Assessing the efficacy of pharmacist-engaged interventions in influencing antibiotic prescribing behavior among general practitioners: meta-analysis

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Abstract

Background: A meta-analysis study was undertaken to examine antibiotic resistance, specifically by assessing the effectiveness of pharmacist interventions in influencing the rate of antibiotic prescriptions compared to their impact on adherence to antibiotic prescribing guidelines.

Objective: Evaluating the effectiveness of pharmacist interventions in influencing the rate of antibiotic prescriptions, in contrast to their impact on adherence to antibiotic prescribing guidelines.

Method: A comprehensive literature review up to the year 2016 was conducted, examining a total of 215 relevant studies. Among these, 15 specific studies were chosen for inclusion, encompassing a population of 298,339 individuals who initially demonstrated antibiotic resistance. Within this group, 134,004 individuals were exposed to interventions involving pharmacist participation, while 164,335 served as controls. The calculation of odds ratios (OR) and 95% confidence intervals (CIs) was employed to assess antibiotic resistance in pharmacists involved in antibiotic prescribing rates as compared to those involved in antibiotic prescribing adherence rates. This analysis utilized dichotomous approaches and employed both fixed and random models.

Result: When pharmacists participated in interventions targeting antibiotic prescribing rates, a considerable reduction in antibiotic resistance was observed (Odds Ratio, 0.86; 95% Confidence Interval, 0.78-0.95, $p<0.00001$). However, these findings exhibited a significant degree of heterogeneity ($I2$ = 90%). Conversely, in interventions focusing on improving antibiotic prescribing adherence rates involving pharmacists, a substantial increase in antibiotic resistance was noted (Odds Ratio, 1.96; 95% Confidence Interval, 1.56-2.45, $p<0.00001$), with similarly high heterogeneity in the results ($I2$ = 91%). These outcomes were specifically evident in individuals grappling with antibiotic resistance issues.

Conclusion: Pharmacist-led interventions targeting antibiotic prescribing rates led to a noteworthy decrease in antibiotic resistance compared to scenarios without pharmacist involvement in such interventions. Nonetheless, it is crucial to approach the interpretation of these results with caution, given the limited sample size in certain studies incorporated into the meta-analysis.

Keywords: antibiotic; pharmacist; physician; pharmacist intervention AMR stewardship

Introduction:

Antibiotic resistance pertains to the capacity of bacteria or other small organisms to endure the impact of antibiotics, rendering the antibiotics ineffective in treating infections caused by these microorganisms. [1]. This phenomenon can occur when bacteria undergo genetic mutations or acquire genes that confer resistance, enabling them to persist and multiply even when exposed to antibiotics. Antibiotic resistance is an escalating issue in public health, as it can lead to the dissemination of infections that become challenging or even impossible to treat, resulting in elevated levels of sickness, hospitalization, and mortality. Pharmacists hold a crucial responsibility in ensuring the responsible and proper utilization of antibiotics. [2]. Pharmacists frequently participate in the distribution of antibiotics and provide guidance to patients on the correct usage of these medications. Furthermore, pharmacists may work alongside healthcare professionals to enhance antibiotic treatment, including ensuring the correct dosage, administration method, and treatment duration. [3].

Pharmacists can also actively participate in antimicrobial stewardship initiatives, whose primary objective is to encourage the responsible utilization of antibiotics to mitigate the emergence of antibiotic resistance. This involvement may encompass activities such as assessing antibiotic prescriptions, delivering educational resources to healthcare providers and patients, and tracking the patterns of antibiotic utilization. [4]. Through close collaboration with healthcare teams, pharmacists can contribute to enhancing antibiotic prescription practices and ensuring that antibiotics are employed solely when they are both necessary and suitable [5].

Effective collaboration between physicians and pharmacists is essential for the proper utilization of antibiotics. While doctors are responsible for prescribing antibiotics to address bacterial infections, pharmacists play a critical role in dispensing these medications and ensuring that patients have a clear understanding of the correct way to take them. [6].

Through a tight-knit collaboration, physicians and pharmacists can jointly advocate for the responsible utilization of antibiotics, thereby decreasing the likelihood of antibiotic resistance. This collaborative effort may encompass the creation and execution of antimicrobial stewardship programs, educating both patients and healthcare providers, and tracking the trends in antibiotic usage to pinpoint areas needing enhancement. By joining forces, doctors and pharmacists can collectively contribute to the appropriate use of antibiotics for infection treatment and the mitigation of antibiotic resistance development. [7].

In recent years, numerous experts have conducted comparative studies examining the impact of pharmacists' involvement in antibiotic prescribing rates versus antibiotic prescribing adherence rates. Furthermore, some meta-analyses have been conducted to assess the advantages and disadvantages of these two strategies. However, a comprehensive assessment of the outcomes of these comparative studies has not yet been carried out, and as a result, definitive conclusions remain elusive. [8]. To compare the impact of pharmacists' involvement in antibiotic prescribing rates with that of antibiotic prescribing adherence rates, a meta-analysis was conducted. The primary objective was to evaluate antibiotic resistance concerning the influence of pharmacists in antibiotic prescribing rates as opposed to their involvement in antibiotic prescribing adherence rates. [9]

During the mid-20th century, antibiotics were celebrated as miraculous drugs with the ability to eliminate disease-causing bacteria without causing harm to the host. The underlying mechanism driving the therapeutic effectiveness of antibiotics is complex, encompassing the inhibition of bacterial cell wall synthesis, protein synthesis, DNA and RNA synthesis, disruption of cell membrane integrity, and various other mechanisms.

