Association Between Selective Decontamination of the Digestive Tract and In-Hospital Mortality in Intensive Care Unit Patients Receiving Mechanical Ventilation
A Systematic Review and Meta-analysis

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IMPORTANCE The effectiveness of selective decontamination of the digestive tract (SDD) in critically ill adults receiving mechanical ventilation is uncertain.

OBJECTIVE To determine whether SDD is associated with reduced risk of death in adults receiving mechanical ventilation in intensive care units (ICUs) compared with standard care.

DATA SOURCES The primary search was conducted using MEDLINE, EMBASE, and CENTRAL databases until September 2022.

STUDY SELECTION Randomized clinical trials including adults receiving mechanical ventilation in the ICU comparing SDD vs standard care or placebo.

DATA EXTRACTION AND SYNTHESIS Data extraction and risk of bias assessments were performed in duplicate. The primary analysis was conducted using a bayesian framework.

MAIN OUTCOMES AND MEASURES The primary outcome was hospital mortality. Subgroups included SDD with an intravenous agent compared with SDD without an intravenous agent. There were 8 secondary outcomes including the incidence of ventilator-associated pneumonia, ICU-acquired bacteremia, and the incidence of positive cultures of antimicrobial-resistant organisms.

RESULTS There were 32 randomized clinical trials including 24,389 participants in the analysis. The median age of participants in the included studies was 54 years (IQR, 44-60), and the median proportion of female trial participants was 33% (IQR, 25%-38%). Data from 30 trials including 24,034 participants contributed to the primary outcome. The pooled estimated risk ratio (RR) for mortality for SDD compared with standard care was 0.91 (95% credible interval [CrI], 0.82-0.99; $I^2 = 33.9%$; moderate certainty) with a 99.3% posterior probability that SDD reduced hospital mortality. The beneficial association of SDD was evident in trials with an intravenous agent (RR, 0.84 [95% CrI, 0.74-0.94]), but not in trials without an intravenous agent (RR, 1.01 [95% CrI, 0.91-1.11]) ($P$ value for the interaction between subgroups = .02). SDD was associated with reduced risk of ventilator-associated pneumonia (RR, 0.44 [95% CrI, 0.36-0.54]) and ICU-acquired bacteremia (RR, 0.68 [95% CrI, 0.57-0.81]). Available data regarding the incidence of positive cultures of antimicrobial-resistant organisms were not amenable to pooling and were of very low certainty.

CONCLUSIONS AND RELEVANCE Among adults in the ICU treated with mechanical ventilation, the use of SDD compared with standard care or placebo was associated with lower hospital mortality. Evidence regarding the effect of SDD on antimicrobial resistance was of very low certainty.

Selective decontamination of the digestive tract (SDD) is a preventive infection control strategy that usually comprises the administration of nonabsorbable, topical antimicrobial agents to the oropharynx and upper gastrointestinal tract, with or without the administration of a short-term course of broad-spectrum intravenous antibiotics.

Since the 1980s, advocates have encouraged the use of SDD in patients receiving mechanical ventilation in the intensive care unit (ICU), primarily to reduce the incidence of ventilator-associated pneumonia. While a body of evidence suggesting reductions in hospital mortality and ventilator-associated pneumonia exists, concerns regarding the effect of SDD on the development of antibiotic resistance have left international guideline panels reluctant to recommend SDD and clinicians reluctant to implement in practice.

Evidence from randomized clinical trials (RCTs), including the Ecological Effects of Decolonisation Strategies in Intensive Care (RGNOSIS) trial and the Selective Decontamination of the Digestive Tract in Intensive Care Unit Patients (SuDDICU) study have recently added substantive weight to the body of evidence. To provide an updated summary of current evidence, this systematic review and meta-analysis was designed to address whether SDD compared with standard care was associated with reduced hospital mortality and other relevant outcomes including the incidence of antimicrobial-resistant organisms in patients in the ICU treated with mechanical ventilation.

Methods

We conducted a systematic review according to a prespecified published protocol (eAppendix 1 in the Supplement), registered at the International Prospective Register of Systematic Reviews (CRD42022309825), and report the review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.

Eligibility Criteria

We included RCTs and cluster RCTs that recruited ICU patients, of whom 75% or more were invasively ventilated, and compared the administration of SDD using antibacterial and/or antifungal agents to the upper gastrointestinal tract, stomach, or proximal small bowel with or without the administration of systemic antibiotics to standard care or placebo. Trials that administered only oral antiseptic agents as the intervention were excluded. Trials that included the routine use of topical antiseptic agents were included in the standard care comparator. We included all reports including studies only reported as abstracts, with no language restriction.

