut microbiome can cause severe diarrhea, abdominal pain, and even life-threatening complications (Ma et al., 2019). The overuse of antibiotics can also be attributed to developing antibiotic resistance, especially even if the cause of the diarrhea is not bacterial; such is the case given in Duong et al., 2017, and Misau et al., 2018. Overuse of antibiotics in cases that are not bacterial can worsen the problem (BinKhamis et al., 2012). One of the major risk factors is antimicrobial use, specifically broad-spectrum agents; CDI is a primary cause of hospital-acquired and community-acquired antibiotic-associated diarrhea (Fuereder et al., 2016; Willems et al., 2012; Alonso & Marr, 2013; Raza et al., 2010). AAD can contribute to prolonged hospital stays, increased healthcare costs, and suboptimal treatment of the underlying infection because of discontinuation of antibiotic therapy. It is severe enough to cause premature discontinuation of antibiotics, thereby affecting the treatment of the original infection (Gu et al., 2022; Gu et al., 2021). AAD is highly skewed toward the elderly, immunocompromised patients, and hospitalized patients, who are at an increased risk of developing complications from AAD (Szajewska et al., 2016).

3. Pharmacist's Role in Prevention

Table 1. Pharmacists' Role in Antimicrobial Stewardship Programs (ASPs)

Intervention	Description	References
Collaborative Practice Agreements	Pharmacists collaborate with physicians to optimize antibiotic prescribing through dose adjustments, de-escalation of therapy, and switching from intravenous to oral administration.	Lee & Bradley, 2023
Point-of-Care Testing	Utilize rapid diagnostic tests, such as procalcitonin, to guide antibiotic decision-making and reduce unnecessary use.	Watkins et al., 2021
Patient Consultations	Provide education on appropriate antibiotic use, adherence, and the risks of resistance.	Lee & Bradley, 2023
Academic Detailing	Engage in one-on-one education and feedback to prescribers about optimal antibiotic prescribing practices.	Lee & Bradley, 2023
Advocacy and Collaboration	Advocate for antimicrobial stewardship principles and collaborate with the multidisciplinary ASP team.	Lee & Bradley, 2023
Expanding Pharmacist Roles	Engage non-ASP pharmacists in stewardship activities to utilize their untapped potential.	Wong et al., 2021
Pharmacy Education and Training	Incorporate antimicrobial stewardship principles into pharmacy education and provide ongoing professional development to support community pharmacists' roles in outpatient antimicrobial stewardship.	Lee & Bradley, 2023; Wong et al., 2021
Program Impact	Pharmacist-led interventions reduce inappropriate antibiotic use, mitigate resistance, and improve patient outcomes.	Lutfiyati et al., 2021; Westerhof et al., 2020; Dionne et al., 2022; Díaz-Madriz et al., 2020

Pharmacists may offer one-on-one counseling with the patients while dispensing antibiotics on educating the patients about possible side effects, such as AAD, and the significance of completion of the full treatment course. Pharmacists may also participate in teaching patients educational materials available as booklets or pamphlets regarding AAD risk and safe prescription of antibiotics (Lutfiyati et al., 2021; Lee & Bradley, 2023). The at-risk population that the pharmacist may identify includes old age and immuno compromised patients to whom pro-active contact can be made for educating them on the prevention and management of AAD (Lee & Bradley, 2023). Pharmacists can work with other healthcare professionals such as physicians and nurses in planning patient education and ensuring that the message is consistent (Lutfiyati et al., 2021). Pharmacists can be involved in public health programs and educational interventions in the awareness of antibiotic resistance and proper use of antibiotics. These are related to the risks of AAD indirectly (Lutfiyati et al., 2021; Lee & Bradley, 2023). Pharmacists can also collaborate with local health officers and community-based organizations to establish and share information on AAD and antimicrobial stewardship (Lutfiyati et al., 2021). This training and professional development of the pharmacists on AAD, antimicrobial stewardship, and patient education might be one of the means that enables them to know better the problems in a position to discuss such matters with the patients effectively (Mudenda et al., 2020). Digital

tools can be in the form of application or internet-based sources which can offer more interactive learning interventions for AAD besides antibiotic use practices among the patients (Zolezzi et al., 2020). Pharmacists also have the availability of digital means such as social media platforms to educate the same demographic about AAD and antimicrobial stewardship in broad terms (Lutfiyati et al., 2021).