Resistance to antibiotics swiftly emerged as a persistent challenge throughout the history of antibiotic development, becoming a universal phenomenon following their discovery and clinical application. No class of antibiotics has remained unaffected by bacterial resistance, [10].

Various organizations, including the World Health Organization (WHO), acknowledge bacterial resistance as a significant concern and have undertaken efforts to mitigate its spread. Nevertheless, global antibiotic resistance remains a persistent challenge with no signs of diminishing. Antibiotics have been instrumental in modern medicine, enabling progress in areas such as organ transplantation, cancer therapy, neonatal care, and major surgeries by managing and preventing bacterial infections. Failing to implement effective global action plans could result in severe social, medical, and economic ramifications, [11].

The primary responsibilities of pharmacists encompass various crucial tasks, such as offering drug-related information, managing medications, preparing and dispensing drugs, providing patient counseling, and devising personalized pharmaceutical care plans to enhance patients' well-being. Pharmaceutical care plans represent a tailored service provided by pharmacists with the goal of improving patients' overall health. Pharmacists occupy a central position within the healthcare system, fulfilling various roles such as academic pharmacists, industrial pharmacists, community pharmacists, clinical pharmacists, hospital pharmacists, veterinary pharmacists, and more. Irrespective of their specific roles, all pharmacists are intricately connected, either directly or indirectly, to the overall health of the population. Ultimately, pharmacists are entrusted with the responsibility of ensuring that the accurate medication reaches the correct patient, at the designated time, in the proper dosage, through the appropriate route, and administered in the correct manner. This emphasizes the indispensable role that pharmacists play within the healthcare system,[12].

The World Health Organization (WHO) has underscored the importance of evaluating and, if needed, strengthening the pharmacist's role as the principal provider and overseer of antibiotics. While numerous initiatives aimed at tackling antibiotic misuse concentrate on improving physicians' prescription practices, other potential avenues of misuse are sometimes neglected. Yet, the manner in which patients employ antibiotics can profoundly influence their efficacy and the likelihood of resistance, [13].

Methods

Eligibility criteria

To generate a summary, we analyze studies investigating the impact of pharmacist interventions on the overall antibiotic prescribing rate, comparing it with the influence on antibiotic prescribing adherence rates, [14, 15].

Information sources

The entirety of the investigation is depicted in Figure 1. The literature was incorporated into the study upon meeting the inclusion criteria.

The research included in the study met specific criteria:

1. The study employed observational, prospective, retrospective, or randomized controlled trial (RCT) designs.
2. Participants selected for the investigation had antibiotic resistance.
3. The intervention assessed the impact of pharmacist involvement on both antibiotic prescribing rates and antibiotic prescribing adherence rates.
4. The study explicitly examined the effect of pharmacist involvement on antibiotic prescribing rates and antibiotic prescribing adherence rates in the management of antibiotic resistance.

Exclusions were made for research that did not highlight the significance of the comparison, studies that did not evaluate the characteristics of antibiotic prescribing rates compared to antibiotic prescribing adherence rates, and those focusing on antibiotic resistance in individuals lacking information on antibiotic prescribing rates and antibiotic prescribing adherence rates.

Search strategy

The search protocol operations were defined based on the PICOS criteria as follows: "population" included individuals with antibiotic resistance, "intervention" or "exposure" involved pharmacists, the "comparison" focused on the antibiotic prescribing rate versus antibiotic prescribing adherence rate in individuals with antibiotic resistance, "outcome" was considered, and there were no restrictions on the "study design" for the proposed investigation, [16, 17].

We conducted a comprehensive search on Google Scholar, PubMed, and various databases until 2023, employing a set of keywords and related terms pertaining to antibiotic resistance, antibiotic prescribing rate, antibiotic prescribing adherence rate, pharmacists, and physicians (refer to Table 1). To ensure the exclusion of studies lacking a clear connection between antibiotic resistance consequences and the comparison of antibiotic prescribing rate versus antibiotic prescribing adherence rate, we excluded replicated papers. The collected studies were organized into an EndNote file, and titles and abstracts were subsequently reviewed.