Search Strategy

We systematically searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL), from inception to September 12, 2022.

The search strategy included multiple medical subject heading terms and keywords to identify critically ill patients, mechanical ventilation, and selective decontamination of the digestive tract (SDD) or selective oral decontamination, combined with sensitive filters to identify RCTs including cluster and crossover RCTs. We limited the search to adult, human studies. We contacted experts and conducted manual searches of reference lists of included studies and other systematic reviews. eAppendix 2 in the Supplement provides details of the electronic search strategy.

Data Collection

Three investigators independently extracted data from each included trial using a standardized data collection form. We extracted all available data as outlined in the protocol, including characteristics of the included studies, design (RCT or cluster RCT), details of the enrolled population including demographics, illness severity, details of the intervention including oral and systemic agents, dose and duration, and comparison group information including use of topical antiseptics. We did not impute missing data. Continuous variables presented in formats not readily amenable to pooling were converted to mean and SD according to published methods. For the SuDDICU trial, we had access to the study data prior to publication. We resolved discrepancies in the data extracted by discussion or, if necessary, adjudication by a fourth reviewer.

Risk of Bias Assessment

Two investigators with no affiliation with the included trials independently assessed risk of bias for each of the included trials using DistillerSR, a tool assessing risk of bias in RCTs, modified to include items specific to cluster randomized trials developed by 3 of the authors (A.D., N.E.H., G.G.) and reported in eAppendix 4 in the Supplement. Disagreements were resolved by discussion and, if necessary, consultation with a third reviewer.

Outcomes

The primary outcome was hospital mortality. For trials in which hospital mortality was not reported, we used mortality reported...
at the closest time point to hospital mortality. Mortality was chosen as the primary outcome because it is not prone to ascertainment bias and is a patient-important outcome. Data were also collected for the following secondary outcomes: mortality at longest follow-up, incidence of ventilator-associated pneumonia, duration of mechanical ventilation, and ICU and hospital length of stay. We attempted to collect data regarding the incidence of positive cultures of antimicrobial-resistant organisms and the incidence of *Clostridioides difficile* using data as reported in the included trials, at both a unit level and an individual patient level. We were also able to obtain specific data regarding the incidence of ICU-acquired bacteremia, again as reported in the included trials.

### Subgroup Analyses

There were 3 prespecified subgroups for the primary outcome. We compared trials where the intervention consisted of SDD with oral and/or enteral agents only compared with SDD that included oral, enteral, and intravenous agents, with the specified hypothesis that there would be a greater reduction in mortality in trials that included intravenous agents as a component of the intervention. We compared trials conducted in surgical ICUs vs medical ICUs vs mixed population ICUs, with the specified hypothesis that there would be a greater reduction in mortality in trials conducted in surgical ICUs. We also compared individual patient--compared with unit-level randomization (ie, cluster and cluster/cluster-crossover), with the specified hypothesis that there would be a greater reduction in mortality in trials that randomized individual patients. We also performed a post hoc subgroup analysis based on publication date (before or after 2000). When results suggested possible subgroup effects, we used the ICEMAN guidelines to assess their credibility.

### Data Synthesis

The primary analysis used a Bayesian random-effects model. A Bayesian approach was chosen as the primary analytic method because it allows a more nuanced and explicit quantitative summary of the data that is potentially open to more intuitive interpretation by clinicians, as well as provides a more robust approach to the estimation of between-study heterogeneity. We performed the primary analysis using vague priors (log of the risk ratio assumed to have a normal distribution with a mean of 0 and an SD of 2) and sensitivity analyses examining treatment effects using weakly informative priors of effect and heterogeneity parameters. The full description of priors is reported in the protocol. In addition, a frequentist random-effects model using Hartung-Knapp-Sidik-Jonkman and Der-Simonian Laird estimates of the between-study variance have been used. Random-effects models for the sensitivity analysis were chosen a priori due to anticipated between-study variation in trial design and implementation of the interventions. We also performed a post hoc pooled secondary analysis limited to studies published as full reports in peer-reviewed journals. Because some of the included trials are cluster-randomized trials, we prospectively adjusted the raw data for the design effect by using an effective sample size approach, defined as the original sample size divided by the design effect. We present results as risk ratios (RRs) for binary outcomes and mean differences (MDs) for continuous outcomes. Along with the pooled estimates of effect sizes and 95% credible intervals (CrIs) for the Bayesian meta-analysis, we report 95% CIs for the frequentist model.

