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Criteria for Switching From Intravenous to Oral Antibiotics in Patients Hospitalized With Community-Acquired Pneumonia: A Rapid Review

Health Quality Ontario

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Evidence Development and Standards Branch at Health Quality Ontario

Criteria for Switching From Intravenous to Oral Antibiotics in Patients Hospitalized With Community-Acquired Pneumonia: A Rapid Review. November 2013; pp. 1–23

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Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, Evidence Development and Standards and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This report was prepared by Health Quality Ontario or one of its research partners for the Ontario Health Technology Advisory Committee and was developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to Health Quality Ontario. It is possible that relevant scientific findings may have been reported since the completion of the review. This report is current to the date of the literature review specified in the methods section, if available. This analysis may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
bpm	Beats per minute
CI	Confidence interval
GI	Gastrointestinal
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HQO	Health Quality Ontario
IV	Intravenous
M-H	Mantel-Haenszel
NS	Not significant
OR	Odds ratio
RCT	Randomized controlled trial
SD	Standard deviation
SWAB/NVALT	Dutch Working Party on Antibiotic Policy and Dutch Association of Chest Physicians

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding (QBF) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to evaluate the criteria for switching from intravenous (IV) to oral antibiotics in adult patients hospitalized with community-acquired pneumonia.

Clinical Need and Target Population

Usually, patients hospitalized with community-acquired pneumonia receive initial empiric therapy with IV antibiotics. (1) A switch from IV to oral antibiotics can occur once there is evidence of clinical improvement. (1)

Technology/Technique

Guidelines

The criteria for switching from IV to oral antibiotics in adults hospitalized with community-acquired pneumonia as recommended by the most current Canadian and international guidelines are summarized in Table 1.

Table 1: Criteria for Switching From IV to Oral Antibiotics in Adults Hospitalized With Community-Acquired Pneumonia: Guideline Recommendations

Guideline	Criteria	Evidence Base
Canadian Infectious Disease Society/Canadian Thoracic Society, 2000 (2)	Satisfactory clinical and laboratory response to initial IV therapy: • resolution of fever • reduction of cough • reduction in respiratory distress • significant reduction of leukocytosis • normally functioning GI tract, especially if patient is being fed through an orogastric tube Exclusions: critically ill patients, especially those who are hemodynamically unstable	Level II evidence (well-designed controlled trials without randomization)

	and require intensive care, should be excluded from switch	
Infectious Diseases Society of America/American Thoracic Society, 2007 (3)	Hemodynamically stable Improving clinically Able to ingest medications Normally functioning GI tract	Strong recommendation, level II evidence
British Thoracic Society, 2009 (4)	Resolution of fever for > 24 hours Pulse rate < 100 bpm Resolution of tachypnea Clinically hydrated and taking oral fluids Resolution of hypotension Absence of hypoxia Improving white cell count Non-bacteremic infection No microbiological evidence of legionella, staphylococcal or Gram-negative enteric bacilli infection No concerns about GI absorption	Recommendation grade B+ (1 or more prospective clinical studies that illuminate but do not rigorously answer the question)
European Respiratory Society, 2011 (5)	Should be considered in all patients except the most severely ill. The optimal time to switch to oral treatment is also unknown; this decision should be guided by the resolution of the most prominent clinical features at admission	Grade A (1 cohort study or more)
SWAB/NVALT (Dutch guidelines), 2011 (6)	Patients should be switched from IV to oral therapy when a substantial clinical improvement, adequate oral intake and GI absorption, and hemodynamic stability are observed: • temperature < 37.8ºC • heart rate < 100 bpm • respiratory rate < 24 breaths/minute • systolic blood pressure > 90 mmHg • arterial oxygen saturation > 90% or partial pressure of oxygen > 60 mmHg on room air • ability to maintain oral intake • normal mental status Exclusions: pneumonia caused by *Staphylococcus aureus* or *Pseudomonas aeruginosa*, a non-drained lung empyema or lung abscess, and disturbed GI resorption are relative contraindications for oral therapy	Level 1 (systematic review of at least 2 independent RCTs)
Swedish Society of Infectious Diseases, 2012 (7)	Switch from IV to oral treatment as soon as clinical condition has improved and patient is afebrile (< 38°C).	Recommendation grade B+ (1 or more prospective clinical studies that illuminate but do not rigorously answer the question)

Abbreviations: bpm, beats per minute; GI, gastrointestinal; IV, intravenous; RCT, randomized controlled trial; SWAB/NVALT, Dutch Working Party on Antibiotic Policy and Dutch Association of Chest Physicians.