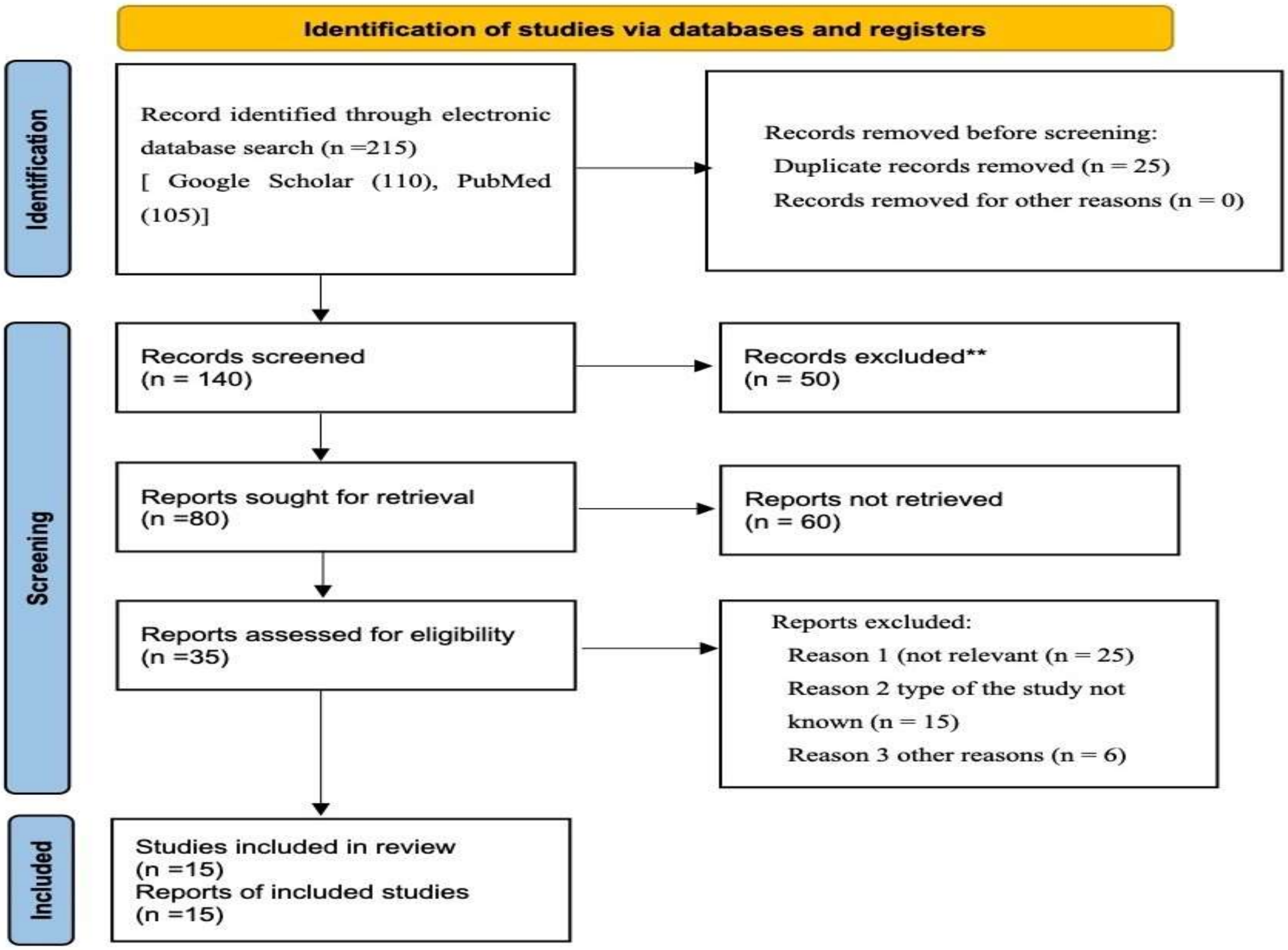

Figure 1. A flow diagram of the investigation process

Selection process

After the epidemiological declaration, a systematic process was established, subsequently structured and analyzed through a meta-analysis procedure.

Data collection process

The data collection criteria encompassed key details such as the primary author, investigation date, year of the study, geographical location, population type, medical and therapeutic characteristics, categories, quantitative and qualitative assessment methods, data sources, outcome estimates, and statistical analyses.

Data items

In cases where investigations incorporated variable values, we systematically gathered data, specifically focusing on the evaluation of antibiotic resistance in relation to both antibiotic prescribing rates and antibiotic prescribing adherence rates.

Investigation risk of bias assessment

The two authors evaluated the methodologies employed in the selected publications to assess potential biases in each investigation. Procedural quality was gauged using the "risk of bias instrument" from the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. Based on the appraisal criteria, each investigation was assigned one of the following bias risks: low - if all quality criteria were met; medium - if one or more requirements were not met or included; and high - if one or more quality needs were either entirely or partially unmet. Additionally, the Ottawa Quality Assessment Scale for cohort studies was utilized to appraise the risk of bias in observational non-randomized trials.

Table 1. Search Strategy for Each Database

Database	Search strategy
Pubmed	#1 antibiotic resistant "[MH]" OR "urinary tract infection"[MH]" OR "pharmacist intervention involved "[MH]". #2 antibiotic prescribing "[TIAB]" "Antimicrobial Stewardship"[TIAB], urinary tract infection "[TIAB]" #3 prescribing behavior"[MH], pharmacist and physician collaboration "[MH].
Google scholar	1. Antibiotic resistant causes "[MH], "urinary tract infection"[MH]" OR "pharmacist intervention involved "[MH]". 2. antibiotic prescribing "[TIAB]" "Antimicrobial Stewardship"[TIAB], urinary tract infection "[TIAB]"
Cochrane library	"pharmacist intervention involved "[MH]", pharmacist and physician collaboration "[MH]", Antimicrobial Stewardship"[TIAB], OR "Antimicrobial Stewardship"[MH]".

Effect measures

Sensitivity analyses were exclusively performed on studies that evaluated and reported antibiotic resistance in comparison with both antibiotic prescribing rates and antibiotic prescribing adherence rates. The aim was to contrast the impact of pharmacists involved in antibiotic prescribing rates with the effect of pharmacists involved in antibiotic prescribing adherence rates. Subclass analysis was employed for this examination.

Synthesis methods

A random- or fixed-effect model was utilized to generate the odds ratio (OR) and a 95% confidence interval (CI) utilizing dichotomous or continuous approaches. Between 0 and 100%, the I2 index was determined. The values at 0%, 25%, 50%, and 75%, respectively, presented no, low, moderate, and high heterogeneity. [18] Other features that show a strong degree of alikeness amongst the related research were also analyzed to make sure the correct model was being utilized. The random effect was used if I2 was 50% or above; if I2 was <50%, the possibility of utilizing fixed-effect rose. [18] A subclass analysis was done by stratifying the initial estimation by the aforementioned consequence groups. A p-value of <0.05 was utilized in the analysis to specify the statistical significance of differences between subcategories.