We assessed quantitative heterogeneity by reporting the posterior estimates of the heterogeneity parameter (tau) with its 95% CrI and the prediction interval of the intervention pooled effect size and by evaluating the proportion of total variability due to heterogeneity rather than due to sampling error (I²). Tests for between-subgroup interaction effects were assessed using the Cochran Q statistic.

Small-study effects were assessed by visual assessment of the contour-enhanced funnel plots and formal Egger regression test.

All statistical analyses were performed using R (for the Bayesian meta-analysis using the package bayesmeta and Stata version 17 (StataCorp LLC).

### Confidence in the Cumulative Evidence

We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to assess the overall certainty of evidence that SDD compared with standard care improves each outcome measure to any degree. We rated certainty in nonzero effects of SDD.
<table>
<thead>
<tr>
<th>Source</th>
<th>Design</th>
<th>Centers</th>
<th>Participants</th>
<th>Population</th>
<th>SDD</th>
<th>Control</th>
<th>Ventilated, %</th>
<th>Primary outcome of trial</th>
<th>Mortality time point</th>
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<tbody>
<tr>
<td>Unertl et al.55 1987</td>
<td>Individual patient RCT</td>
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<td>39</td>
<td>Mixed medical surgical</td>
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<td>Standard care</td>
<td>100</td>
<td>Colonization and respiratory infection</td>
<td>ICU</td>
</tr>
<tr>
<td>Kerver et al.54 1988</td>
<td>Individual patient RCT</td>
<td>1</td>
<td>96</td>
<td>Mixed medical surgical</td>
<td>Oral: every 6 h until oropharyngeal and tracheal cultures negative • Polymyxin E, 2%; tobramycin, 2%; amphotericin, 2% Enteral: every 6 h until oropharyngeal and tracheal cultures negative • Polymyxin E, 200 mg; tobramycin, 80 mg; amphotericin B, 200 mg Intravenous: 5 d • Cefotaxime, 50-70 mg/kg/d</td>
<td>Standard care</td>
<td>100</td>
<td>Prevention of colonization</td>
<td>ICU</td>
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<tr>
<td>Ulrich et al.53 1989</td>
<td>Individual patient RCT</td>
<td>1</td>
<td>100</td>
<td>Mixed medical surgical</td>
<td>Oral: 4 times/d until potentially pathogenic organism could no longer be isolated • Polymyxin E, 2%; norfloxacin, 2%; amphotericin, 2% Enteral: 4 times/d until potentially pathogenic organism could no longer be isolated • Polymyxin E, 100 mg; tobramycin, 80 mg; amphotericin B, 500 mg Intravenous: daily until potentially pathogenic organism could no longer be isolated • Trimethoprim, 500 mg</td>
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<td>80</td>
<td>Prevention of ICU-acquired infection</td>
<td>ICU</td>
</tr>
<tr>
<td>Rodríguez-Roldán et al.52 1990</td>
<td>Individual patient RCT</td>
<td>1</td>
<td>28</td>
<td>Mixed medical surgical</td>
<td>Oral: every 6 h • Polymyxin E, 2%; tobramycin or netilmicin, 2%; amphotericin B, 2%</td>
<td>Placebo</td>
<td>100</td>
<td>Colonization and infection in the respiratory system</td>
<td>ICU</td>
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<td>Aerdts et al.51 1991</td>
<td>Individual patient RCT</td>
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<td>56</td>
<td>Mixed medical surgical</td>
<td>Oral: 1 g every 6 h • Amphotericin, 2%; norfloxacin, 2%; polymyxin E, 2% Enteral: 4 times/d via nasogastric tube • Polymyxin E, 200 mg; norfloxacin, 50 mg; amphotericin B, 500 mg Intravenous: 3 times/d for 3 d • Cefotaxime, 500 mg</td>
<td>Standard care</td>
<td>100</td>
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<td>ICU</td>
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<td>Blair et al.50 1991</td>
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<td>331</td>
<td>Mixed medical surgical</td>
<td>Oral: 4 times/d for duration of ICU • Oral polymyxin, 2%; tobramycin, 2%; amphotericin, 2% Enteral: 4 times/d for duration of ICU • Polymyxin, 100 mg; tobramycin, 80 mg; amphotericin B, 500 mg Intravenous: 4 d • Cefotaxime, 50 mg/kg/d</td>
<td>Standard care</td>
<td>93</td>
<td>Infection</td>
<td>ICU</td>
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<tr>
<td>Gaussorgues et al.49 1991</td>
<td>Individual patient RCT</td>
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<td>118</td>
<td>Mixed medical surgical</td>
<td>Enteral: 4 times/d for duration of ventilation • Gentamicin, 20 mg; colistin, 36 mg; vancomycin, 50 mg; amphotericin B, 500 mg</td>
<td>Standard care</td>
<td>100</td>
<td>Nosocomial bacteremia</td>
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<td>Pugin et al.48 1991</td>
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<td>79</td>
<td>Surgical</td>
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<td>Cockerill et al.47 1992</td>
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<td>Oral: 4 times/d for duration of ICU • Gentamicin, 2%; polymyxin B, 2%; nystatin, 1 × 10^5 U/g Enteral: 4 times/d for duration of ICU • Gentamicin, 80 mg; polymyxin B, 100 mg; nystatin, 2 million units Intravenous: 3 times/d for 3 d • Cefotaxime, 1 g</td>
<td>Standard care</td>
<td>84.7</td>
<td>Infection rates</td>
<td>Hospital</td>
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</table>

