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Audit and Feedback Interventions for Antibiotic Prescribing in Primary Care: A Systematic Review and Meta-analysis

Alice X. T. Xu,[1,2] Kevin Brown,[1,2] Kevin L. Schwartz,[1,2,3] Soheila Aghlmandi,[4] Sarah Alderson,[5] Jamie C. Brehaut,[6,7] Benjamin C. Brown,[8] Heiner C. Bucher,[9] Janet Clarkson,[10,11] An De Sutter,[12] Nick A. Francis,[13] Jeremy Grimshaw,[6,14] Ronny Gunnarsson,[15,16,17] Michael Hallsworth,[18,19] Lars Hemkens,[9,20,21,22] Sigurd Høye,[23] Tasneem Khan,[5] Donna M. Lecky,[24] Felicia Leung,[25] Jeremy Leung,[26] Morten Lindbæk,[23] Jeffrey A. Linder,[27] Carl Llor,[28,29,30] Paul Little,[13] Denise O'Connor,[31] Céline Pulcini,[32,33] Kalisha Ramlackhan,[1] Craig R. Ramsay,[34] Pär-Daniel Sundvall,[15,16,17] Monica Taljaard,[6,7] Pia Touboul Lundgren,[35] Akke Vellinga,[36] Jan Y. Verbakel,[37,38] Theo J. Verheij,[39] Carl Wikberg,[15,16] and Noah Ivers[40]

[1]Public Health Ontario, Toronto, Ontario, Canada; [2]Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada; [3]Li Ka Shing Knowledge Institute, Unity Health Toronto, Toronto, Ontario, Canada; [4]Paediatric Research Center, University Children's Hospital Basel (UKBB), Basel, Switzerland; [5]Leeds Institute of Health Sciences, University of Leeds, Leeds, United Kingdom; [6]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada; [7]School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada; [8]Centre for Primary Care and Health Services Research, School of Health Sciences, University of Manchester, Manchester, United Kingdom; [9]Pragmatic Evidence Lab, Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), Basel, Switzerland; [10]School of Dentistry, University of Dundee, Dundee, United Kingdom; [11]NHS Education for Scotland, Dundee, United Kingdom; [12]Department of Public Health and Primary Care, Center for Family Medicine UGent, Ghent University, Ghent, Belgium; [13]Primary Care Research Centre, University of Southampton, Southampton, United Kingdom; [14]Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada; [15]General Practice / Family Medicine, School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [16]Research, Education, Development & Innovation, Primary Health Care, Region Västra Götaland, Gothenburg, Sweden; [17]Centre for Antibiotic Resistance Research (CARe), University of Gothenburg, Gothenburg, Sweden; [18]The Behavioural Insights Team, Brooklyn, New York, USA; [19]Center for Social Norms and Behavioral Dynamics, University of Pennsylvania, Philadelphia, Pennsylvania, USA; [20]Pragmatic Evidence Lab, Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel and University of Basel, Basel, Switzerland; [21]Meta-Research Innovation Center Berlin (METRIC-B), Berlin Institute of Health, Berlin, Germany; [22]Meta-Research Innovation Center at Stanford (METRICS), Stanford University, Stanford, California, USA; [23]Antibiotic Centre for Primary Care, Department of General Practice, Institute of Health and Society, University of Oslo, Oslo, Norway; [24]Primary Care & Interventions Unit, HCAI, Fungal, AMR, AMU& Sepsis Division, UK Health Security Agency, London, United Kingdom; [25]Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada; [26]Faculty of Science, McGill University, Montreal, Quebec, Canada; [27]Division of General Internal Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; [28]University Institute in Primary Care Research Jordi Gol, Via Roma Health Centre, Barcelona, Spain; [29]CIBER de Enfermedades Infecciosas, Instituto de Salud Carlos III, Madrid, Spain; [30]Research Unit for General Practice, Department of Public Health, University of Southern Denmark, Odense, Denmark; [31]School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia; [32]Université de Lorraine, APEMAC, Nancy, France; [33]Université de Lorraine, CHRU-Nancy, Centre régional en antibiothérapie du Grand Est AntibioEst, Nancy, France; [34]Health Services Research Unit, University of Aberdeen, Aberdeen, United Kingdom; [35]Department of Public Health, Nice University Hospital, Nice, France; [36]CARA Network, School of Public Health, Physiotherapy and Sports Science, University College Dublin, Dublin, Ireland; [37]Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium; [38]NIHR Community Healthcare Medtech and IVD cooperative, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom; [39]Julius Center for Health Sciences and Primary Care, UMC Utrecht, Utrecht, The Netherlands; and [40]Women's College Hospital, Toronto, Ontario, Canada

Background. This systematic review evaluates the effect of audit and feedback (A&F) interventions targeting antibiotic prescribing in primary care and examines factors that may explain the variation in effectiveness.

