



Pharmacist-Led Antimicrobial Stewardship

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The value of critical care pharmacists has been well documented. Various studies have shown that critical care pharmacists reduce medication errors, improve patient outcomes, reduce costs and waste, and decrease mortality rates among patients with thromboembolic diseases or infections [1,2]. Antimicrobial resistance (AMR) causes prolonged illness, greater risk of infection spread, increased morbidity, and higher mortality rates, which result in increased expenses to the government, healthcare services, and individuals. It is estimated that around 700,000 people die annually from drug-resistant infections, with experts predicting an alarming possible increase to 10 million deaths each year by 2050 and major future challenges to the way we practice medicine and surgery. Resistance has been associated with increasing mortality, treatment failure and healthcare costs [3,4]. This alarming rate exceeds the annual number of deaths caused by cancer (8.2 million) and is almost ten times that of motor vehicle accidents (1.2 million) [5]. In the United States, in addition to significant mortality, antimicrobial resistance adds \$20 billion in excess direct health care costs and up to \$35 billion in annual societal costs as a result of lost productivity [6]. Antibiotic stewardship was established to combat this trend and was recognized in 1996 to draw attention to the rising incidents in mortality and morbidity associated with inappropriate use of antibiotics [7]. Antibiotic stewardship is a core part of critical care, and many times, the physician will rely on the pharmacist's recommendations and expertise. Antibiotic Stewardship Recommendations include constituting a team, close coordination between teams, audit, formulary restriction, de-escalation, optimizing dosing, active use of information technology among other measure [8]. The Infectious Diseases Society of America guidelines on antimicrobial stewardship recommend that the core multidisciplinary stewardship team include an infectious diseases

(ID) physician and a clinical pharmacist with ID training [9]. Antibiotic prescribing in outpatient settings exceeds that of inpatient prescribing, with more than 150 million antibiotic prescriptions annually; of these prescriptions, more than 30% are either unnecessary or inappropriately prescribed [10-12]. Orally administered antimicrobials accounted for approximately 90% of total consumption: oral third-generation cephalosporins, macrolides, and fluoroquinolones accounted for approximately 77% of oral consumption. Therefore, pharmacists must extend their support for the appropriate use of antimicrobials prescribed by attending physicians to not only hospitalized patients but also outpatients [13]. As the regulations for antibiotic stewardship in outpatient settings continue to evolve and optimal stewardship strategies are defined, pharmacists must be leaders in the implementation of these programs [14]. Stewardship programs can help, reduce inappropriate prescription and broad-spectrum use of antimicrobials, improve, clinical outcomes for the population as a whole, slow down the emergence of antimicrobial resistance and conserve healthcare resources [3]. The WHO Global Action Plan on Antimicrobial Resistance recommends countries work together to improve awareness and understanding of antimicrobial resistance, including through social media. The 2018 World Antibiotic Awareness Week campaign used Twitter to tailor media messages about the Global Action Plan [15]. Social media have become important information channels, but may not reach people with low knowledge and/or low interest in the subject. Within the EU, countries with low use of antibiotics, such as Sweden and The Netherlands, show a higher population knowledge level [16]. The use of community antibiotic stewardship programs (ASPs) is rising. ASPs involving pharmacists are effective in decreasing antibiotic prescribing and increasing guideline-adherent antibiotic prescribing by GPs [17]. Evidence in

China and Netherlands showed that antibiotic stewardship program was associated with more less 80% and more than 25% decrease in cost of antibiotic prophylaxis per procedure respectively [18]. The issue of antimicrobial resistance is worse in low and middle-income countries (LMIC), as the incidence of infectious diseases is high compared to high-income countries. In low and middle-income countries, the mortality rates due to antimicrobial-resistant bacteria are under-reported, however, available data in India, Nigeria, Pakistan, and Congo indicate that a huge number of neonatal deaths resulted from drug-resistant sepsis [19]. Annually, more than 50,000 newborns are estimated to die from sepsis due to pathogens resistant to first-line antibiotics [20]. In European countries, antimicrobial resistance is also on the rise and considered to be responsible for about 25,000 deaths annually [21]. Pharmacists are core AMS team members where there is an ongoing need to align continuing education for health professionals with realities of practice. However, antimicrobial stewardship (AMS) is not comprehensively and fully taught in medical or pharmacy curricula and little is known about the relevance of pharmacist training to meet AMS needs [22]. Critically, there is a need for establishing sustainable funding for AMS teams working beyond hospital settings that is not solely derived from cost savings through reduced drug expenditure. Instead, funding for developing and supporting AMS teams should be considered within the patient safety and healthcare-quality-related spending [23]. More recently, the introduction of national stewardship guidelines, and an increased focus on stewardship as part of the UK five-year antimicrobial resistance strategy, have accelerated and embedded developments. Antimicrobial pharmacists have been instrumental in effecting changes at an organizational and national level [24]. A pharmacist dispensing antimicrobials without a prescription is 83–100% of the time unaware of a patient's allergies status [19]. Inaccurate allergy labelling results in inappropriate antimicrobial management of the patient, which may affect clinical outcome, increase the risk of adverse events and increase costs. Inappropriate use of alternative antibiotics has implications for antimicrobial stewardship programs and microbial resistance. du Plessis et.al, 2019 recommended that a pharmacist-led allergy management service is a safe option to promote antimicrobial stewardship and appropriate allergy labelling [25]. Cheon., *et al.* 2018 suggested broader adoption for the role of pharmacists in the provision of penicillin skin testing. This would help expand the service and maximize the potential benefits of penicillin skin testing [26].