Reporting bias assessment

The bias in the studies was assessed both statistically and qualitatively using the Egger regression test and funnel plots, which illustrate the logarithm of the odds ratios (ORs) against their standard errors (the presence of bias was considered if p≥0.05).

Certainty assessment

Two-tailed testing was employed to examine each p-value. The graphs and statistical analyses were generated using Review Manager Version 5.3 (The Nordic Cochrane Centre, the Cochrane Collaboration, Copenhagen, Denmark).

Results

15 publications, published between 1994 and 2016, from a total of 215 connected investigations that met the inclusion criteria were chosen for the investigation. [19-33] The results of these researches are presented in Table 2. 298339 individuals with antibiotic resistant were in the chosen investigations' starting point, 134004 of them were utilizing pharmacists involved intervention, and 164335 were utilizing individual's control. The sample size was between 130 and 154250 Individuals. Pharmacists involved intervention in antibiotic prescribing rate had significantly lower antibiotic resistant (OR, 0.86; 95% CI, 0.78-0.95, p<0.00001) with high heterogeneity (I2 = 90%), and individuals control, pharmacists involved intervention in antibiotic prescribing adherence rate had significantly higher antibiotic resistant (OR, 1.96; 95% CI, 1.56-2.45, p<0.00001) with higher heterogeneity (I2 = 91%) compared to those with pharmacists involved intervention in antibiotic prescribing rate in individuals

with antibiotic resistant as shown in Figures 2 and 3. The sample size was between 130 and 154250 individual. The absence of data prevented the use of stratified models to examine the effects of specific factors, such as age and ethnicity, on comparison outcomes. No evidence of investigation bias was found (p = 0.84) using the quantitative Egger regression test and the visual interpretation of the funnel plot as shown in Figures 4 and 5 and Tables 3 and 4. However, the majority of the implicated RCTs were found to have poor procedural quality and no bias in selective reporting.

Table 2. Characteristics of the selected investigations for the meta-analysis

Investigations	Country	Total	Pharmacist intervention	Individual control
Santis, 1994	Australia	802	357	445
Stålsby Lundborg, 1999	Sweden	3737	1857	1880
Saint, 1999	USA	2128	1883	245
Ilett, 2000	Australia	16916	7262	9654
Veninga, 2000	Netherland	5598	2760	2838
Coenen, 2004	Belgium	898	80	818
Welschen, 2004	Netherland	1723	905	818
Martens, 2006	Netherland	1138	652	486
Van Driel, 2007	Belgium	130	70	60
Smeets, 2009	Netherland	2000	1000	1000
Esmaily, 2010	Iran	13480	8052	5428
Weiss, 2011	Canada	2000	1000	1000
Wilf-Miron, 2012	Palestine	91875	47500	44375
Vervloet, 2016	Netherland	154250	59483	94767
Vellinga A, 2016	Canada	1664	1143	521
	Total	298339	134004	164335

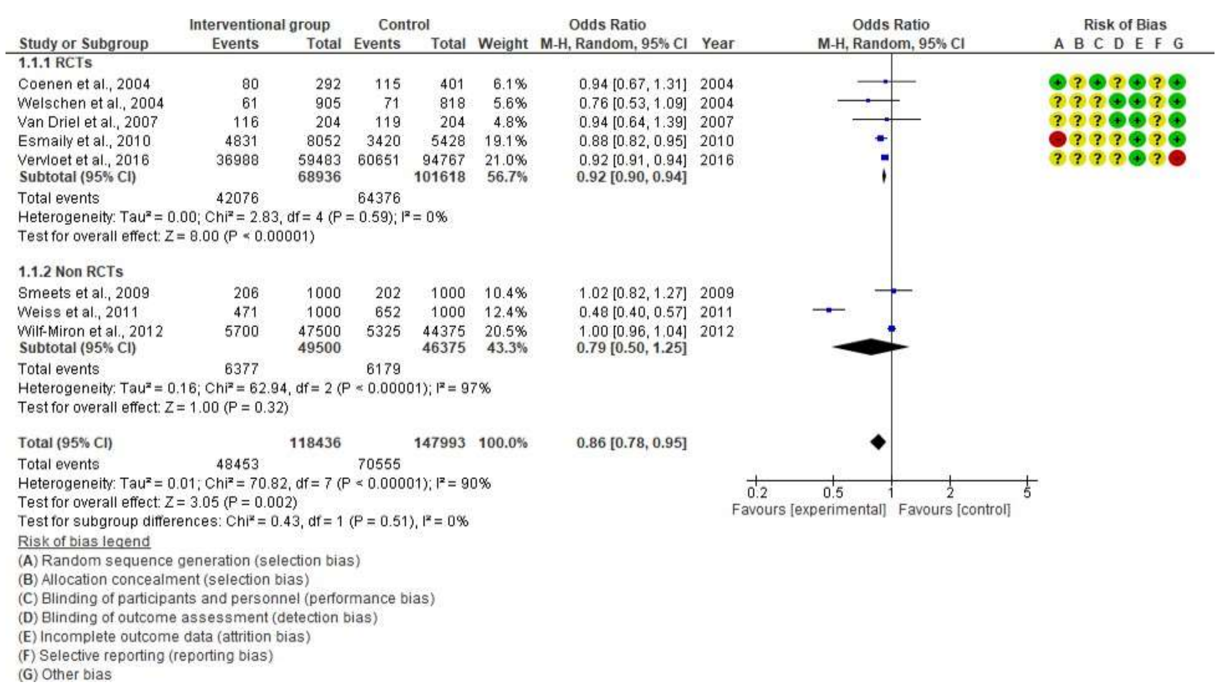

Figure 2. The effect's forest plot of pharmacists involved intervention in antibiotic prescribing rate, and individual control compared pharmacists involved intervention in antibiotic prescribing adherence rate in antibiotic resistant

