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Interventions to improve antibiotic prescribing practices for hospital inpatients

Cochrane Review | Antibiotics | Carrie L. Scott, Jennifer Cooper, Kristy McNeil, Kevin Brown, Ian M Gould, Craig A Ramsay, Mark Pallett | Cochrane Infectious Diseases Group
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differences.

We chose to use the mean difference for RCTs and ratios of means (ROMs) for other studies, which accounts for baseline differences. We used random-effects meta-analysis to combine effect sizes across studies. We assumed that the intervention effect would be similar regardless of the type of study and that heterogeneity would be due to clinical or methodological diversity. We used Hartung-Knapp-Sidik-Jonkman variance estimation and 95% CIs to account for the uncertainty in our estimates of heterogeneity.

We conducted a sensitivity analysis to assess the effect of the assumption that the intervention effect was fixed for all studies. We expected that the observed scale of the intervention effect would be proportional to the baseline risk of the outcome, so we used a fixed-effect ratio of means (FE-ROM) meta-analysis to combine the ratios of means across studies. We used the Knapp-Hartung adjustment to the standard error of the FE-ROM estimate and 95% CIs to account for the uncertainty in our estimate of the intervention effect. We expected the fixed effect of the intervention to be proportional to the baseline risk of the outcome, so we used a random-effects meta-analysis of the natural logarithm of the ratio of means (RE-lnROM) to combine effect sizes across studies. We used the Knapp-Hartung adjustment to the standard error of the RE-lnROM estimate and 95% CIs to account for the uncertainty in our estimate of the intervention effect. We back-transformed the RE-lnROM estimate and its 95% CI to the original scale for ease of interpretation.

We assessed the impact of interventions on mortality using risk ratios (RRs) and risk differences (RDs). We used the Mantel-Haenszel method to combine these effect sizes across studies. We did not include zero-event studies because this method uses the total number of events in the calculation of the RR and RD. We used the Sidik-Jonkman variance estimator and 95% CIs to account for the uncertainty in our estimates of heterogeneity.

We assessed the impact of interventions on ventilator-free days using the Gray proposal, which generalises the Wilcoxon test to incorporate ties and censoring. We did not include censored observations in the analysis. We used the Sidik-Jonkman variance estimator and 95% CIs to account for the uncertainty in our estimates of heterogeneity.

We assessed the impact of interventions on ordinal outcomes using proportional odds ratios (POR) and 95% CIs. We used the Sidik-Jonkman variance estimator and 95% CIs to account for the uncertainty in our estimates of heterogeneity.

We assessed the impact of interventions on time-to-event outcomes using the Peto method, which is a variant of the Mantel-Haenszel method that uses the observed minus expected number of events and the hypergeometric variance. We did not include zero-event studies because this method uses the total number of events in the calculation of the RR and RD. We used the Sidik-Jonkman variance estimator and 95% CIs to account for the uncertainty in our estimates of heterogeneity.

Sensitivity analysis

We used sensitivity analysis to assess the robustness of our results to the following decisions: choice of effect measure for dichotomous outcomes (RR versus RD), choice of effect measure for time-to-event outcomes (HR versus RD), choice of effect measure for continuous outcomes (MD versus SMD), choice of meta-analysis model for continuous outcomes (random-effects versus fixed-effect), choice of meta-analysis model for ratio of means outcomes (RE-lnROM versus FE-ROM), choice of variance estimator for the random-effects meta-analysis (Sidik-Jonkman versus DerSimonian-Laird), choice of variance estimator for the random-effects meta-analysis (Knapp-Hartung versus Wald-type), and choice of cut-point for ordinal outcomes (POR for adjacent versus cumulative categories).

Subgroup analysis and investigation of heterogeneity

We used meta-regression to investigate potential effect modifiers. In meta-regression, the outcome variable is the effect estimate (e.g., mean difference or risk ratio). We used covariates to explain some of the variation in the effect estimates across studies. We used the Knapp-Hartung adjustment to the standard error of the meta-regression estimate and 95% CIs to account for the uncertainty in our estimates of the effect of the covariate. We used the Sidik-Jonkman variance estimator and 95% CIs to account for the uncertainty in our estimates of heterogeneity.

We assumed that the subgroups are exchangeable. We used the following covariates in our meta-regression analyses:

- interventions that included tracheostomy versus those that did not;
- interventions that included a tracheostomy versus usual care;
- enabling interventions that included feedback versus those that did not;
- feedback interventions that included goal setting versus those that did not.