Pharmacists may be tasked to lead ASP development and implementation with little or no support from an infectious diseases (ID) physician and other hospital personnel whose involvement on ASP teams is recommended (e.g., clinical microbiologists, infection control specialists, hospital epidemiologists) [27]. Pharmacists and other health care professionals should collaborate within multidisciplinary teams (MDTs) to reduce the risk of antimicrobial resistance, thereby reducing the economic burden, improving patients' quality of life, and reducing hospitalization due to infections [19]. In a UK study, almost 60% of pharmacist's contributions are made during the MDT round [28]. Research has shown that pharmacists play an important role in the (Emergency Department) ED, but there is a need for data supporting this in specific patient outcomes as the majority of the literature addresses adverse drug event prevention and cost-containment [29]. Critical care pharmacists are recognized in the guidelines from the Society of Critical Care Medicine (SCCM) as essential team members for the delivery of care for critically ill patients. In fact, the return on investment of an ICU pharmacist's salary approached in multiple studies of critically ill patients with infection [30]. Including critical care pharmacists in the multidisciplinary ICU team improved patient outcomes including mortality, ICU length of stay in mixed ICUs, and preventable/nonpreventable adverse drug events [31]. Although factors, such as a lack of financial resources, may be beyond the control of the pharmacy profession, other factors, such as increased documentation in patient records and increased scholarly work demonstrating pharmacists' contributions, can and should be addressed more consistently by all critical care pharmacists [32]. The critical care pharmacist ensures the discontinuation of these medications in patients who no longer have an indication. Unfortunately, these medications are sometimes started by the ward team and continued on discharge. Additionally, home maintenance medications are often not resumed on hospital admission and/or subsequent discharge, increasing the risk of death, emergency department visit, or hospitalization. A critical care pharmacist integrated into the ICU-Recovery Center (ICU-RC) may take attempt to identify and treat the types of medication errors found in a population of high-risk ICU [33]. In addition, pharmacists who are often the first point of care, dispense antibiotics without a physician prescription, offer alternative antibiotics even when patients present with a prescription. Within the hospitals lack of monitoring of antibiotic use is one of the major factors driving the spread of resistance [34]. The implementation of antimicrobial stewardship programs in primary health care is

suboptimal. This negatively affects the global efforts to control antimicrobial resistance. There is a need to institutionalize national guidelines for AMS in primary health care [35]. Multiple randomized controlled trials (RCTs) have found that shorter courses of antibiotic therapy result in similar cure rates as traditional courses for many types of infections, including UTIs, SSTIs, and pneumonia. Unfortunately, familiarity with short-course therapy as a stewardship tool is limited. A recent study found that only one-third of infectious diseases practitioners from 58 countries recommended short-course therapies [36]. Consequently, some countries have recommended shortening the duration of antibiotic treatment of community-acquired pneumonia (CAP). No significant differences in adverse events were reported. However, none of the trials reported on the impact on the development of resistant bacteria [37]. As with the cost of climate change, estimates of total AMR costs are fraught with uncertainty and may be far too low. This cost depends on various factors: which drug and pathogen are involved, the mechanism of antibiotic resistance, the prevalence of that pathogen, the types of infections it causes and their level of transmissibility, the health burden of those infections, and whether alternative treatments are available [38]. AMS can help pharmacists improve the quality of patient care and improve patient safety through increased infection cure rates, reduced treatment failures, and increased frequency of correct prescribing for therapy and prophylaxis. The cost of employing a pharmacist at the recommended minimum staffing level is approximately £20 per patient per day. Several studies find that the role reduces overall expenditure through more efficient use of medicines and the avoidance of direct costs of iatrogenic harm, with additional savings made from avoiding payouts arising from damages claims [19,27].

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