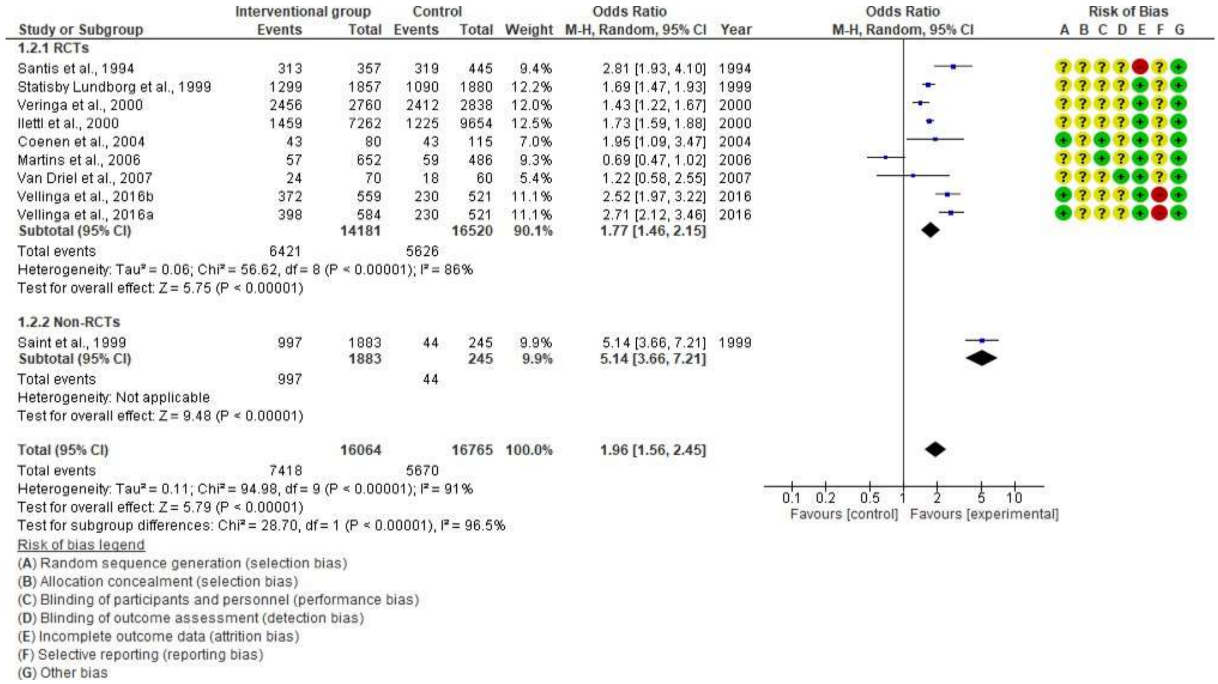

Figure 3. The effect's forest plot of the pharmacists involved intervention in antibiotic prescribing adherence rate and individual control compared with pharmacists involved intervention in antibiotic prescribing rate in antibiotic resistant

Table 3. Risk of bias assessment for RCTs using the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0

	Random seq. generation	Rand conc.	Blinding participants	Blinding outcome	Incomplete outcome	Selective reporting	Others
Marcia Vervloet1	u	u	u	u	l	u	h
C. Stålsby Lundborg	u	u	u	u	l	u	l
C.C.M. Veningaa	u	u	u	u	l	u	l
Samuel Coenen	l	u	l	u	l	u	l
HAMIDEH M. ESMAILY	H	u	u	u	l	u	l
M L van Driel	u	u	u	l	l	u	l
Jody D Martens	u	u	l	u	l	u	l
Akke Vellinga	l	u	u	u	l	H	l
Ineke Welschen	u	u	u	l	l	u	l
Kenneth F. Ilett	u	u	u	u	l	u	l
Giovanna De Santis	u	u	u	u	H	u	l

Table 4. Risk of bias for the observational non-randomized trials New - Ottawa Quality Assessment Scale for cohort studies.

Study_ID	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascert. Of exposure	Outcome_not present at start	Comparability	Assess. Of outcome	followup period	Adeq. Followup	Total
Rachel Wilf-Miron	*	*	*	*	*	*	*	*	8
FM Smeets	*	*	*	*	*	*	*		7
Sanjay Saint	*	*	*	*	*	*	*	*	8
Karl Weiss	*	*	*	*	*	*	*	*	8