We used the following ordinal variables in the meta-regression because they might influence the size of intervention effect:

- 5-year year of publication;
- 5-year year of recruitment;
- sedation intensity (light versus deep);
- sedation agent (propofol versus benzodiazepine);
- ventilation mode (pressure versus volume);
- ventilation duration (short versus long);
- mortality;
- length of hospital stay;
- length of ICU stay;
- ventilator-associated pneumonia;
- negative cardiovascular effects.

We also assessed the evidence from the meta-regression in terms of the extent to which we believed it helped explain variation of effect. We included the following effect modifiers in our analysis:

- 5-year year of publication;
- 5-year year of recruitment;
- sedation intensity (light versus deep);
- sedation agent (propofol versus benzodiazepine);
- ventilation mode (pressure versus volume);
- ventilation duration (short versus long);
- mortality;
- length of hospital stay;
- length of ICU stay;
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- sedation agent (propofol versus benzodiazepine);
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- ventilation duration (short versus long);
- mortality;
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- length of ICU stay;
- ventilator-associated pneumonia;
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- sedation agent (propofol versus benzodiazepine);
- ventilation mode (pressure versus volume);
- ventilation duration (short versus long);
- mortality;
- length of hospital stay;
- length of ICU stay;
- ventilator-associated pneumonia;
- negative cardiovascular effects.

Results

Description of studies

Results of the search

The combined results of all literature searches are described in the study flow diagram (Figure 1).

Figure 1.

Figure 14: Study flow diagram.

Included studies

The Characteristics of included studies table lists 38 studies, of which 37 used the Intensive Care Unit-based design to evaluate the intended effect of intervention. Of the 38 studies, 34 RCTs, 3 cluster RCTs, 1 cohort, and 0 RCTs. The remaining 1 studies were designed to identify unintended consequences of interventions and used the following designs: 0 cohort (Cohort 2007, Dissertation 2014). Intensive Care Unit-based studies included a total of 4 000 participants, 2 000 in intervention and 2 000 in control (Collins 2003), and 1 participant (Jones Unpublished) in Intensive Care Unit-based RCTs (NCT 2011).

Geographical location of study

Ward-based studies included 152 participants. The remaining 152 were from Europe (n=0), includes Israel, Asia (n=0), South America (n=0), Australia (n=0), and East Asia (n=0). The number of studies by country (including the countries in Asia multinational studies) is: Canada (n=1), China (n=0), Denmark (n=0), Finland (n=0), France (n=0), Germany (n=0), Ireland (n=0), Israel (n=0), Italy (n=0), Netherlands (n=0), Norway (n=0), Spain (n=0), Sweden (n=0), Switzerland (n=0), Taiwan (n=0), Thailand (n=0), UK (n=0), USA (n=1).

Number of hospitals

A total of 20 (70%) studies were conducted in one hospital, 8 studies in 2 hospitals, 0 studies in 3 to 5 hospitals, and 0 studies in 6 or more hospitals.

Delivery of intervention

Of the 20 interventions, 0 (0%) were designed and delivered by a multidisciplinary team, 0 (0%) by specialist physicians (critical care, anesthesiologists), 0 (0%) by department physicians (e.g. emergency department or critical care), and 20 (100%) by nonspecialist physicians.

Funding

Five studies received some funding from manufacturers of drugs or devices (Jones Unpublished). The remaining 33 studies were funded by government agencies. No participating hospitals. Details are provided in the Characteristics of included studies table.

Power calculations

Details of power calculations are provided in Appendix 3.

Excluded studies

We excluded 114 ineligible studies from the review because they did not contain relevant or interpretable data. Reasons for studies for details, see the Characteristics of excluded studies.

Risk of bias in included studies

All 38 (100% and 100% were at high risk of bias (Figure 2). High risk of bias was more common in RCTs (34/34, 100%) than in ITS (0/0, 0%), CBA (0/0, 0%), or NRSI (0/0, 0%). Most of the risk were ITS studies (Figure 3). Among RCTs, high risk of bias was most common due to bias in outcome assessment (34/34, 100%) and bias in selection of participants (34/34, 100%). Bias in selection of participants was the most common reason for high risk of bias in ITS studies (0/0, 0%). Bias in selection of participants was the most common reason for high risk of bias in CBA studies (0/0, 0%). Bias in selection of participants was the most common reason for high risk of bias in NRSI studies (0/0, 0%). Bias in selection of participants was the most common reason for high risk of bias in Intensive Care Unit-based studies (34/34, 100%). Bias in selection of participants was the most common reason for high risk of bias in Ward-based studies (0/0, 0%). Bias in selection of participants was the most common reason for high risk of bias in studies with the intended effect of intervention (34/34, 100%). Bias in selection of participants was the most common reason for high risk of bias in studies with the intended effect of intervention (0/0, 0%). Bias in selection of participants was the most common reason for high risk of bias in studies with unintended consequences (0/0, 0%). Bias in selection of participants was the most common reason for high risk of bias in studies with unintended consequences (0/0, 0%).