(continued)
Results

We retrieved 7586 records. Figure 1 presents the results of the search and reasons for trial exclusion. The 32 eligible trials included 24389 participants, most of whom were enrolled in 3 cluster-crossover trials (18 335/24 389). The Table (and eTable 1 in the Supplement) present the characteristics of included trials. One trial was published only as an abstract, all other trials were published in peer-reviewed journals. Apart from the results of the SuDDICU trial, no additional unpublished data were

Table. Included Study Characteristics (continued)

<table>
<thead>
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<th>Primary outcome of trial</th>
<th>Mortality time point</th>
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<tbody>
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<td>Gastinne et al.46, 1992</td>
<td>Individual patient RCT</td>
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<td>445</td>
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<td>Placebo</td>
<td>100</td>
<td>Mortality at day 60</td>
<td>Hospital</td>
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<td>Jacobs et al.45, 1992</td>
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<td>76</td>
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<td>Standard care</td>
<td>100</td>
<td>Prevention of nosocomial pneumonia</td>
<td>ICU</td>
</tr>
<tr>
<td>Rocha et al.44, 1992</td>
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<td>101</td>
<td>191</td>
<td>Neurosurgical</td>
<td>Oral: 4 times/d for duration of ICU (max, 15 d) • Polymyxin E, 2%; tobramycin, 2%; amphotericin B, 2% Enteral: 4 times/d for duration of ICU • Polymyxin E, 100 mg; tobramycin, 80 mg; amphotericin, 500 mg Intravenous: 4 d • Cefotaxime, 2 g/d</td>
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<td>100</td>
<td>Infection rate</td>
<td>Hospital</td>
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<td>191</td>
<td>Neurosurgical</td>
<td>Oral: 4 times/d for duration of ventilation or commencement of enteral nutrition • Polymyxin E, 2%; tobramycin, 2%; amphotericin B, 2%; vancomycin, 2% Enteral: 4 times/d for duration of ventilation (max, 15 d) • Polymyxin E, 100 mg; tobramycin, 80 mg; amphotericin, 500 mg</td>
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<td>100</td>
<td>Duration of hospitalization and cost of antibiotic therapy</td>
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<td>Langlois-Karaga et al.42, 1995</td>
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<td>97</td>
<td>Trauma</td>
<td>Oral: 4 times/d for duration of ventilation or commencement of enteral nutrition • Colistin, gentamicin, amphotericin B Enteral: 4 times/d for duration of ventilation or commencement of enteral nutrition • Colistin, gentamicin, amphotericin B</td>
<td>Placebo</td>
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<td>148</td>
<td>Trauma</td>
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<td>ICU</td>
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<td>Abele-Horn et al.39, 1997</td>
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<td>148</td>
<td>Trauma</td>
<td>Oral: every 6 h for duration of ventilation • Amphotericin, 2%; tobramycin, 2%; polymyxin E, 2% Intravenous: 3 times/d for 3 d • Cefotaxime, 2 g</td>
<td>Standard care</td>
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<td>Colonization and infection rates</td>
<td>ICU</td>
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<th>Source</th>
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<th>Control</th>
<th>Ventilated, %</th>
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<td>578</td>
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<td>100</td>
<td>VAP ICU</td>
<td>ICU</td>
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<td>271</td>
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<td>100</td>
<td>VAP ICU</td>
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<td>226</td>
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<td>100</td>
<td>VAP Hospital</td>
<td>ICU</td>
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<td>Krueger et al, 2002</td>
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<td>527</td>
<td>Surgical</td>
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<td>100</td>
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<td>934</td>
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<td>Placebo</td>
<td>100</td>
<td>Time to VAP</td>
<td>NR</td>
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obtained directly from study authors. The 32 included trials had a median of 133 trial participants (IQR, 81-366). The median age of participants in the included studies was 54 years (IQR, 44-60), and the median proportion of female trial participants was 33% (IQR, 25%-38%), as shown in eTable 1 in the Supplement.