4. Clinical Interventions

The consensus is reached in several meta-analyses and systematic reviews concluding that probiotics significantly reduce the risk of AAD development when compared to the placebo (Videlock & Cremonini, 2012; Goodman et al., 2021). Among those, some of the most promising candidates are Saccharomyces boulardii, Lactobacillus acidophilus, and Lactobacillus rhamnosus (Goodman et al., 2021). The maximum probiotic dosages of more than 5 × 10^9 CFU per day have been indicated to be associated with improved efficacy in the prevention of AAD (Agamennone et al., 2018). Horosheva et al. suggested the dose-effect relationship in 2014, which indicated that the therapeutic success of probiotics depends on the specific probiotic strain used and the dose administered. Probiotics have been proven to prevent AAD in pediatric as well as adult populations, which include the elderly and critical patients (Drago et al., 2020; Guo et al., 2018). Probiotics might work in preventing AAD through gut microbiome restoration, suppression of the growth of opportunistic pathogens, and regulation of the immune response (Videlock & Cremonini, 2012; Goodman et al., 2021). The use of probiotics appears to be safe with low side effects and adverse reaction incidents reported for the prevention of AAD (Adnan et al., 2023).

Table 2: Probiotic Strains for AAD Prevention.

Probiotic Strain	Effectiveness	Recommended Dose
Saccharomyces boulardii	Reduces risk of AAD in pediatric and adult patients	≥5 × 10^9 CFU per day
Lactobacillus acidophilus	Restores gut microbiome and inhibits pathogen growth	≥5 × 10^9 CFU per day
Lactobacillus rhamnosus	Prevents AAD in critically ill and elderly patients	≥5 × 10^9 CFU per day

The high-risk populations that pharmacists can identify involve the elderly, immunocompromised patients, and patients on broad-spectrum antibiotics (Haran et al., 2014; Elseviers et al., 2015). Pharmacists can thus target high-risk patients who will be provided with AAD preventive and management interventions. Pharmacists can collaborate with prescribers to ensure antibiotic selection and dosing, particularly in high-risk populations, to reduce the risk of AAD (Haran et al., 2014). It is thus achievable by offering alternative antibiotics that have a low risk for AAD, or dosing and antibiotic treatment might be adjusted. A therapeutic drug monitoring that may integrate AUC monitoring for the case of vancomycin may use a therapist to ensure proper medication of antibiotics for the safety of patients, especially through reducing adverse reactions such as AAD. According to Joseph et al. (2021). According to Naletto et al. 2019 and Osemene et al. (2012), pharmacists can inform their patients on how to use antibiotics appropriately and why adherence is important as well as the fact that a patient

should be able to recognize and handle cases of AAD, which would enable the patient to participate actively in his care by recognizing early signs of AAD. The patient with a high chance of developing AAD should be counseled on probiotics use. According to Wronowski et al. (2021), and Elseviers et al. (2015), some of the adequate strains to be used comprise Saccharomyces boulardii or Lactobacillus species. Appropriate advice regarding the right dosage and duration of a suitable probiotic strain must be given by the pharmacists to the patients. Pharmacists can actively monitor patients for the development of AAD as well as other adverse effects related to antibiotic use (Osemene et al., 2012).

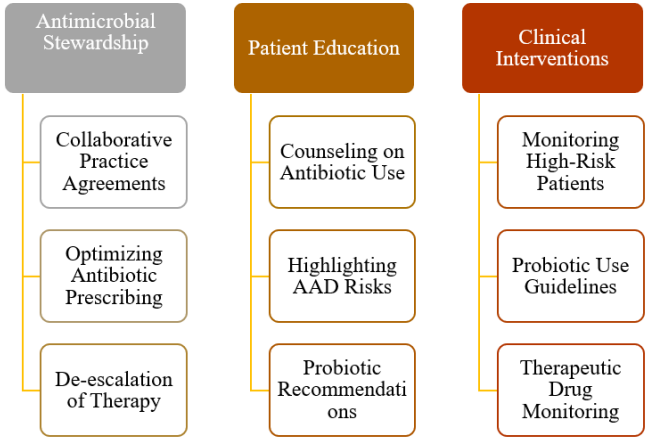

Figure 1. Pharmacist's Role in Preventing Antimicrobial-Associated Diarrhea.