Methods. Randomized controlled trials (RCTs) involving A&F interventions targeting antibiotic prescribing in primary care were included in the systematic review. Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, and ClinicalTrials.gov were searched up to May 2024. Trial, participant, and intervention characteristics were extracted independently by 2 researchers. Random effects meta-analyses of trials that compared interventions with and without A&F were conducted for 4 outcomes: (1) total antibiotic prescribing volume; (2) unnecessary antibiotic initiation; (3) excessive prescription duration, and (4) broad-spectrum antibiotic selection. A stratified analysis was also performed based on study characteristics and A&F intervention design features for total antibiotic volume.

Results. A total of 56 RCTs fit the eligibility criteria and were included in the meta-analysis. A&F was associated with an 11% relative reduction in antibiotic prescribing volume (N = 21 studies, rate ratio [RR] = 0.89; 95% confidence interval [CI]: .84, .95; I2 = 97); 23% relative reduction in unnecessary antibiotic initiation (N = 16 studies, RR = 0.77; 95% CI: .68, .87; I2 = 72); 13% relative reduction in prolonged duration of antibiotic course (N = 4 studies, RR = 0.87 95% CI: .81, .94; I2 = 86); and 17% relative reduction in broad-spectrum antibiotic selection (N = 17 studies, RR = 0.83 95% CI: .75, .93; I2 = 96).

Conclusions. A&F interventions reduce antibiotic prescribing in primary care. However, heterogeneity was substantial, outcome definitions were not standardized across the trials, and intervention fidelity was not consistently assessed.

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Correspondence: N. Ivers, Women's College Hospital, 76 Grenville St, Toronto, ON M5S1B2 Canada (Noah.Ivers@wchospital.ca).

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The burden of antimicrobial resistance (AMR) continues to rise, with 1.27 million attributable deaths to bacterial AMR worldwide in 2019 [1]. Overprescribing and inappropriate prescribing of antibiotics is associated with AMR, along with increased risk of adverse effects, and increased healthcare costs [2]. Antimicrobial stewardship aims to optimize antimicrobial use to achieve the best clinical outcomes and combat the AMR crisis [3]. Primary care settings account for a vast majority of human antibiotic consumption worldwide, making it a crucial target for antimicrobial stewardship activities [4–6]. It is estimated in some regions that at least one-quarter of antibiotics prescribed in primary care settings are unnecessary [7, 8], making this a viable target for quality improvement interventions.

Audit and feedback (A&F) is a quality improvement strategy that involves measuring of professional performance, with results subsequently provided to clinicians and/or their teams to encourage positive change in clinical practice [9]. A&F interventions can be effective antibiotic stewardship strategies by including content that targets the underlying psychosocial reasons for inappropriate prescribing behaviors, including perceived patient expectations, clinician habits, and lack of accountability [10]. However, a variety of implementation details can impact the effectiveness of the interventions [11–13]. A number of randomized control trials (RCTs) have evaluated antibiotic A&F specifically in the context of primary care, which resulted in inconsistent findings with regards to the extent of the effectiveness of antibiotic A&F, likely due to varying study and intervention designs [14–16].

Antimicrobial stewardship interventions have been systematically reviewed for hospital settings [17, 18]. As a crucial setting for quality improvement, we sought to evaluate the evidence within the more narrow context of primary care. This systematic review aimed to summarize the effects of A&F interventions on the volume and appropriateness of antibiotic prescribing in primary care. We further aimed to describe how the effects of A&F interventions vary by study and intervention characteristics.

METHODS

The reporting of this systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist [19]. The protocol for this study was registered and published with Prospero [CRD42022298297].

Search Strategy

We searched within the included studies of the latest A&F Cochrane Review update [20], which were originally identified through electronic database searches in Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (Ovid), EMBASE (Ovid), CINAHL (Ebsco), and ClinicalTrials.gov up to June 2020. No language restriction was applied to the searches. The A&F Cochrane Review update includes all professional behavior change outcomes. The present meta-analysis enabled a more focused and detailed analysis of A&F targeted antibiotic prescribing in primary care. An updated search of the same databases was conducted in February 2022 and May 2024. An additional manual search of references of was conducted following the February 2022 search.

Using a web-based collaboration software platform, COVIDence [21], 2 reviewers (A. X. and F. L.) independently screened the titles and abstracts of search results from the updated literature search. Full texts of potentially eligible studies and all included studies from the Cochrane review were then assessed against the eligibility criteria. Discrepancies were resolved by discussion and/or consultation with third reviewer (N. I.) for final decision.

Eligibility Criteria

Types of studies: RCTs of any type of design (parallel, crossover, stepped wedge) and unit of analysis (individual, cluster).

Types of participants and settings: Healthcare professionals including, but not restricted to, general practitioners (GPs), family physicians, pediatricians, nurse practitioners, and dentists, responsible for antibiotic prescribing in primary care settings, which is defined as any primary contact with health care services.

Types of interventions and comparators: Interventions featuring A&F alone or as part of a multi-component intervention targeting improvements in antibiotic prescribing behavior in at least 1 arm of the RCT. Comparators include no intervention or usual care, or other non-A&F interventions aimed to reduce antibiotic prescribing.