Figure 2.

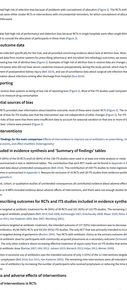

Figure 3.

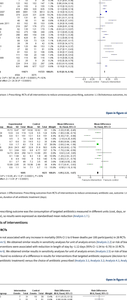

Figure 4.

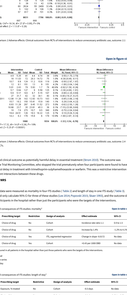

Figure 5.

Figure 6.

Figure 7.

Figure 8.

Figure 9.

Figure 10.

Figure 11.

Figure 12.

Figure 13.

Figure 14.

Allocation

Most of the RCTs had high risk of selection bias because of problems with concealment of allocation (Figure 5). The RCTs with low risk of selection bias used adequate methods for concealment of allocation (concealed by an external party, sealed opaque envelopes, or sealed, numbered containers).

Blinding

Most of the RCTs had high risk of performance and detection bias because of bias in RCTs is a single hospital were other single-blind and it was difficult to increase the allocation of participants in these trials (Figure 6).

Incomplete outcome data

The RCTs varied bias substantially for the risk and of provided convincing evidence about lack of attrition bias. Most of the RCTs had high risk of attrition bias because of problems with missing data (Figure 7). Attrition bias was the most common reason for high risk of attrition bias (Figure 7). Examples of high risk of attrition bias in studies were: the number of participants who did not have serum creatinine measure postoperatively during the study period, which may have underestimated the incidence of postoperative AKI (Jones 2006); the number of participants who underwent a follow-up chest x-ray was lower in the intervention arm (Kress 2000); and the number of participants who underwent a follow-up chest x-ray was lower in the intervention arm (Kress 2000). Most of the RCTs had low risk of attrition bias because of problems with the other RCTs

Hospital	1.000	1.000	1.000
Other	1.000	1.000	1.000

Intervention with a restrictive component

Prolong	0.667	0.667	Measures that facilitate suitable dosing patients with Cystic fibrosis	Pulmonary function	0.667	Moderate	Moderate
Prolong	0.667	0.667		Mortality	0.667	Moderate	Moderate
Prolong	0.667	0.667		Pulmonary function	0.667	Moderate	Moderate
Prolong	0.667	0.667		Mortality	0.667	Moderate	Moderate

CI95: confidence-bound pseudomedian
CI: confidence interval
OR: odds ratio
CI95: 95% CI on the pseudomedian OR

There was a restriction component to the intervention in seven studies. This study assessed the effectiveness of antimicrobial stewardship programmes in Cystic fibrosis patients. Two studies assessed the effectiveness of a restrictive component in Cystic fibrosis patients (0.667). The remaining five studies all assessed antimicrobial consequences of interventions that included antibiotics. Others by requiring prior approval, as follows.

- Negative antibiotical culture through treatment in trial and communication (Kayser 2012), Collins 2003, Conner 2001, Lindell 2003).
- Delay to time to first antibiotic (Kayser 2012, Kayser 2012, Kayser 2012, Kayser 2012).
- Delay in cultures (Kayser 2012).

In three studies (Friedberg 2009, Kayser 2007, Kayser 2008), the intervention was a national financial incentive to the GP and was intended to reduce time to first antibiotic dose for people admitted to hospital with community-acquired pneumonia (CAP). Two studies (Kayser 2007, Kayser 2008) reported a reduction in time to first antibiotic dose for people with CAP and antibiotic treatment. In two single studies, there was a decrease in the percentage of participant with correct diagnosis of CAP based on prospective criteria (Kayser 2007, Kayser 2008). In contrast, a single, multicentre study reported no evidence of an effect on time to first antibiotic dose for people with CAP (Kayser 2008) (0.667, moderate).