**Risk of Bias**

eTable 2 in the Supplement presents the risk of bias assessments. No trials were adjudicated as low risk of bias in all domains. The risk of bias was adjudicated as low for 28 of 30 trials contributing data regarding hospital mortality. We rated down the certainty in other outcomes due to risk of bias as shown in eTable 3 in the Supplement.

**Primary Outcome**

There were 30 trials (24,034 participants) that contributed data to the primary outcome. Ten trials (n = 20,467 participants) reported hospital discharge mortality and 20 (n = 3567 participants) reported mortality at ICU discharge. Using a bayesian random-effects model with vague priors, the pooled estimated RR for hospital mortality for SDD was 0.91 (95% CrI, 0.82-0.99; tau = 0.10; I² = 33.9%) compared with standard care, with a 99.3% posterior probability that SDD was associated with lower hospital mortality (Figures 2 and 3; eFigure 2 in the Supplement). The certainty in the evidence was adjudicated as moderate (eTable 3 in the Supplement). The results were similar for the sensitivity analyses using semi-informative priors and the specified frequentist methods (Figures 2 and 4; eTable 4 in the Supplement). There was no evidence of small-study effects on visual inspection of the funnel plot or the Egger test (eFigure 1A in the Supplement).

**Subgroup Analysis**

The primary outcome of hospital mortality was assessed in 3 a priori subgroups (Figure 4; eFigures 2-4 in the Supplement). There was evidence that the pooled estimate for...
mortality was different (P value for the between-subgroup interaction test = .02) for trials that included an intravenous agent as a component of SDD (RR, 0.84 [95% CrI, 0.74-0.94]) compared with those with no intravenous agents (RR, 1.01 [95% CrI, 0.91-1.11]) as shown in eFigure 2 in the Supplement. We judged the credibility of the potential effect modification as moderate to high certainty. There was evidence that the pooled estimate for mortality was different (P value for the between-subgroup interaction test = .02) for cluster-randomized (RR, 1.00 [95% CrI, 0.79-1.23]) compared with individual patient randomized trials as shown in eFigure 3 in the Supplement. We judged the credibility of the potential effect modification as low. Details of the credibility assessments are presented in eAppendices 5 and 6 in the Supplement. There was no evidence of a differential estimate of the association with mortality (P value for the between-subgroup interaction test = .89) in trials comparing surgical, trauma, and mixed ICU populations, with no data available from medical ICUs (eFigure 4 in the Supplement). Data were not available to permit an assessment of the potential heterogeneity by study design (cluster randomized compared with individual patient randomized trials) on the estimated incidence of positive cultures for antimicrobial-resistant organisms. There was no evidence of a differential association (P value for the between-subgroup interaction test = .99) in trials published before or after 2000 (eFigure 5 in the Supplement). The pooled estimate of the association with mortality and uncertainty around the estimate were similar in pooled analysis limited to studies published as full reports in peer-reviewed journals (eFigure 6 in the Supplement).

Secondary Outcomes

Figure 3 and eTables 3 and 4 in the Supplement present the results of all secondary outcomes with assessment of small-study bias.
Compared with standard care, SDD was associated with a reduced risk of ventilator-associated pneumonia (RR, 0.44 [95% CrI, 0.36-0.54]; very low certainty; eFigure 7 in the Supplement), a reduced risk of ICU-acquired bacteremia (RR, 0.68 [95% CrI, 0.57-0.81]; low certainty; eFigure 8 in the Supplement), a reduction in the duration of mechanical ventilation (mean difference, −0.73 days [95% CrI, −1.32 to −0.09 days]; moderate certainty; eFigure 17 in the Supplement), and duration of ICU admission (mean difference, −0.86 [95% CrI, −1.73 to 0.00 days]; moderate certainty; eFigure 10 in the Supplement). There was no association with duration of hospital stay (mean difference, −0.52 days [95% CrI, −2.23 to 1.20 days]; moderate certainty; eFigure 11 in the Supplement).
The pooled estimated RR for mortality at longest follow-up for SDD compared with standard care was 0.93 (95% CrI, 0.86-1.00) (eFigure 12 in the Supplement). Only 3 trials28,34,35 provided additional data regarding mortality beyond hospital discharge, 1 completed follow-up at 90 days,28 1 at 1 year,34 and 1 had a median follow-up duration of 3.5 years.35