Dehydration will also impact many of the patients suffering from AAD, as diarrhea results in excessive fluid loss Cohen et al., 2010 Liao et al., 2020). Pharmacists help the patients obtain information on hydration status that has to be followed in proper hydration such as high fluids intake in form of water, electrolyte-based beverage solutions, or oral hydration solution Castro et al., 2020; Liao et al., 2020). Pharmacists can educate patients on signs and symptoms of dehydration and when to seek medical care. Some dietary changes may help manage the symptoms of AAD and facilitate the recovery of the gut microbiome (Liao et al., 2020; Łukasik et al., 2020). During the acute phase of AAD, pharmacists can advise a patient to take easily digestible and low-fiber foods: bananas, rice, applesauce, or toast; probiotic-rich food sources: yogurt, kefir, or fermented vegetables; that will help restore their gut microbiome (Liao et al., 2020; Łukasik et al., 2020; McFarland et al., 2018; Wang et al., 2016). Pharmacists can advise on probiotics, such as Saccharomyces boulardii or Lactobacillus species, to prevent and manage AAD (Castro et al., 2020; McFarland et al., 2018; Doar, 2023). Pharmacists can advise appropriate probiotic strain, dose, and duration of use to optimize the effectiveness in preventing and managing AAD. Pharmacists can help in actively monitoring symptoms, hydration, dietary changes, and the reporting of worsening symptoms to healthcare providers (Liao et al., 2020; Łukasik et al., 2020). Pharmacists may also monitor patient adherence to hydration and dietary strategies and provide support as needed. Pharmacists will collaborate with the physicians, the nurses, and all others in the healthcare profession together to cooperate

in their bid to educate their patients using a consistent message given by the patients (Shen et al., 2017; McDonald et al., 2018). Collaboration increases the effectiveness of patient education and leads to better AAD management. As it enables them to take a patient lead in education on hydration and diet, pharmacists also play a role in improving effective management of antimicrobial-associated diarrhea, thus improving better outcomes for patients and therefore supporting antimicrobial stewardship efforts (Silverman et al., 2017).

Microbial Insights

Antibiotics cause an imbalance in the intestinal microbiota either by inhibition or promotion of various bacteria (Li et al., 2021; Meng et al., 2017). This subsequently leads to the opportunistic pathogens such as Clostridium difficile, which cause diarrhea that becomes severe (Darkoh et al., 2019). Antibi-otics can sharply chan-ge the gut mi-crobio-ta, fa-vor-i-zing a decrease in bene-fi-cial bac-te-ri-a and an increase in po-ten-tial-ly pa-tho-gène-nous bac-te-ria, such as Pro-teo-bac-teri-a, (Darkoh et al., 2019; Gao et al., 2021). Such chan-ges in the gut mi-cro-bio-ta can de-grade the in-tegri-ty and fun-ction of the gut im-mune re-spon-sa of AAD (Fröhlich et al., 2016). This state of gut dysbiosis caused by antibiotics can last even after the cessation of the antibiotic treatment. It hampers the restoration of the healthy gut microbiome (Oh et al., 2016; Zhang et al., 2021). The extended disruption of gut microbiota makes one more susceptible to AAD and other adverse conditions of the gastrointestinal system. The existence of antibiotics enhances the growth of antibiotic-resistant bacteria, which eventually outgrow the gut. This further impairs the development of AAD (Borgo et al., 2016; Wang et al., 2021). Antibiotic-induced gut dysbiosis impacts the composition of gut metabolites, including short-chain fatty acids, and affects the barrier function of the intestine as well as inflammation (Wang et al., 2021). Lower abundance of Bifidobacterium and Lactobacillus species has been associated with increased risk of diarrheal disease (Solano-Aguilar et al., 2013).