Types of outcome measures: Studies evaluating antibiotic prescribing volume and/or appropriateness of antibiotic prescribing (unnecessary antibiotic initiation, excessive prescription duration, and broad-spectrum antibiotic selection) were considered.

Data Extraction

We used a predefined extraction spreadsheet and at least 2 reviewers independently extracted data. Extracted data included study characteristics, participant characteristics, A&F intervention details, and outcome results.

Risk of Bias Assessment

At least 2 reviewers independently assessed the risks of bias of included studies using the revised Cochrane risk of bias tool for randomized trials (RoB 2) [22]. Additional considerations for cluster-randomized trials and stepped-wedge designs were assessed accordingly [23]. All included studies were assessed for bias arising from the randomization process, the identification or recruitment of participants into clusters, deviations from intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result. Using the RoB 2 tool, each study was given a judgement of low risk of bias, some concerns, or high risk of bias. Discrepancies were resolved by consensus and/or consultation with third reviewer (N. I.) for final decision.

Outcomes

Four outcome metrics were identified and analyzed: antibiotic prescribing volume (primary outcome for this review), unnecessary antibiotic initiation, prolonged antibiotic prescription course, and broad-spectrum antibiotic selection. For the outcomes related to antibiotic appropriateness and selection, we used the trial authors' definition for the outcomes. For example, some authors defined unnecessary based on specific billing codes for typically viral infections and the specific approach varied across trials. In some studies, the intervention to reduce broad-spectrum antibiotics focused on reducing floroquinolones, in others, it sought to limit use of a wider range of antibiotics. For the prolonged antibiotic prescription outcome, we defined >7 days as long duration.

Stratification Variables

We included the following variables to generate stratified effect estimates of A&F on antibiotic prescribing volume: level of feedback (team vs individual clinician); year of study publication (before vs after 2010); risk of bias (low, some concerns, high); primary care patient population (pediatric, nursing home, general public); multifaceted intervention (A&F alone vs as part of a multifaceted intervention); high income country (based on World Bank definitions [24]); feedback frequency (single feedback episode vs multiple episodes); feedback interval if multiple episodes (monthly [>0 to 2 month intervals], quarterly [3 to 5 month intervals], annually [≥ 6 month intervals]); diagnostic focus (urinary, respiratory, other, or mixed); study design (stepped-wedge, pre-post, post-only); baseline total antibiotic use in the country of conduct (defined daily doses [DDD] per person year < 9 [median] vs DDD per person year ≥ 9); number of clusters (<100, 100–999, ≥ 1000).

Analysis

We conducted a random effects meta-analysis using the contrast-based generalized linear mixed models framework [25]. Prior to conducting the meta-analysis, results from each study were reanalyzed using separate Poisson regression models to estimate prescribing rate ratios (RR). For studies without baseline data, covariates included the study arm only (ie, with A&F or without A&F). For studies with baseline data, covariates included the arm (as above) and whether the measurement was part of the pre-intervention baseline or the follow-up period. Case counts were adjusted to account for estimated intracluster correlation (ICC) using the approach outlined by the Cochrane Collaborative [26], using the reported ICC, or falling back to an ICC of 0.10, the median of the reported ICCs. For the only crossover trial, we extracted data at the end of the first period. For factorial trials, we compared arms with audit to arms without audit and feedback. Stepped-wedge studies could not be reanalyzed based on tabulated data and as such we used study derived estimates. These study-specific effects (derived and reported) were then used for the subsequent meta-analyses. We fit a random effects meta-analysis model for each of the 4 outcomes, with each outcome treated separately.

We also conducted stratified analyses to examine whether the observed antibiotic prescribing volume differed according to pre-planned variables, as well as sensitivity analyses to examine the impact of the median ICC assumption used in the primary analysis. The stratified estimates were estimated from 12 separate models that included the stratification variable as the only variable in the model. To better understand the impacts of the assumed ICC for studies not reporting ICC on our results, we redid our analyses using ICCs corresponding to the 25th (0.05) and 75th (0.25) percentile of reported ICCs, when studies did not report the ICC.

Funnel plots were constructed using the sample size and effect size of studies for each of the 4 outcomes to evaluate the possibility of publication bias.

All analyses were conducted in R, version 4.3.2, and the metafor package [27].

Finally, we applied GRADE to assess the overall confidence in our findings for each of the 4 outcomes, specifically considering the domains of risk of bias, consistency of effect, imprecision, indirectness, and publication bias to upgrade or downgrade the stated confidence in results [28].

RESULTS

The search and selection process are shown in Figure 1. Within the included studies of the A&F Cochrane review, from the June 2020 database search, we applied the eligibility criteria and excluded 262 studies due to ineligible participant setting or outcome measures. From the February 2022 database search, 4447 titles and abstracts were screened, and 222 full texts were assessed using the eligibility criteria. An additional search update was conducted in May 2024. In total, 56 trials were included: 31 studies from the Cochrane review; 11 studies from the June 2020 literature search; 9 studies from the May 2024 search; and 5 studies from manual reference reviews.