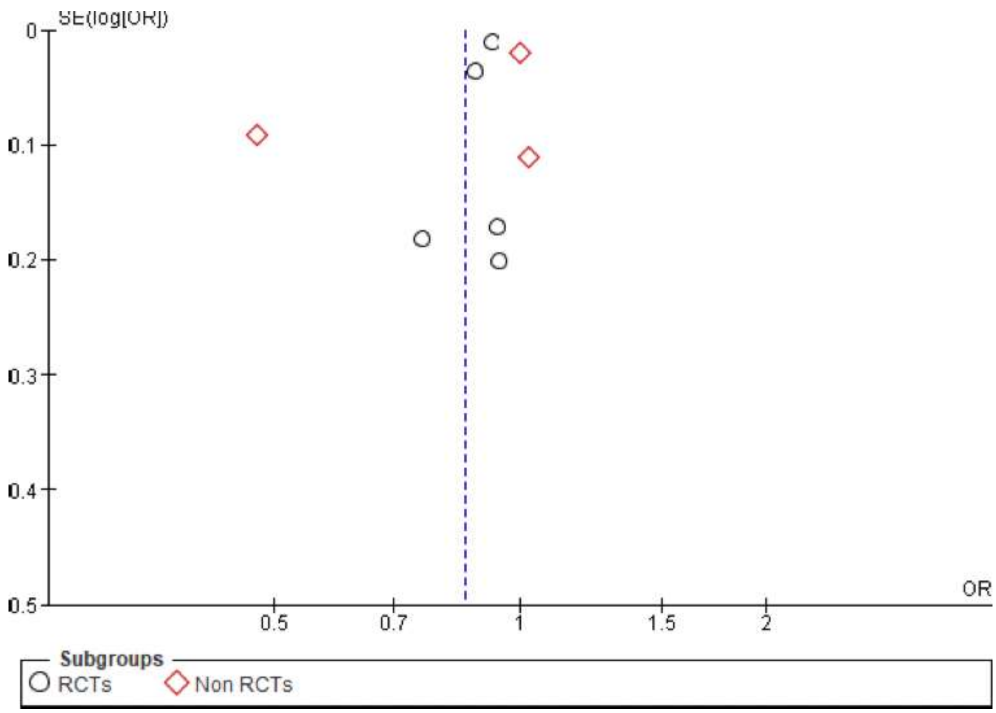

Figure 4. The funnel plot of The effect's forest plot of pharmacists involved intervention in antibiotic prescribing rate, and individual control compared pharmacists involved intervention in antibiotic prescribing adherence rate in antibiotic resistant.

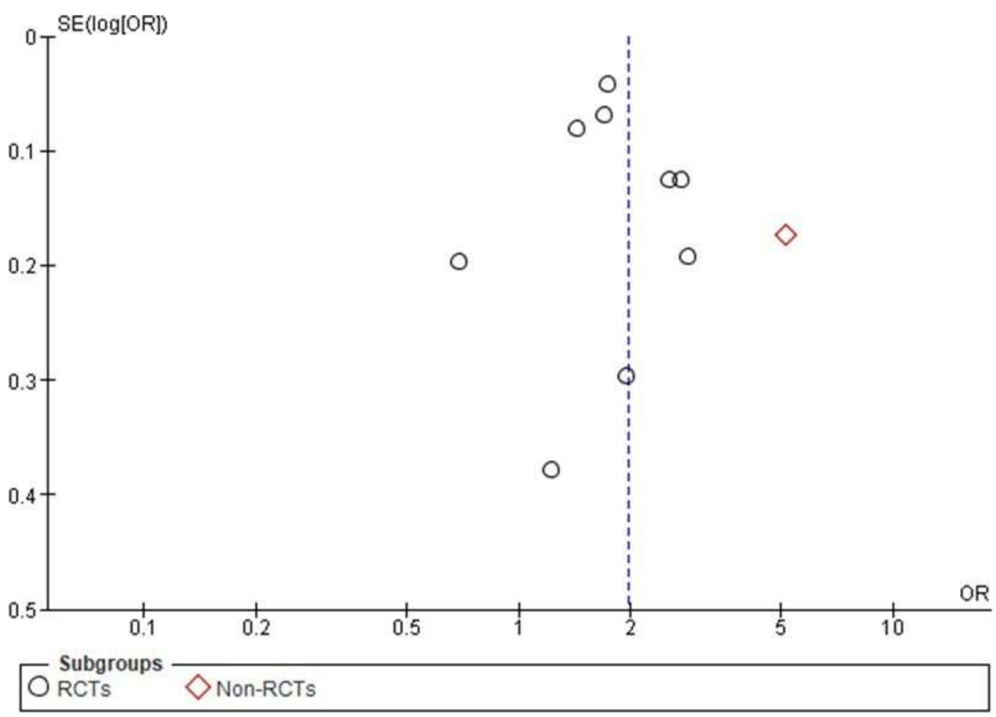

Figure 5. The funnel plot The effect's forest plot of the pharmacists involved intervention in antibiotic prescribing adherence rate and individual control compared with pharmacists involved intervention in antibiotic prescribing rate in antibiotic resistant.

Discussion

In investigations that were considered for the meta-analysis, individuals with antibiotic resistant were in the chosen investigations' starting point, 134004 of them were utilizing pharmacist involved in antibiotic prescribing rate and adherence rate, [19-33] and 164335 were utilizing indivisual control, pharmacists involved intervention in antibiotic prescribing rate had significantly lower antibiotic resistant, and indivisual control compared pharmacists involved intervention in antibiotic prescribing adherence rate in individuals with antibiotic resistant.

We identified 35 antibiotic stewardship intervention trials conducted in the USA, UK,
Australia, Europe, and Asia, where pharmacists played a key role in optimizing antibiotic prescribing practices by General Practitioners (GPs). Our comprehensive meta-analysis provided compelling evidence, with moderate to high certainty, that Antibiotic Stewardship Programs (ASPs) involving pharmacists led to reduced Antimicrobial Prescription Rates (APR) and increased adherence to Antimicrobial Prescribing Appropriateness Rates (APAR). [34]

Effective strategies included GP education combined with feedback on prescribing and interactive group meetings between GPs and pharmacists. These approaches effectively lowered APR and raised APAR among GPs. Our findings align with a review by Davey et al., which noted that interactive meetings outperformed didactic lectures and contributed to improvements in laboratory resources. [35]