Explaining heterogeneity in the intended effect of interventions

Meta-regression of RCTs

Meta-regression of RCTs (Figure 7) shows that the effectiveness of interventions (Analysis 1.1) Figure 3). Outcomes for all or those with a particular exposure to control of antibiotic prescribed were associated with a positive effect (and participants. We did not perform meta-regression on 12 RCTs with continuous prescribing outcomes because the outcomes were too heterogeneous (Figure 8). We did not perform meta-regression on 10 RCTs with continuous prescribing outcomes because the outcomes were too heterogeneous (Figure 9).

Meta-regression results for 24 RCTs with dichotomous outcomes

In the meta-regression, unadjusted, restriction, targeting antibiotic choice versus exposure and high risk of bias were significantly associated with greater intervention effect in univariate analysis, and they all remained significant in multivariate analysis (Figure 7).

Figure 7 Open in figure viewer

Meta-regression for effect modifiers for 24 RCTs. A positive value for Beta indicates enhanced intervention effect. Unadjusted RCTs including and restriction component in the intervention (Figure 7).

OR for 24 RCTs of enabling interventions, four also included feedback (Lonsdale 2019, Schouten 2010, Schouten 2007, Tonkin 2005). All four of these RCTs targeted antibiotic choice, as we have compared their effects with other RCTs targeting other intervention targets. We did not perform meta-regression on 12 RCTs with continuous prescribing outcomes because the outcomes were too heterogeneous (Figure 8). We did not perform meta-regression on 10 RCTs with continuous prescribing outcomes because the outcomes were too heterogeneous (Figure 9).

Figure 8 Open in figure viewer

Meta-regression for effect modifiers for 24 RCTs. A positive value for Beta indicates enhanced intervention effect. Unadjusted RCTs including and restriction component in the intervention (Figure 8).

Figure 9 Open in figure viewer

Meta-regression for effect modifiers for 24 RCTs. A positive value for Beta indicates enhanced intervention effect. Unadjusted RCTs including and restriction component in the intervention (Figure 9).

Meta-regression of RCTs analysis

Do interventions that involve audit and feedback have greater intended effect?

There were 107 RCTs studies with data that could be used for meta-regression of prescribing outcomes at one, six, or 12 months' post-intervention. We used multivariable meta-regression to identify effect modifiers in 79 studies including data about prescribing as an outcome: randomisation, Audit and feedback, Target 1 Audit and feedback and restriction were independently associated with greater intervention effect (Figure 11). In comparison with interventions targeting different antibiotics, interventions that targeting choice were associated with greater effect (-0.45 (-0.7 to -0.2) Figure 11). Of studies (Figure 12). Of studies (Figure 13). Of studies (Figure 14). The National Institute's suggestion that restriction and targeting were not effective (Figure 11 Figure 12). The National Institute's suggestion that restriction and targeting were not effective (Figure 11 Figure 12).

Figure 10 Open in figure viewer

Meta-regression of prescribing outcomes by effect modifiers for 107 studies of interventions that included restriction.

Figure 11 Open in figure viewer

Meta-regression of prescribing outcomes by effect modifiers for 107 studies of interventions that included restriction.

Figure 12 Open in figure viewer

Meta-regression of effect modifiers for 107 studies of interventions that included restriction for one intervention. Outcomes in others are prescribing for a particular antibiotic. Are the four studies with Medium and Low risk of bias and prescribing outcomes. Any included restriction.

Are interventions that include feedback more effective than those that do not?

Feedback was included in 4 (12%) of 33 RCTs (Figure 3) and 20 (67%) of 30 RCTs studies (Figure 12). Of enabling interventions that included feedback, three (Figure 13). Of studies (Figure 14). Of studies (Figure 15). Of studies (Figure 16). Of studies (Figure 17). Of studies, audit and feedback was combined with review and recommendation changes in antibiotic prescribing. Interventions that included feedback were more effective than those that did not. However, there were no free studies with gain setting or action planning to assess their effect in addition to feedback.

There were only two RCTs studies with data that could be used for meta-regression of effect on antibiotic consumption to an effective intervention. Interventions that included feedback were more effective than those that did not.