Study Characteristics

Table 1 provides the basic characteristics of all 56 included studies, which were all clustered RCTs, conducted in 16 different countries. The publication years ranged from 1982 to 2024, with 66% (N = 37) published in the last 10 years. Patient populations varied between adult (N = 46), pediatric (N = 5), and

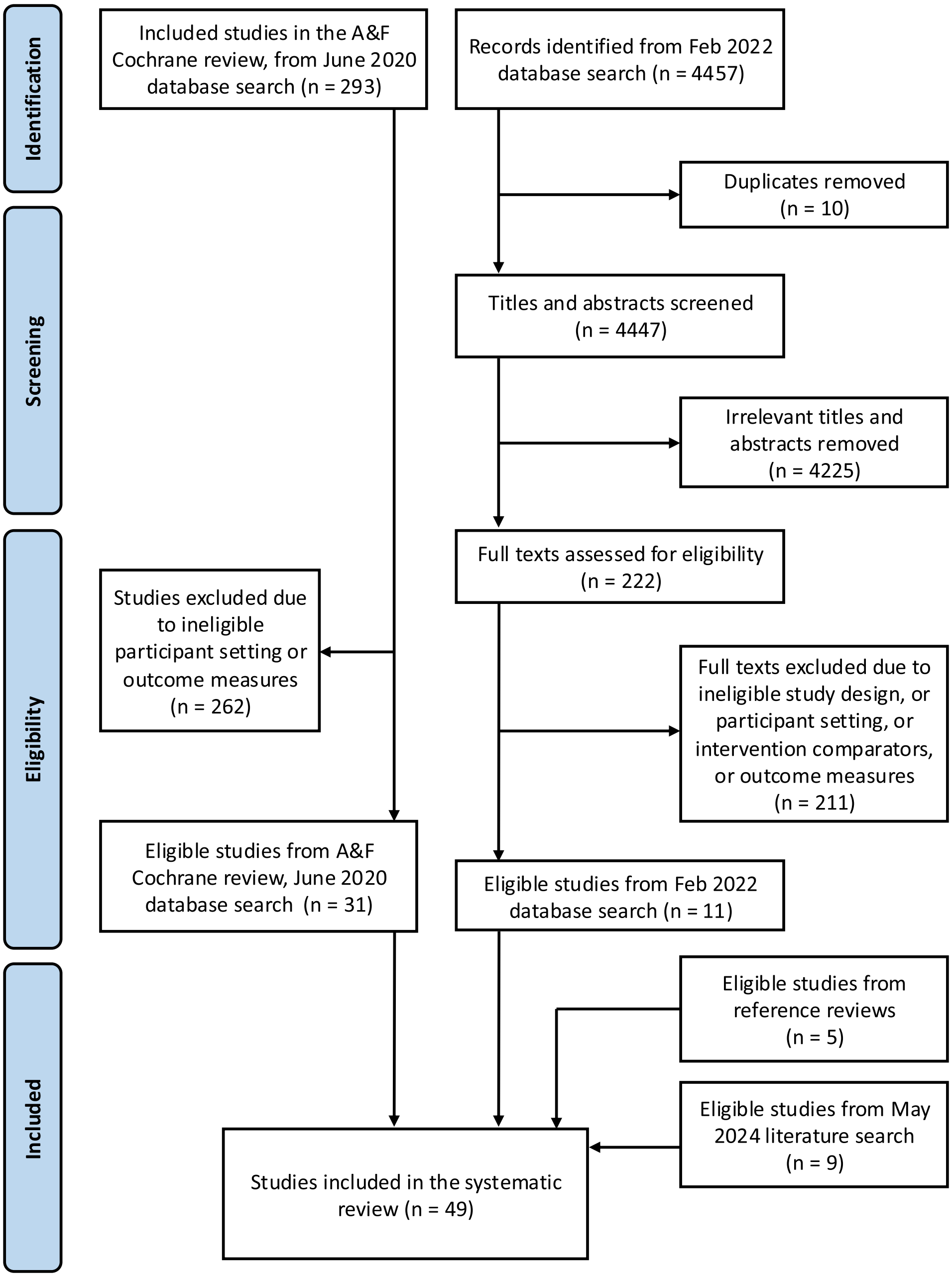

Figure 1. PRISMA flow diagram for the study selection process. Abbreviation: A&F, audit and feedback.

nursing homes (N = 5). Over half of the included studies had interventions with multiple feedback episodes (60.7%, N = 34), although other studies only had interventions with a single feedback episode (39.3%, N = 22).