We also observed that GP education, academic detailing, and workshop training involving pharmacists were effective in enhancing GP APAR. Overall, ASPs involving pharmacists consistently produced gradual improvements in the quality of antibiotic prescribing by GPs. While we couldn't definitively establish the superiority of specific intervention strategies, our results underscore the importance of exploring diverse approaches and implementation methods involving pharmacists in future research. [36]

Our research revealed that Antibiotic Stewardship Programs (ASPs) involving pharmacists were more effective in increasing guideline-compliant antibiotic prescribing by GPs than in reducing overall antibiotic prescribing. [37] Understanding the factors contributing to this difference, including their impact on GPs' prescription behaviors, warrants further investigation. [38]

It's worth noting that there is limited literature available on ASP implementation approaches within community settings. Most of the ASPs analyzed in our meta-analysis followed a team-based implementation approach. Our analysis indicated that interventions were more likely to succeed in reducing the Antimicrobial Prescription Rate (APR) and improving the Antimicrobial Prescribing Appropriateness Rate (APAR) when facilitated jointly by a pharmacist and a GP. Additionally, interventions involving pharmacists and other infectious disease healthcare professionals were effective in enhancing the APAR. While there were limited studies on pharmacist-led ASPs, our findings still suggested their effectiveness in improving the APAR. [39]

Though the precise quantification of pharmacists' impact on intervention success remains challenging, it is clear that pharmacists can significantly contribute to the implementation of community-based Antimicrobial Stewardship Programs (ASPs) in collaboration with General Practitioners (GPs). This assertion is substantiated by a study revealing substantial improvements in stewardship facilitated by pharmacists, even in settings with limited infectious disease resources. [40]

Our review underscores the valuable expertise of pharmacists in delivering effective antibiotic prescribing education and training to GPs. This education can take various forms, including academic detailing, consensus group meetings, and workshop training. When a trained pharmacist provides GPs with education covering topics such as antibiotic pharmacotherapy, pharmacokinetics, pharmacodynamics, problem-based case studies, antibiotic spectra, resistance patterns, and evidence-based local or disease-specific antibiotic guidelines, it can have a positive influence on GPs' antibiotic prescribing behavior. [41]

Furthermore, involving pharmacists in interdisciplinary guideline development and implementing these guidelines using audit and feedback strategies, as is done in the inpatient setting, could prove beneficial in implementing Antibiotic Stewardship Programs (ASPs) in GP settings. However, to effectively implement ASPs involving pharmacists, it is crucial to establish a system-supported network between GPs and pharmacists and to implement a structured mechanism for providing feedback on antibiotic prescribing. [42]

In summary, advocating for the role of pharmacists in the implementation of ASPs among GPs can support the promotion of optimal antibiotic prescribing practices, contribute to the sustainability of available antibiotics, and help mitigate the threat of antimicrobial resistance within the community. [43]

Our review underscores the importance of establishing a policy-driven collaboration between General Practitioners (GPs) and pharmacists to address obstacles to optimal antibiotic prescribing. The WHO European survey, covering 15 European countries, highlights the positive impact of GP-pharmacist network groups in shaping desired antibiotic prescribing behaviors in general practice settings. [44]

While our review has identified models for involving pharmacists in GP Antibiotic Stewardship Programs (ASPs), there remains a need for more substantial evidence regarding the direct influence of pharmacists on GPs' day-to-day antibiotic prescribing practices. Additionally, it is crucial to evaluate the feasibility, long-term sustainability, and acceptability of such interventions within specific local contexts. [45]

In summary, this review underlines the existing gaps in evidence for interventions aimed at enhancing the quality of antibiotic prescribing by GPs and offers recommendations for future research to address these gaps in the context of pharmacist-involved ASPs. [46]

This review has several limitations that need to be considered. Firstly, although we initially identified 45 eligible studies, our ability to conduct a comprehensive meta-analysis was hampered by the lack of interpretable data in 15 of these studies. This limitation was primarily due to incomplete data reporting, limited author responses, and a high risk of bias. Consequently, our meta-analysis was not as extensive as desired, even though many of the excluded studies did report positive effects for the outcomes under investigation. [47]

Secondly, we were unable to evaluate the effectiveness of individual components within multicomponent Antibiotic Stewardship Programs (ASPs) because many studies reported combined results for interventions. Additionally, we could not determine the potential superiority of one intervention component over others. [48]

Thirdly, our ability to calculate the Antimicrobial Prescribing Appropriateness Rate (APAR) at the level of specific antibiotic doses or regimens was constrained because APAR measurement was typically based on GPs' adherence to guidelines or recommendations in choosing antibiotics. [49]

Fourthly, we couldn't precisely quantify the absolute impact of pharmacist involvement in ASPs due to methodological complexities in intervention design, delivery, and components across different studies. Moreover, there were no studies directly comparing the effectiveness of ASPs with and without pharmacist involvement. [50]

Fifthly, we observed substantial heterogeneity among the included studies, but we couldn't identify the specific factors contributing to this variabilit y. Likely sources of heterogeneity could include the complex settings in which GPs operate, variations in study designs, and the diverse nature of interventions and their implementation strategies. Sixthly, we conducted numerous subgroup analyses, which can increase the risk of Type I errors. [51]

However, these analyses were conducted according to our published protocol and should be viewed as exploratory, providing a basis for further research in this area.Lastly, it's important to note that our findings may not be fully generalizable to low- and middle-income countries, as our review primarily focused on higher- income settings. Our review possessed several notable strengths. It represents the first systematic review, as far as our knowledge extends, that systematically evaluated the impact of Antibiotic Stewardship Programs (ASPs) involving pharmacists on the enhancement of antibiotic prescribing practices by General Practitioners (GPs). To ensure rigor and transparency, we registered this review with PROSPERO and conducted thorough searches across eight prominent medical databases to identify pertinent studies. [33]