Summary of interventions for the studies included in meta-regression

In comparison with RCTs, 24 RCTs studies were more likely to have restriction components. 36 (34%) of 56 RCTs studies (Figure 11). Of studies (Figure 12). Of studies (Figure 13). Of studies (Figure 14). Of studies (Figure 15). Of studies (Figure 16). Of studies (Figure 17). Of studies (Figure 18). Of studies (Figure 19). Of studies (Figure 20). Of studies (Figure 21). Of studies (Figure 22). The National Institute's suggestion that restriction and targeting were not effective (Figure 11 Figure 12

Microbial outcomes

Interventions were consistently associated with reduction in CDI, but less consistently associated with reduction in infection by resistant bacteria. However, intervention effects on microbial outcomes could only be analysed reliably in planned interventions (Figure 13), and our meta-analysis was limited by four technical challenges.

1. Each study had considerable variance because of the small number of microbial events in each time point.
2. Studies rarely had stable pre-intervention data, so that extrapolation of the pre-intervention trend throughout the postintervention phase was probably unreliable.
3. We analysed a single prescribing outcome for each study (even if more were reported). The criteria for selection of the prescribing outcome were determined by the analysis plan for the effect of interventions on prescribing behaviour. However, these criteria may not have been correct for analysis of the relationship between changes in prescribing and microbial outcomes.
4. We could only analyse the relationship between prescribing and microbial outcomes at fixed time points. We chose six and 12 months, respectively, imposing a six-month time lag for all interventions. However, the time lag will likely vary by prescribing and microbial outcomes, and by intervention context (Vernaz 2008).

Quality of the evidence

We found high-certainty evidence that interventions increase appropriate use of antibiotics, reduce duration of antibiotic treatment, and shorten hospital stay without increasing the risk of mortality. There was low-certainty evidence that these interventions can delay treatment and create a negative professional culture (summary of findings Table for the main comparison). High risk of bias was associated with greater intervention effect in RCTs (Figure 7) for the outcome of compliance with desired practice. However, we have presented separate analysis of effects for RCTs at low or medium risk of bias (Analysis 1.3; Analysis 1.6; Analysis 2.3; Analysis 2.6). These analyses provide evidence supporting our decision not to downgrade for risk of bias, since excluding studies at high risk of bias did not substantively change the direction of effect. We did not downgrade for inconsistency since the direction of effect across the studies was consistent, and our meta-regression provides some explanation for the high levels of statistical heterogeneity between the results of the studies. The certainty of evidence about adverse effects was more variable, with particular concerns about the unintended consequences of restrictive interventions, namely delays in treatment and negative professional culture, for which we have low-certainty evidence.

The quality of reporting of interventions was poor, which makes it difficult for professionals and clinical teams to reliably implement interventions that have been shown to be useful and for other researchers to replicate or build on research findings (Hoffmann 2014). We found high-certainty evidence that enablement and restriction both enhanced the effectiveness of interventions. However, we found only moderate-certainty evidence for the effectiveness of feedback, and there were too few studies with action planning and goal setting to provide any reliable information about the combined effects of these behaviour change techniques.

In the analysis of risk of bias equal weight is given to all criteria (Figure 2). Our results for microbial outcomes clearly showed that the risk of bias from unplanned interventions is much greater than the risk from other infection control interventions (Figure 13; Figure 14).

We found that some NRS study designs provided important additional evidence about intervention effects and sustainability in routine clinical practice (ITS studies) and about unintended consequences (case control, cohort, and qualitative studies). However, we found no useful evidence from CBAs or NRTs and suggest that these study designs should not be included in updates to this review.

Heterogeneity of intervention effect

We found that two intervention functions, enablement and restriction, explained some of the variation in targeted prescribing behaviour. However, we found little evidence that behaviour change theory had been used to design interventions (Charani 2011). There were too few interventions with explicit goals or action planning to include these variables in meta-regression.

There was no consistent evidence that intervention setting or target explained variation in the effect of interventions (Figure 7; Figure 10)

Potential biases in the review process

Our decision not to use adjusted data for cluster RCTs for the primary analysis could be contested. The consequences of using unadjusted data would be to assign too much weight to cluster studies in the analysis, potentially biasing the effect from our analyses to their results (Higgins 2011). We believe that taking clustering into account is unlikely to impact on the strength of the results in such a way as to change the conclusions of the review. Our sensitivity analyses provide some indirect support for the approach we have undertaken. In comparison to unadjusted results, analyses based on the effective sample sizes calculated from assumed ICCs consistently gave a larger average intervention effect (Analysis 1.1 versus Analysis 1.2; Analysis 2.1 versus Analysis 2.2; Analysis 2.4 versus Analysis 2.5).The increased effect size could be explained by the lower weight assigned to the cluster studies, which tended to have smaller effects than the individually randomised studies.