Intervention Characteristics

Each RCT had at least 1 study arm that included A&F alone or as part of a multifaceted intervention. Specific intervention characteristics are summarized at the arm level. A total of 142 study arms were identified from the 56 included studies, including 59 arms without A&F as an intervention (treated as control arms). Out of the 83 arms with A&F as an intervention, 22 arms only provided team level feedback to healthcare professionals, 50 arms only provided individual prescriber feedback, and 11 arms provided both team and prescriber level feedback. In terms of feedback frequency, 33 arms provided a single episode of feedback, whereas 50 arms provided multiple episodes of feedback, with frequency ranging from every 10 days (eg, electronic dashboard updates), to monthly, quarterly, semi-annually, and annually.

Table 1. Study Characteristics of all Included Studies (N = 56)

Study_ID	Country of Conduct	Patient Population	Number of Clusters	Intervention Duration (months)	Feedback Frequency
Aghlmandi 2023 [39]	Switzerland	Adult	3170	24	Multiple
Awad 2006 [40]	Sudan	Adult	20	3	Multiple
BETA 2018 [41]	Australia	Adult	3198	6	Single
Carney 2023 [42]	Canada	Adult	2378	12	Single
Chang 2020 [43]	China	Adult	31	7	Multiple
Chappell 2021 [31]	New Zealand	Adult	1260	3	Single
Curtis 2021 [44]	UK	Adult	1392	12	Multiple
Daneman 2021 [45]	Canada	Nursing home	1238	12	Multiple
Daneman 2022 [38]	Canada	Nursing home	1263	3	Multiple
Dutcher 2022 [46]	USA	Adult	30	6	Multiple
Du Yan 2021 [47]	USA	Adult	45	11	Multiple
Elouafkaoui 2016 [34]	UK	Adult	1988	12	Multiple
Eltayeb 2005 [48]	Sudan	Adult	80	5	Single
Finkelstein 2001 [49]	USA	Pediatric	12	12	Single
Finkelstein 2008 [50]	USA	Pediatric	16	36	Multiple
Gerber 2013 [51]	USA	Pediatric	18	12	Multiple
Gjelstad 2013 [52]	Norway	Adult	79	12	Single
Gold 2022a [32]	UK	Adult	920	6	Single
Gold 2022b [53]	UK	Adult	688	6	Single
Gonzales 2013 [54]	USA	Adult	22	6	Single
Gulliford 2019 [55]	UK	Adult	79	12	Multiple
Hallsworth 2016 [14]	UK	Adult	1581	6	Single
Hemkens 2017 [15]	Switzerland	Adult	2814	24	Multiple
Hurlimann 2015 [56]	Switzerland	Adult	136	24	Multiple
Hux 1999 [57]	Canada	Adult	250	6	Multiple
Kahan 2009 [58]	Israel	Adult	298	4	Single
Kronman 2020 [59]	USA	Pediatric	19	16	Multiple
Lagerlov 2000 [60]	Norway	Adult	196	12	Single
Linder 2010 [61]	USA	Adult	27	9	Multiple
Lundborg 1999 [62]	Sweden	Adult	36	12	Single
McConnell 1982 [63]	USA	Adult	33	6	Single
Meeker 2016 [64]	USA	Adult	47	18	Multiple
Mitchell 2021 [65]	USA	Nursing home	28	12	Multiple
Mortrude 2021 [66]	USA	Adult	8	3	Single
Nace 2020 [67]	USA	Nursing home	22	12	Multiple
Naughton 2009 [68]	Ireland	Adult	98	6	Single
O'Connell 1999 [69]	Australia	Adult	2440	12	Multiple
Persell 2016 [70]	USA	Adult	28	12	Multiple
Pettersson 2011 [71]	Sweden	Nursing home	46	7	Single
Poss-Doering 2021 [72]	Germany	Adult	14	24	Multiple
Schmiemann 2023 [73]	Germany	Adult	110	12	Multiple
Schwartz 2021 [16]	Canada	Adult	3465	12	Single
Schwartz 2024 [74]	Canada	Adult	5046	6	Single
Shen 2018 [75]	China	Adult	24	12	Multiple
Singer 2022 [76]	Canada	Adult	178	24	Multiple
Soleymani 2019 [77]	Iran	Adult	809	3	Single
Sondergaard 2003 [78]	Denmark	Adult	181	24	Single
Trietsch 2017 [79]	Netherlands	Adult	21	36	Multiple
van der Velden 2016 [80]	Netherlands	Adult	86	12	Multiple
Vellinga 2016 [81]	Ireland	Adult	30	6	Multiple
Vervloet 2016 [82]	Netherlands	Adult	8	12	Single
Wei 2017 [83]	China	Pediatric	25	6	Multiple
Welschen 2004 [84]	Netherlands	Adult	12	12	Multiple
Yang 2014 [85]	China	Adult	20	6	Multiple
Yang 2023 [86]	China	Adult	328	3	Multiple
Zwar 1999 [87]	Australia	Adult	156	24	Multiple