Furthermore, we adhered to best practices for systematic reviews, aligning with the PRISMA-P guidelines and employing the TIDieR template to comprehensively describe the interventions under investigation. To assess the quality of evidence, we applied the GRADE framework, ensuring a robust evaluation process. [32]

Our review offers recommendations for future research endeavors in the realm of pharmacist-involved Antibiotic Stewardship Programs (ASPs). It suggests a focus on optimizing implementation strategies through feasibility studies conducted within various contexts. These studies should explore pharmacist-led interventions, those co-led by pharmacists and GPs, and those led by a collaboration between pharmacists and infectious disease health professionals in the context of antibiotic stewardship. [31]

In addition, future research should delve into assessing guideline compliance in antibiotic prescribing at the level of specific doses and dose regimens. The outcomes of interest should encompass changes in the prescription of broad- spectrum antibiotics by GPs and patient safety indicators, including clinical outcomes, allergy occurrences, and side effects. [30]

To enhance the robustness of future research, it is advisable to include comprehensive reporting of antibiotic prescribing data from both pre- and post- intervention periods for both control and intervention groups. Furthermore, the design of future ASPs should consider incorporating both pharmacy and non- pharmacy intervention arms for a more comprehensive assessment. [29]

Lastly, evaluating the impact of reductions in antibiotic prescribing and adherence to guidelines by GPs on reducing the prevalence of antibiotic resistance within the community is crucial. This assessment can serve as a measure of ASP effectiveness and contribute to building an evidence base for the development of collaborative GP-pharmacist team- based care models for implementing community-based ASPs. [28]

To summarize, our meta-analysis has provided evidence supporting the effectiveness of Antibiotic Stewardship Programs (ASPs) involving pharmacists in reducing antibiotic prescribing and promoting guideline-adherent antibiotic prescribing by General Practitioners (GPs), particularly in the short term. Promising ASP strategies that engage pharmacists include GP education combined with prescribing feedback, group meetings, workshop training, and academic detailing, all of which contribute to enhancing the quality of antibiotic prescribing in community settings. [27]

Implementing team-based ASPs with pharmacists and exploring the barriers to changing GPs' antibiotic prescribing behavior are essential steps for planning and executing future, more complex ASPs in general practices. The dissemination of our findings has the potential to influence policy, promoting greater collaboration between GPs and pharmacists in ASPs. [26]

To further bridge the evidence gap and emphasize the role of pharmacists, there is a need for more high-quality ASP trials involving pharmacists, particularly in the GP and community contexts. These trials should not only focus on generating evidence but also prioritise the utilisation of pharmacists in the effective implementation and sustainability of community ASPs. [25]

Lastly, our study underscores the importance of establishing a comprehensive intervention framework within a collaborative GP-pharmacist network to better evaluate appropriate antibiotic prescribing measures. This approach should encompass considerations of feasibility, acceptability, and sustainability within GP ASPs. [24]

This meta-analysis confirmed the efficacy involving the intervention of pharmacists on antibiotic prescribing rate and antibiotic prescribing adherence rate on the management of antibiotic resistant. More inspection is still desirable to clarify these feasible influences. This was also emphasised in former investigations that utilised a related meta-analysis procedure and originate equivalent values of the efficacy. Although the meta-analysis was incapable to discover if differences in these characteristics are related to the outcomes being researched, properly-led RCTs are vital to consider these aspects as well as the mixture of different ages, and ethnicities of individuals. In conclusion, pharmacists involved intervention in antibiotic prescribing rate had significantly lower antibiotic resistant, and individual control compared pharmacists involved intervention in antibiotic prescribing adherence rate. [23]

As we mentioned the 15 studies that were included in our research, those studies had different titles and research topics but were all reaching the same point that our research based on which is including the antibiotic resistant either this were related to the urinary or respiratory tract infection as in some studies included in our research, the education intervention and other topics but all related to the main purpose of our research related to the intervention can lower and end the antibiotic resistant, we managed to collect different kind of studies to analyse the different intervention and targeting the pharmacists as if there intervention will assess with the general physicians to lower and stop the antibiotic resistant , we got the significant outcome of how the pharmacist intervention can make a huge different as part of the health system. [22]

Limitations

Since some of the investigations involved in the meta-analysis were not included, there might have been selection bias. The omitted publications, however, did not fulfil the necessities for inclusion in the meta-analysis. Also, we lacked the expertise to determine whether factors like age, and ethnicity influenced results. The purpose of the investigation was to measure the effect of pharmacists intervention involved in antibiotic prescribing rate and the efficacy of the pharmacists interventions involved in antibiotic prescribing adherence rate on the management of antibiotic resistant. Bias may have grown because incomplete or incorrect data from earlier research were included. Possible sources of bias involved the individuals' nutritional status in addition to their race, and age. Unwontedly, incomplete data and certain unpublished work may distort the value that is being examined.

Conclusions

Pharmacists involved intervention in antibiotic prescribing rate had an influence significantly, and individual control compared pharmacists involved intervention in antibiotic prescribing adherence rate. However, care must be exercised when dealing with these values due to the low sample size of some of the nominated for the meta-analysis. That would affect the level of significance of the evaluation studied. We are really going to use our research as a start to make a different with the antibiotic misuse and over use and with the cooperation between the physicians and the pharmacists there will be a bigger chances to success and also applying such a program like the antibiotic stewardship in our countries will have a huge impact in a long term.

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