Rapid Review

Research Question

What are the criteria for switching from IV to oral antibiotics in adult patients hospitalized with community-acquired pneumonia?

Research Methods

Literature Search

Search Strategy

A literature search was performed on June 25, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews, for studies published from January 1, 2008, to June 25, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2008, and June 25, 2013
- systematic reviews, meta-analyses, and health technology assessments
- evaluating the switch from IV to oral antibiotics in patients hospitalized with community-acquired or nursing home–acquired pneumonia
- evaluating at least 1 of the outcomes of interest
- in adult patients

Exclusion Criteria

- studies in children
- studies in patients with chronic obstructive pulmonary disease or in immunocompromised patients
- studies in patients with ventilator-associated or hospital-acquired pneumonia

Outcomes of Interest

- length of stay
- clinical cure

Expert Panel

In April 2013, Health Quality Ontario's (HQO's) Expert Advisory Panel on Evidence-Based Episodes of Care for Pneumonias Presenting to Hospitals was struck. Members of the panel included physicians, nurses, allied health professionals, and personnel from the Ministry of Health and Long-Term Care.

The role of HQO's Expert Advisory Panel on Evidence-Based Episodes of Care for Pneumonias Presenting to Hospitals was to contextualize the evidence produced by Health Quality Ontario and provide advice on the appropriate clinical pathway for a patient with pneumonia in the Ontario health care setting. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (8) Details on the outcomes of interest were abstracted from the selected review, and primary studies were referenced as needed.

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (9) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (9) For more detailed information, please refer to the latest series of GRADE articles. (9)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 643 citations published between January 1, 2008, and June 25, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

One systematic review met the inclusion criteria. (10) The reference list of the included study was hand-searched to identify other relevant studies, but no additional citations were included.

For each included study, the study design was identified and is summarized below in Table 2, which is a modified version of a hierarchy of study design by Goodman. (11)

Table 2: Body of Evidence Examined According to Study Design

Study Design	Number of Eligible Studies
RCTs	
Systematic review of RCTs	1
Large RCT	
Small RCT	
Observational Studies	
Systematic review of non-RCTs with contemporaneous controls	
Non-RCT with non-contemporaneous controls	
Systematic review of non-RCTs with historical controls	
Non-RCT with historical controls	
Database, registry, or cross-sectional study	
Case series	
Retrospective review, modelling	
Studies presented at an international conference	
Expert opinion	
Total	1

Abbreviation: RCT, randomized controlled trial.

The systematic review evaluated the outcomes of switching from IV to oral antibiotics compared with maintaining IV antibiotics in patients hospitalized with community-acquired pneumonia. (10) The review received an AMSTAR score of 7/11, which is considered fair (Appendix 2). (8)

Six RCTs were included in the systematic review: in 3, detailed criteria for switching from IV to oral antibiotics were presented; in the remainder, the switch occurred either on a day stipulated by a treatment protocol or as the result of a physician's subjective assessment. (10) Different antibiotics were evaluated in each study. (10) Patients presented with either moderate-to-severe or severe pneumonia. (10) The hospital stay was shorter in patients who switched from IV to oral antibiotics compared with maintaining IV antibiotics (Table 3). (10)

In a meta-analysis of the 6 included RCTs, the authors did not find a statistically significant difference in treatment success between the 2 groups. (10) Table 3 summarizes the findings of the systematic review and its component studies.