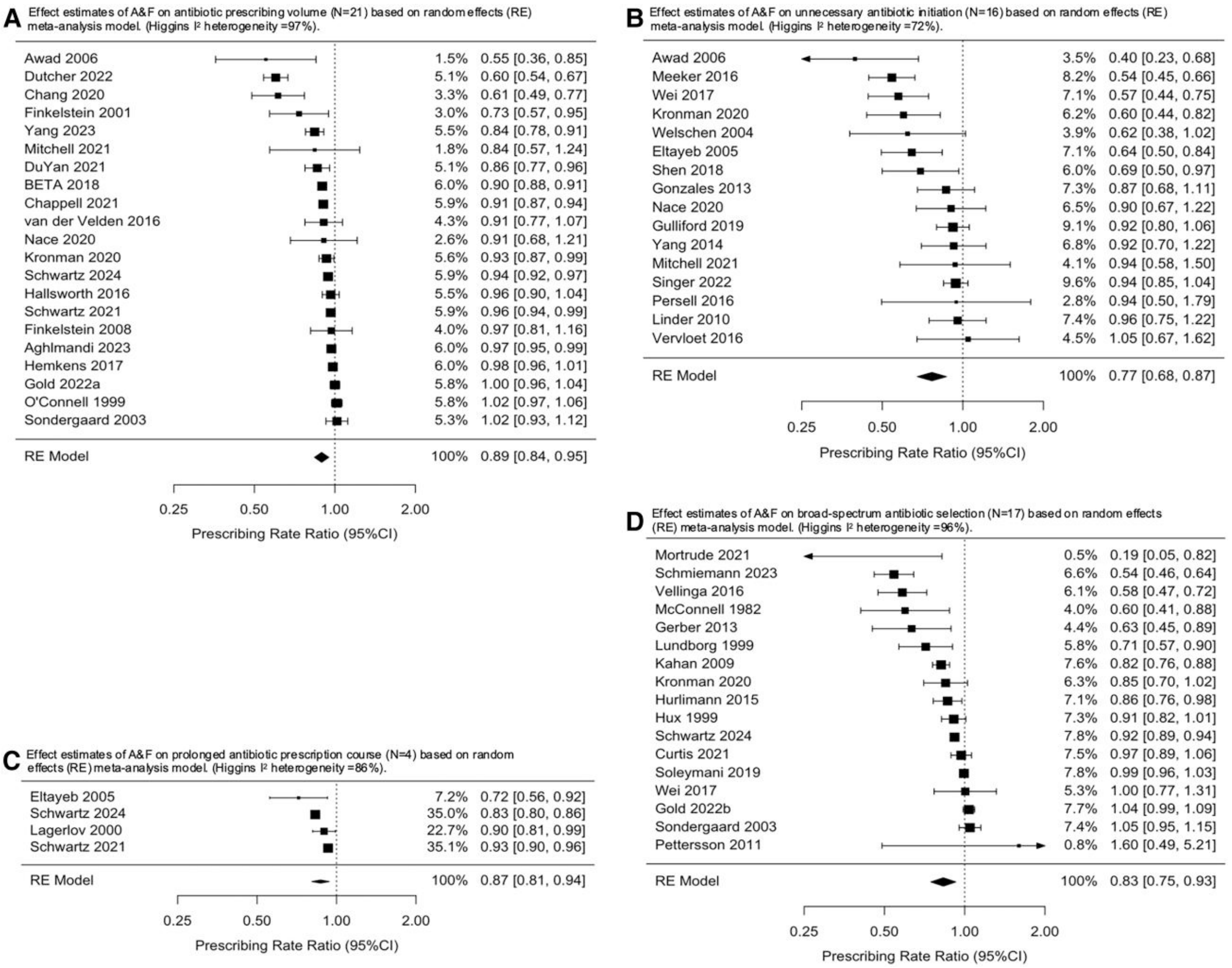

Figure 2. *A*, Effect estimates of A&F on antibiotic prescribing volume (N = 21) based on RE meta-analysis model (Higgins I^2 heterogeneity = 97%). *B*, Effect estimates of A&F on unnecessary antibiotic initiation (N = 16) based on RE meta-analysis model (Higgins I^2 heterogeneity = 72%). *C*, Effect estimates of A&F on prolonged antibiotic prescription course (N = 4) based on RE meta-analysis model (Higgins I^2 heterogeneity = 86%). *D*, Effect estimates of A&F on broad-spectrum antibiotic selection (N = 17) based on RE meta-analysis model (Higgins I^2 heterogeneity = 96%). Abbreviations: A&F, audit and feedback; RE, random effects.

Risk of Bias

Seven studies were judged as high risk of bias, 14 studies had some concern, and 35 studies had low risk of bias. Among the 7 high risk studies, 5 studies had high risk of bias in the domain measurement of the outcome. Commonly, this related to manual extraction of prescription data by unblinded research team members. Details for each study are summarized in Supplementary Table 1.