The study done by Solano-Aguilar et al. proved that high abundance of these species correlates with the low probability of clinical diarrhea. Low abundance of the Bacteroides fragilis group, essential for intestinal homeostasis, correlated with diarrheal disease as well (Solano-Aguilar et al., 2013). B. fragilis population does depend more upon the diverse environmental demands. In some places it is observed, in different studies. Enhanced abundance of Proteobacteria, for instance, such as that associated with species Escherichia coli and Klebsiella, has been reported for people with AAD, Yang et al., (2022). The increased Proteobacteria abundance would imply a lot of disorders of the digestive system which could be presented as diarrhoea. Clostridium difficile overgrowth is an established cause of antibiotic-associated diarrhea and colitis (Cohen et al., 2010). This is widely held in the literature. Elevations in SCFAs, which enhance neutrophil migration and inflammation, have been tied to the development of AAD (Jiang et al., 2023). Jiang et al showed that patients with AAD had higher levels of SCFAs compared with healthy controls. This study confirms the association between SCFAs and AAD. Antibiotic-resistant organisms, including those in the phylum of Proteobacteria, predispose an individual to AAD (Borgo et al., 2016; Wang et al., 2021). This is supported by a number of studies that show antibiotic resistance complicates treatment and increases the risk of diarrhea. There has been a significant shift in the composition of the overall gut microbiome, including

a reduction in Firmicutes and an increase in Bacteroidetes, in people with AAD (Yang et al., 2022).

According to the references listed, the key barriers to prevention of antimicrobial-associated diarrhea among the pharmacists in clinical practice are:

The pharmacists are not involved in the stewardship of antimicrobial:

While pharmacists are well placed to support decision making and optimization of antibiotics, they often are not formally involved in antimicrobial stewardship programs (Broom et al., 2015) Wong et al., 2021). The doctors may stay in an unfortunate position in relation to use of antibiotics if they need to bear all the responsibilities concerning decisions regarding choice, dosage, and duration (Broom et al., 2015).

Suboptimal knowledge and practice of the pharmacist:

Some of them lack in-depth understanding or misunderstanding about diarrhea's proper treatment directs them to the un-selective use of antibiotics. Suggestions like zinc supplementation and RHA supplementation are neglected (Rani et al., 2022; Hamadouk et al., 2021). -Non-pharmacological counseling such as change of lifestyle are unlikely to be complied with an antibiotic prescription, the most work done by a pharmacist is a dispensing of a drug product (Mikhael et al., 2023).

Lack of structured pharmacist-led interventions:

Pharmacist-led interventions have been shown to be effective in promoting the switch from intravenous to oral antibiotics and reducing antibiotic use, but such structured approaches are not always implemented in clinical practice (Nguyễn et al., 2023; Giesler et al., 2022).

Interprofessional and role-based challenges:

They will find it hard to work effectively with other professions in health care, most probably other physicians, because of the aspects of antimicrobial stewardship (Broom et al., 2015). There are role-related issues and antibiotics are peripheral rather than clinical core for pharmacists on the matter of decision- making over antibiotics (Broom et al., 2015). There could also be a lack of proper provision of resources, support for pharmacist.

Finding qualified and experienced professionals to lead clinical pharmacy education and training programs, more so in developing countries is a big challenge (Sakeena et al., 2018).- The knowledge and skills of the pharmacist may not be quickly assimilated into the healthcare system in the developing countries, thus limiting his or her contribution to efforts at antimicrobial stewardship efforts (Sakeena et al., 2018).

Table 3: Challenges and Barriers Faced by Pharmacists.

Challenge	Description	References
Limited Involvement in Stewardship	Pharmacists are often excluded from antimicrobial stewardship programs	Broom et al., 2015

Knowledge Gaps	Misconceptions about diarrhea management and antibiotic use	Rani et al., 2022
Resource Limitations	Lack of resources and structured pharmacist-led interventions	Sakeena et al., 2018
Interprofessional Challenges	Difficulties collaborating with other healthcare professionals	Broom et al., 2015
Guideline Gaps	Insufficient guidance on pharmacist-led strategies in clinical practice	Wong et al., 2021