The electronic literature search did not identify 42 (19%) of the 221 included studies, highlighting some of the challenges in constructing sensitive search terms for reviews of behavioural interventions and the identification of non-randomised studies. It is possible that additional eligible studies have not been retrieved by the search process we undertook for this review.

We did not find evidence of publication bias in the RCTs, however publication bias is more likely in the ITS studies because the decision to publish may have been made after the analysis of intervention effect.

Agreements and disagreements with other studies or reviews

Agreements

Ivers 2012 included and analysed 140 RCTs that compared any intervention in which audit and feedback was a core, essential component to usual care and evaluated effects on professional practice. The review concluded that interventions were more effective if they also included goal setting and action planning. We were unable to reproduce their analysis because only four of our RCTs included feedback (Figure 8). Although 20 ITS studies included feedback (Figure 12), there were not enough studies with goal setting or action planning for reliable analysis.

Our findings are similar to a previous review that found that behavioural determinants and social norms were not given due consideration in the design and evaluation of interventions to change antibiotic prescribing (Charani 2011).

Sustainability of intervention effect

We found evidence that removal of restriction, in Himmelberg 1991, Kallen 2009, Kim 2008, and Skrlin 2011, or of review and recommend change (enablement, Standiford 2012) was associated with reversal of intervention effect (Table 7). Three previous studies have shown that removal of financial incentives is associated with reversal of intervention effects in primary care (Avery 2012; Dreischulte 2016; Lester 2010). This is an important issue because the attractiveness of interventions will be reduced if improvement resources cannot be moved on to new priorities. Restriction is a relatively low-cost intervention, but it is worrying that an enabling intervention (review and recommend change) apparently had no sustained effect on clinical teams after being in place for seven years (Standiford 2012). Review and recommend change is a time-intensive process that was included in 36 (54%) of 67 of the enabling interventions in ITS studies.

Disagreements

A systematic review on current evidence about antimicrobial stewardship objectives reported that "guideline-adherent empirical therapy was associated with a reduction for mortality (odds ratio 0.65, 95% CI 0.54-0.80)" (Schuts 2016). Only two of the 39 studies in this review reported an intervention: one was invalid because it was an uncontrolled before-after study (Garcia 2007), and the other was a CBA (Dean 2006). The remaining 37 studies used case control study or cohort designs to compare the outcomes of participants with and without guideline-adherent antibiotic treatment, and did not include an intervention to change professional practice. The results of this review are in marked contrast to our analysis of mortality in 11 RCTs targeting antibiotic choice (Analysis 3.1). The most likely explanation for the discrepancy between our results and Schuts 2016 is confounding by indication. It is likely that participants with less complex or severe illness were more likely to receive guideline-adherent antibiotic treatment and that there was residual confounding after adjustment for available clinical information.

A systematic review on the effect of antibiotic stewardship programmes on CDI reported that interventions were associated with a consistent, significant protective effect (pooled risk ratio for CDI 0.48, 95% CI 0.38 to 0.62) (Feazel 2014). Of the 16 studies included in this systematic review, four were ITS studies that were also included in our review (Elligsen 2012; Fowler 2007; Price 2010; Talpaert 2011), and the remaining 12 studies were either uncontrolled before-after or inadequate ITS studies. The statistical analysis in this review was not appropriate (Feazel 2014). Calculation of risk ratios for the post- versus pre-intervention periods is an uncontrolled before-after analysis, which does not provide a reliable estimate of intervention effect.

Additional details about the disagreements with Feazel 2014 and Schuts 2016 can be found in Appendix 7.

Limitations

There are five weaknesses in the current evidence.

1. Evidence of intended effects is unbalanced towards reducing unnecessary treatment (compliance with guidelines that are intended to reduce use of broad-spectrum antibiotics or shorten duration of treatment). More evidence is required about finessing effective treatment of sepsis without also causing excessive use of antibiotics.
2. The limited evidence regarding adverse effects of restrictive interventions suggests that they can be associated with delay in essential treatment. There is a need for better patient safety outcome measures that can be used in studies of interventions in clinical practice.
3. The majority of the interventions do not use effective behaviour change techniques such as action planning or feedback.
4. Given the critical role of junior doctors in antimicrobial stewardship in hospitals, it is surprising that there is only a single example of an intervention that involved junior doctors in self monitoring and reflection on feedback about their prescribing (Price 2010).
5. Analysis of the impact of interventions on microbial outcomes requires large, multihospital RCTs.

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