Effects on Antibiotic Prescribing

All 56 studies directly compared A&F versus no A&F and were included in the meta-analyses; these included a total of 36 547 randomized clusters (ie, prescribers or clinics). Of the 56 studies, 21 contributed to the antibiotic prescribing volume outcome (23 792 clusters), 16 contributed to the unnecessary initiation outcome (639 clusters), 4 contributed to the prolonged duration outcome (8787 clusters), and 17 contributed to the broad-spectrum antibiotic selection outcome (9125 clusters); studies could contribute to multiple outcomes. Figure 2 presents the meta-analysis results for effect estimates of A&F on antibiotic prescribing volume (2A), unnecessary initiation of antibiotic prescribing (2B), prolonged duration of antibiotic prescribing (2C), and broad-spectrum antibiotic selection (2D). A&F was associated with a reduced risk for all 4 antibiotic prescribing outcomes. The RR for antibiotic prescribing volume was 0.89 (95% confidence interval [CI]: .84 to .95) with a Higgins I^2 of 97%; unnecessary antibiotic initiation RR = 0.77 (95% CI: .68 to .87) with a Higgins I^2 of 72%; prolonged antibiotic prescription course RR = 0.87 (95% CI: .81 to .94) with a Higgins I^2 of 86%; broad-spectrum antibiotic selection RR = 0.83 (95% CI: . 75 to .93) with a Higgins I^2 of 96%.

Figure 3 presents the effect estimates of A&F on antibiotic prescribing volume (N = 21) stratified by prespecified covariates. Most variables evaluated demonstrated consistent effect

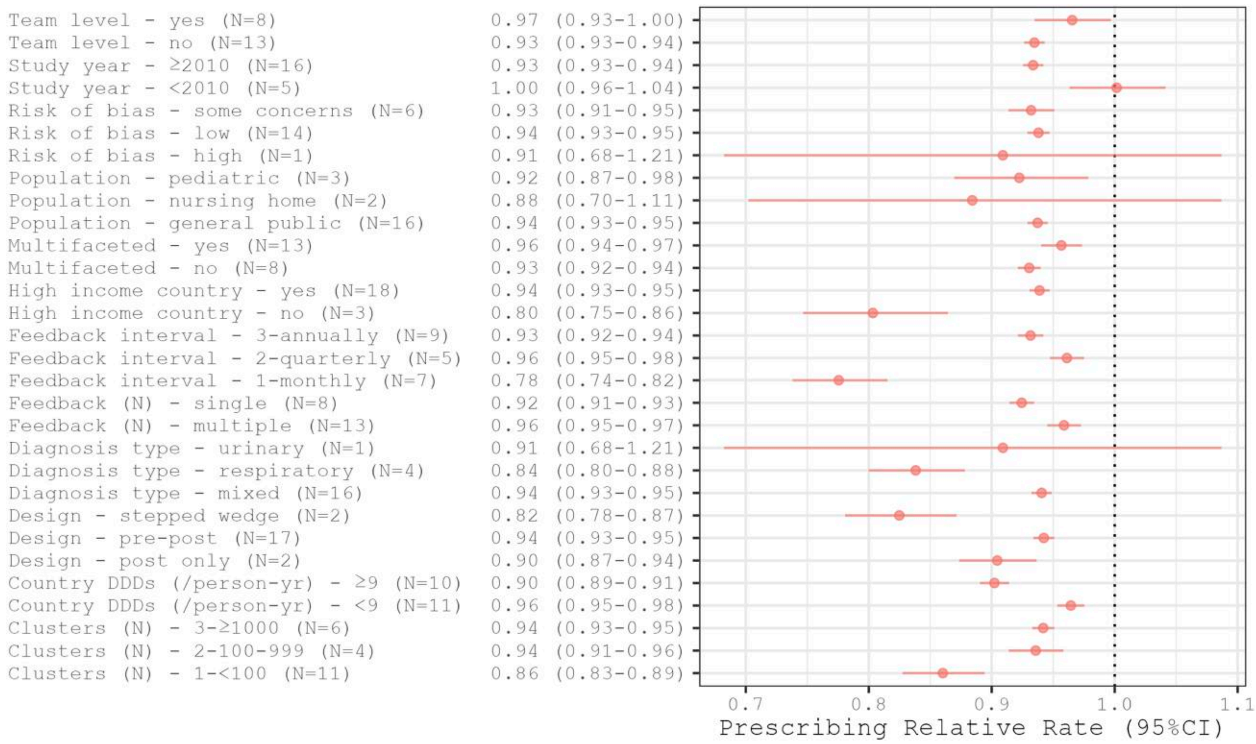

Figure 3. Stratified effect estimates of A&F on antibiotic prescribing volume. Abbreviations: A&F, audit and feedback; CI, confidence interval.

sizes for antibiotic A&F in primary care, including risk of bias, multifaceted intervention. All stratified *P*-values were significant (<.05) except ROB and patient population. Low income countries compared to high income countries, and countries with higher antibiotic use, compared to those with lower antibiotic use, appeared to have larger effect sizes. Effect sizes appeared larger for monthly (RR 0.78; 95% CI: .74–.82) compared with quarterly (RR 0.96; 95% CI: .95–.98) or annually (RR 0.93; 95% CI: .92–.94) administered feedback trials; however, differences should be interested cautiously as these represent indirect comparisons.