5. Challenges and Barriers

While pharmacists are well-positioned to make the contribution to decision making and optimization of antibiotics, often, they are not formally included in antimicrobial stewardship programs (Broom et al., 2015) Wong et al., 2021). It has been suggested that doctors will not be out of the difficult situation regarding antibiotic use if all the responsibility of decisions such as choice, dosage, and duration is left solely to them (Broom et al., 2015). Some pharmacists may not know or have inadequate knowledge of how to properly manage diarrhea. This can cause them to use antibiotics in a careless manner without prescriptions like zinc and rehydration therapy, according to reports by Rani et al. in 2022 and Hamadouk et al. in 2021. This is because pharmacists have been found to major in dispensing pharmacological agents and neglect non-pharmacological prescriptions such as lifestyle changes during the management of diarrhea, as was reported by Mikhael et al. in 2023. Although it has been shown that interventions adopted by pharmacists are effective in switching intravenous antibiotics to oral antibiotics and lower antibiotic prescriptions, such systematic practices are not always adopted in the clinical field (Nguyễn et al., 2023; Giesler et al., 2022). Pharmacy practice could be interfered with because a pharmacist is not able to properly liaise with other health-care providers such as doctors over the implementation of antimicrobial stewardship (Broom et al., 2015). A perception that the decisions on the use of antibiotics are an edge rather than the clinical decision core may result from role-based problems for the pharmacists (Broom et al., 2015). In particular, identifying well-qualified and experienced professionals to lead clinical pharmacy education and training programs is highly challenging, especially in developing countries (Sakeena et al., 2018). For instance, the integration of pharmacists' knowledge and expertise into the healthcare system would be challenging for developing countries, thereby further limiting the participation of pharmacists in stewardship (Sakeena et al., 2018). The references reflect that pharmacists, even in areas where they are most influential, like antimicrobial stewardship, generally do not have a representation in the development of high-impact clinical practice guidelines (Freeman et al., 2018).

The above reason can make guidelines not address the role of a pharmacist in the prevention and management of AAD. Some guidelines may indicate that pharmacists have a role to play in antimicrobial stewardship, but specific recommendations about pharmacist-led interventions to prevent AAD are sometimes not present or are applied differently (Wong et al., 2021). The

references suggest that guidelines sometimes do not clarify the implementation of pharmacist-led strategies such as the use of clinical decision support systems or structured pharmacist-led interventions (Wong et al., 2021). The references further indicate that some pharmacists have little or wrong knowledge about the management of diarrhea, and they use antibiotics indiscriminately (Ogbo et al., 2014). The available guidelines are deficient in the elucidation of the role and responsibilities of the pharmacists to instruct the patient on the right use of antibiotics, diagnosis of AAD, and other non-pharmacological interventions (Mikhael et al., 2023). Based on references, it is assumed that guidelines for some of the conditions, such as glucocorticoid-induced osteoporosis, may vary significantly, with content or recommendation changes based on different countries or regions (Ishihara, 2024; Laurent et al., 2022). This will raise the challenges of the harmonization of pharmacists with consistent, evidence-based practice for the prevention of AAD, especially in the cases of patient populations that have a higher risk. As can be seen from the references, there are some particular patients' population with higher risks of developing AAD. Examples of these particular patient populations include the critically ill and immunocompromised patients (Lee & An, 2021). However, guidelines at present do not make specific recommendations or provide specific guidance about the role of the pharmacist in monitoring and managing high-risk patients to prevent AAD.

6. Future Directions

Pharmacogenomic testing helps in identifying genetic factors responsible for an individual's response to antibiotics, and therefore pharmacists can select the best antibiotic and optimize the dose to minimize the risk of AAD (Ramadan, 2024; Crown et al., 2020). Through this data from pharmacogenomics, pharmacists can tailor the patient's antibiotic therapy to the patient's genetic profile to minimize the risk of an adverse event, such as AAD (Frick et al., 2018; Gammal et al., 2022). Such pharmacogenomic information would enable pharmacists to identify patients at a higher risk of developing AAD, and hence proactively advise them to use certain probiotic strains or combinations that would help prevent or manage the condition (Brown et al., 2018). The selection of the most likely probiotics for a patient would depend on the genetic profile of the patient and their susceptibility to AAD. This will allow pharmacists to assimilate knowledge and skills in respect to the application of pharmacogenomics, in order to maximize benefits in the care of their patients by avoiding AAD through application of this technology, as stated by Frick et al. (2018), Loudon et al. (2021), and Hicks et al. (2019). Pharmacogenomic information can empower pharmacists by giving them the knowledge and tools to interpret and apply this kind of data so they can be actively involved in more activities on antimicrobial stewardship and prevention of AAD (Balogun, 2024). The management of the patients likely to be at a risk for AAD can in collaboration with other health service providers like physicians and geneticists integrate pharmacogenomics data (Hicks et al., 2019). Therefore, this collaboration would prevent the misuse of pharmacogenomic data in guiding the choices of antibiotics, dosages, and adjunctive therapies such as probiotics for managing and preventing AAD. Pharmacists can use this knowledge to counsel patients on the need for personalized antibiotic therapy, the role of probiotics, and the diagnosis and treatment of AAD (Ramadan, 2024; Rahma et al., 2020). Further research is needed in evaluating the effectiveness of some