Table 3: Systematic Review and Component RCTs—Summary

Study, Year N	Intervention/Control	Criteria for Switching From IV to Oral Antibiotics	Mean Length of Stay, days (SD)[a]	Clinical Cure, n (%)[a]
Systematic Review (6 RCTs)				
Athanassa et al, 2008 (10)	Intervention: switch from IV to oral antibiotics Control: maintain IV antibiotics	Most common criteria: • absence of fever[b] (50%) • improvement of symptoms (50%) • normal GI absorption (33%)	Weighted mean difference[c]: −3.3 (95% CI, −4.4 to −2.3)	*Treatment success* OR 0.92 (95% CI, 0.61–1.39)[c]
RCTs Included in the Systematic Review				
Castro-Guardiola et al, 2001 (12) N = 103	Intervention: different options Control: different options	Switch on day 2	Intervention: 6 (4) Control: 11 (3) *P* < 0.001	*Treatment success* Intervention: 36 (75) Control: 42 (76)
Omidvari et al, 1998 (13) N = 95	Intervention: IV cefamandole, switch to oral cefaclor Control: IV cefaclor	Switch following physician's subjective assessment of patient response	Intervention: 7.3 Control: 6.9 NS[c]	*Improvement* Intervention: 55 (95) Control: 36 (97)
Siegel et al, 1996 (14) N = 73	Intervention: IV and oral cefuroxime, switch on day 2 (intervention 1); or IV and oral cefuroxime, switch on day 5 (intervention 2) Control: IV cefuroxime	Switch on day 2 or day 5	Intervention 1: 6 (3) Intervention 2: 8 (2) Control: 11 (1) *P* < 0.05	*Therapeutic success* Intervention 1: 18 (90) Intervention 2: 17 (85) Control: 16 (94)
Norrby et al, 1998 (15) N = 619	Intervention: IV and oral levofloxacin Control: IV ceftriaxone	Improvement in clinical signs and symptoms	Intervention: 9 Control: 8 NS[c]	*Clinical response* Intervention: 239 (76) Control: 229 (75) NS[d]
Oosterheert et al, 2006 (16) N = 265	Intervention: IV amoxicillin/ clavulanate or 2nd/3rd generation cephalosporin, switch to oral amoxicillin/clavulanate Control: IV amoxicillin/clavulanate or 2nd/3rd generation cephalosporin	Decrease in temperature > 1ºC Respiratory rate < 25 breaths/minute Oxygen saturation > 90% or arterial pressure > 55 mmHg Hemodynamically stable Absence of mental confusion Ability to take oral drugs	Intervention: 9.6 (5.0) Control: 11.5 (4.9) Mean difference: 1.9 (95% CI, 0.6–3.2)[c]	*Clinical cure* Intervention: 110 (83) Control: 113 (85) Mean difference: 2.0% (95% CI, −7.0 to 10.0)[c]
Yakub et al, 2005 (17) N = 50	Intervention: IV and oral amoxicillin/clavulanate Control: IV amoxicillin/clavulanate	Afebrile ≥ 8 hours Symptom improvement No abnormal GI absorption	Intervention: 4.1 (0.92) Control: 8.2 (1.1)[c]	*Clinical cure* Intervention: 23 (92) Control: 22 (88)

Abbreviations: CI, confidence interval; GI, gastrointestinal; IV, intravenous; NS, not significant; OR, odds ratio; RCT, randomized controlled trial; SD, standard deviation.
[a]Unless otherwise specified.
[b]Different definition used in each study.
[c]*P* value not provided.
[d]Based on the CI provided.

In the studies that used detailed criteria for switching, the switch from IV to oral antibiotics occurred on average 3 to 4 days after initiation of IV antibiotics. (15-17) In 1 study that used a protocol specifying a switch to oral antibiotics on day 2, 4 patients (8.3%) could not be switched due to insufficient improvement, and 4 patients (8.3%) had to be switched back to IV antibiotics due to worsening of pneumonia. (12) The authors of the review concluded that the switch back may have been the result of switching patients to oral antibiotics before they reached clinical stability. (10)

After grouping the studies according to the use of detailed criteria for switching (Figure 1), no statistically significant difference in clinical cure was observed between patients who switched from IV to oral antibiotics compared to those treated with IV antibiotics in either subgroup (overall relative risk, 1.00; 95% confidence interval, 0.94–1.05).