Sensitivity Analyses

We observed strong asymmetry for the volume and selection outcomes based on funnel plots, with significant Egger tests computed for both these outcomes (Supplementary Figure). Based on 24 ICCs reported from 9 studies, the median ICC was 0.10 (p25 = 0.048, p75 = 0.250). We observed comparable effect estimates for all 4 outcomes when using alternative ICC values for studies that didn't report ICCs (Supplementary Table 2).

Certainty of Findings

We downgraded confidence in results for antibiotic volume and antibiotic selection to low due to unexplained inconsistency in results beyond those described in the stratified results, and potential risk of reporting bias. We downgraded confidence in results for antibiotic appropriateness from high to moderate due to inconsistency. For antibiotic duration, we downgraded confidence in results to low due to inconsistency and because 1 of the 4 studies (the 1 with greatest effects) was at high risk of bias.

DISCUSSION

Our meta-analysis of 56 studies on A&F for antibiotic prescribing in primary care settings identified improvement in all four antibiotic prescribing outcomes evaluated. We observed an 11% relative reduction in antibiotic prescribing volume, 23% relative reduction in unnecessary antibiotic initiation, 13% relative reduction in prolonged duration of antibiotic course, and 17% relative reduction in broad-spectrum antibiotic selection. Although the included studies were conducted across a range of contexts and tests a variety of intervention components, the similarity across outcomes is striking. It is certainly possible that future studies would lead to adjustments in these estimates of effects but given the number, size, and quality of included trials, it seems unlikely that future trials would reverse the direction of effects observed.

Findings from our meta-analysis are consistent with existing evidence to support the effectiveness of A&F interventions in reducing the number of antibiotic prescriptions [12]. Zeng et al reported an overall rate difference of 4% for social norm feedback [12]; similarly, Ivers et al generally reported relative small improvements in professional practice performance for A&F interventions [29]. It is challenging to directly compare these absolute risk reductions to the relative effect sizes calculated in our meta-analyses. However, our findings of greater effects in lower income countries and in jurisdictions with greater antibiotic use fits with prior evidence suggesting that A&F is more effective when recipients have greater room for improvement.

The specific components of A&F interventions likely contributes to the effectiveness of the intervention [11, 30]. In the stratified analysis on antibiotic volume, we attempted to delineate the potential effect modifiers related to greater effect sizes for A&F interventions. Of note, studies providing monthly feedback, compared to quarterly or annual feedback [14, 16, 31, 32], appeared to have larger effect sizes. This finding highlights the importance of repeating A&F interventions, which is consistent with published best practice guidelines for feedback delivery [33]. There is a paucity of direct evidence in the literature to demonstrate the ideal frequency of feedback delivery. Indirect comparisons may be affected by available resources and the context-specific nature of A&F interventions. In fact, 1 trial directly testing repetition of antibiotic A&F to dentists (0, 6, and 9 months vs 0 and 6 months) did not show a difference [34], highlighting the need for ongoing head-to-head studies to advance best practices for A&F.

Our results contribute to the growing evidence base for the effectiveness of A&F interventions to modify prescribing behaviors for antibiotics in primary care settings. To advance the field of A&F, there may no longer be clinical equipoise to conduct 2-arm trials with a control arm without antibiotic A&F, especially in jurisdictions where there are substantial over-prescribing of antibiotics in primary care [35, 36]. Future work should focus on comparing different ways to deliver antibiotic prescribing feedback to address numerous unanswered questions [33]. Though our stratified analyses did not find that high risk of bias studies reliably produced in greater effect estimates, it is important that future trials blind outcome assessors and/or apply computerized assessment of prescribing quality.

This review has some limitations. Heterogeneity was substantial. The use of outcome definitions of antibiotic appropriateness as defined by the original study authors likely resulted in the observed heterogeneity in the outcomes between studies. We did not conduct further analyses of co-interventions of A&F in the included study arms, and these co-interventions may have contributed to the observed effectiveness of A&F intervention [37]. It is unclear which types of co-interventions work best to produce the most significant reductions in inappropriate antibiotic prescribing behavior, although we observed that studies with A&F alone as an intervention were similar to those of studies with multifaceted interventions. Furthermore, we did not assess the quality of the A&F intervention implementation and engagement with the feedback; which can both contribute to the observed effectiveness of the trials. Prior studies have identified relatively low engagement with A&F interventions [38]. There may be several other intervention characteristics that contribute or affect the effectiveness of A&F that were not extracted and analyzed in the present meta-analysis; including the presence of peer group discussion of feedback on prescribing, the nature of feedback delivery (ie, passive delivery via an electronic dashboard or active request of data from prescribers), and the types of guidance on behavioral change [37].

CONCLUSION

A&F can improve antibiotic prescribing in primary care settings, especially if delivered frequently in contexts with greater room for improvement. If data are available, repeated interventions that include A&F should be prioritized in AMR national action plans.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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