pharmacist-led interventions, like clinical decision support systems, structured pharmacist-led interventions, and care models in collaborative care against AAD Wong et al. (2021) Nguyễn et al., 2023; Giesler et al., 2022).

Comparative, highly informative studies would look at the effectiveness of pharmacist-led interventions compared to standard care or other approaches led by other healthcare providers (Agomo, 2011). Further research is required to identify challenges that hinder pharmacists from being more proactive in the stewardship of antimicrobial agents and prevention of AAD, which include lack of engagement in guideline development, role-based challenges, and resource-related barriers (Broom et al., 2015; Wong et al., 2021; Sakeena et al., 2018). Identification of facilitators that would help the pharmacists overcome such barriers and further their contribution to the prevention of AAD would be helpful (Skowron et al., 2011). Further research is needed to establish the efficacy of patient education led by a pharmacist regarding appropriate antibiotic use, identification of AAD, and non-pharmacological measures including diet and probiotic intake (Mikhael et al., 2023; Ogbo et al., 2014). More studies are needed to clarify the impact of these pharmacist-led education interventions on patient adherence, clinical outcomes, and antimicrobial stewardship (MacDougall et al., 2016). Further studies into this area should be conducted on the appropriate probiotic strain, dose, and the duration of treatment that prevents AAD and the role played by a pharmacist in recommending such prophylaxis (Elseviers et al., 2015; Blaabjerg et al., 2017; Goli et al., 2019).

The cost-effectiveness analysis of the use of probiotics for the prevention of AAD, what the pharmacist can do for promoting their proper use, would turn out to be of great use (Elseviers et al., 2015). Research will help understand how further developments in pharmacogenomics can push forward pharmacist-led interventions for AAD: personal antibiotic selection and dosing, targeted probiotic recommendations, and how it affects patient education and outcomes (Ramadan, 2024; Crown et al., 2020; Frick et al., 2018; Gammal et al., 2022; Brown et al., 2018). This would add pharmacogenomic data into pharmacist-led antimicrobial stewardship programs and their implications on preventing AAD. The evidence this would provide would be very significant (Hicks et al., 2019; Balogun, 2024).

7. Conclusion

Thereby, pharmacists play the crucial role in solving this more complex problem of AAD. The roles range from optimizing antimicrobial use through advising and educating patients and their health care providers on potential threats and preventive strategies for AAD. Clinical interventions encompass the use of probiotics, as well as keeping an eye on high-risk patients, integrating with what the pharmacist is doing. These pharmacists are, however limited from their potential by issues of lack of involvement in the antimicrobial stewardship program, a lack of resource, and interprofessional obstacles. These can be removed by systemic changes; thus, including pharmacists within stewardship initiatives with training and clinical guidelines clear and emphasis on contributions. With pharmacogenomics now integrated, the management of AAD would promise more specific antibiotic therapy that will further reduce the risk and better outcomes. The implementation of these benefits requires cooperation between healthcare

professionals to comprehensively address the issue of AAD. As a gatekeeper to antimicrobial use, the pharmacist can act as a critical bridge to overcome gaps in care and contribute to diminishing the burden of AAD while promoting efforts to defeat antibiotic resistance across the world. This paper emphasizes the need for greater engagement of pharmacists and supports systemic initiatives to leverage them in AAD prevention and management in the best possible way.

Author Contributions

Even though the original text was written by the corresponding author, all authors made significant contributions by gathering information and conducting a literature search for the article. Each author took responsibility for all parts of the manuscript, took part in its critical review, and approved the final draft.

Acknowledgments
The authors thank and are very grateful to the publishers, open access databases, web portals, and writers whose works provided the literature needed to complete this article.

Conflict of Interest

The authors declare they don’t have any conflict of interest.

Ethical Approval

Not Applicable

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