Data were unavailable at a unit level to facilitate a pooled analysis of the association of SDD with the emergence of antimicrobial-resistant organisms; available data are qualitatively summarized in eTable 5 in the Supplement. None of the 3 cluster-randomized trials9,10,27 reported an increase in positive cultures of antimicrobial-resistant organisms at a unit level.

Of the studies that reported data at an individual patient level, data were available to provide a pooled estimate of the incidence of positive cultures of antimicrobial-resistant organisms (estimated RR, 0.65 [95% CrI, 0.46-0.92]; very low certainty; eFigure 13 in the Supplement), incidence of positive cultures of methicillin-resistant Staphylococcus aureus (estimated RR, 1.06 [95% CrI, 0.56-1.98]; very low certainty; eFigure 14 in the Supplement), and vancomycin-resistant enterococcus (estimated RR, 0.62 [95% CrI, 0.18-2.06]; very low certainty; eFigure 15 in the Supplement).

The pooled estimated RR for Clostridioides difficile was 0.52 (95% CrI, 0.15-1.80; eFigure 16 in the Supplement). eTable 5 in the Supplement summarizes data not amenable to pooling. Fourteen trials28,31-35,39,40,43,47,48,51,52,55 reported no increase in detection of antimicrobial-resistant organisms from clinical or surveillance cultures, 6 trials36,37,41,44,50,53 reported an increase in antimicrobial-resistant organisms detected, and 9 trials26,29,30,38,42,45,46,49,54 did not report the incidence of detection of antimicrobial-resistant organisms.

Discussion

In this systematic review and meta-analysis, the use of SDD in patients receiving mechanical ventilation in the ICU is likely associated with a reduced risk of hospital mortality. This reduction in mortality was evident in trials that included an intravenous agent as a component of the intervention. The results provide evidence that the use of SDD may result in a reduced incidence of ventilator-associated pneumonia and ICU-acquired bacteremia; however, this evidence was of lower certainty. It was also found that SDD was probably associated with a small reduction in the duration of mechanical ventilation, but little or no reduction in the duration of ICU admission. There was no evidence that SDD was associated with an increase in the incidence of antimicrobial-resistant organisms; however, the association between SDD and the emergence of antimicrobial-resistant organisms remains very uncertain.

The findings of reduced risk of mortality and incidence of ventilator-associated pneumonia are consistent with the results of a recent Cochrane review.4 The addition of 2 recent trials9,10 has more than doubled the sample size, increasing confidence in the primary finding of a reduction in mortality associated with the use of SDD, as well as reporting pooled data for additional outcomes. The use of bayesian methods in this review provides the quantitative framework for clinicians and policymakers to interpret the uncertainty regarding the overall results of recent trials, as they consider the overall risks and benefits of implementing this intervention.9,10 Concern that the widespread use of broad-spectrum antibiotics might promote antimicrobial-resistant organisms has been a barrier to the adoption of SDD.7,8 In keeping with previous literature,7,9 no evidence was found to support the concern, but the available evidence is of very low certainty and is insufficient to rule out that possibility. Methodologically sound, long-term observational studies designed to overcome the limitations identified in the current body of research regarding the ascertainment of the effect of SDD on the development of antimicrobial-resistant organisms is a priority for future research.

Our review has several strengths. The inclusion of recent large trials has substantially increased the number of included
participants, allowing the assessment of a broader range of outcomes than have been previously reported. The use of Bayesian and frequentist analyses provides confidence that the results are robust to the methods used to pool data.

Limitations This study has several limitations. First, consistent with previous trials, the prevalence of antimicrobial resistance was uniformly low, consequently, the results may not be applicable in health care settings with a higher rate of antimicrobial resistance. Second, evidence regarding the association of SDD with secondary outcomes, in particular outcomes related to the incidence of antimicrobial-resistant organisms, was adjudicated as very low certainty, largely due to lack of blind

Conclusions Among adults in the ICU treated with mechanical ventilation, the use of SDD compared with standard care or placebo was associated with lower hospital mortality. Evidence regarding the effect of SDD on antimicrobial resistance was of very low certainty.

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