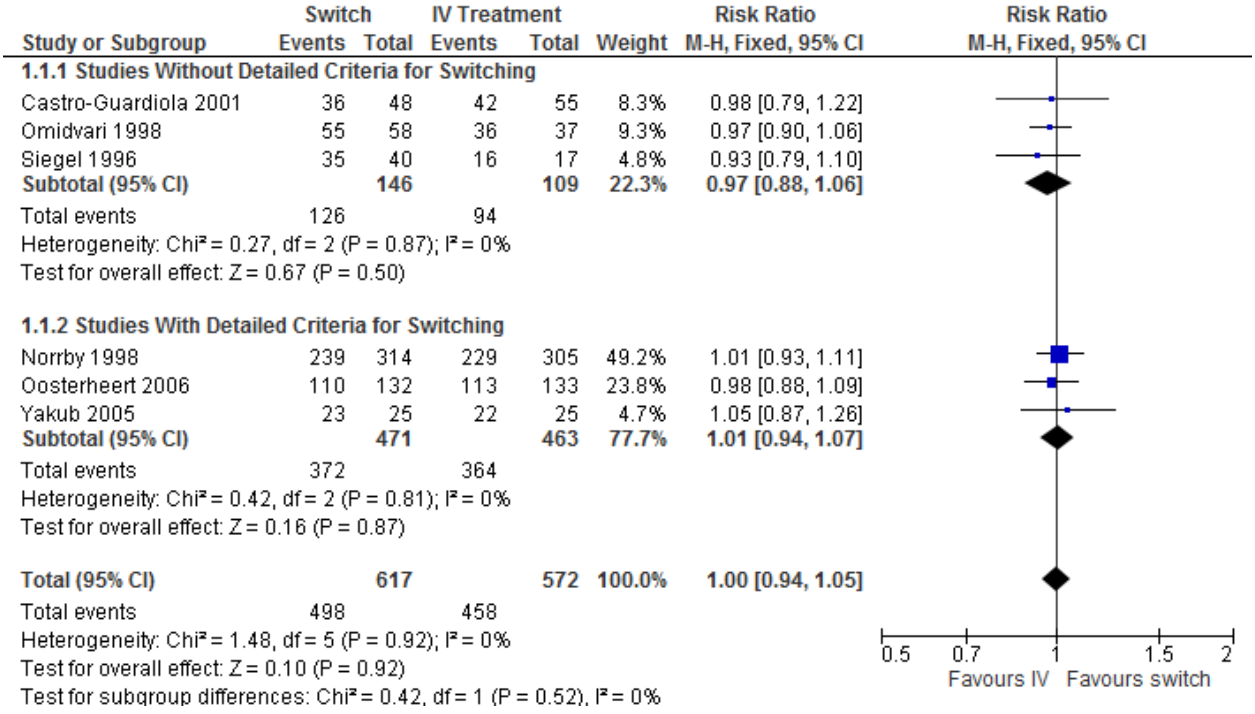

Figure 1. Clinical Cure in Patients Who Switched From IV to Oral Antibiotics Compared to IV Antibiotics

Abbreviations: CI, confidence interval; IV, intravenous; M-H, Mantel-Haenszel

Because these studies were not designed to specifically evaluate criteria for switching, only indirect evidence was available. Therefore, the quality of evidence according to GRADE was low (Appendix 2).

Conclusions

In patients hospitalized for community-acquired pneumonia, RCTs that evaluated switching from IV to oral antibiotics using a detailed set of criteria showed a shorter length of hospital stay in patients who switched to oral antibiotics, but no statistically significant difference in clinical cure compared with maintaining IV antibiotics. The criteria for switching commonly included hemodynamic stability, absence of fever, and ability to take oral drugs. The quality of the evidence was low.

Acknowledgements

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HQO's Expert Advisory Panel on Evidence-Based Episodes of Care for Pneumonias Presenting to Hospitals

Panel Members	Affiliation(s)	Appointment(s)
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Dr Dan Ricciuto	Lakeridge Health	Physician Lead, IPAC and Antimicrobial Stewardship
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Cathy Relf	Trillium Health Partners – Mississauga Hospital	Physiotherapist
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Tania Larsen	London Health Sciences	Intensive Care Physiotherapist

Decision Support and Case Costing Specialist		
Linda Welham	Southlake Regional Health Centre	Decision Support and Case Costing Specialist

Appendices

Appendix 1: Literature Search Strategies

Search date: June 25, 2013
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; All EBM Reviews - Cochrane DSR, ACP Journal Club, DARE, CCTR, CMR, HTA, and NHSEED
Limits: 2008-current; English
Filters: Meta-analyses, systematic reviews, health technology assessments

Databases: EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 2013, EBM Reviews - ACP Journal Club 1991 to May 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2013, EBM Reviews - Cochrane Central Register of Controlled Trials April 2013, EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012, EBM Reviews - Health Technology Assessment 2nd Quarter 2013, EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2013, Embase 1980 to 2013 Week 21, Ovid MEDLINE(R) 1946 to May Week 4 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations May 29, 2013

#	Searches	Results
1	exp Pneumonia/	251440
2	(pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab.	297852
3	or/1-2	411044
4	exp Anti-Bacterial Agents/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	535990
5	exp antibiotic agent/ use emez	889642
6	(((anti?bacterial or anti?mycobacterial or bacteriocidal) adj agent) or antibiotic* or bacteriocide*).ti,ab.	499674
7	or/4-6	1617053
8	Meta Analysis.pt.	43474
9	Meta-Analysis/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Technology Assessment, Biomedical/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	52430
10	Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez	83182
11	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	362020
12	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	4816
13	or/8-12	414910
14	3 and 7 and 13	2156
15	limit 14 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	2018
16	limit 15 to yr="2008 -Current" [Limit not valid in DARE; records were retained]	895
17	remove duplicates from 16	677

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Score of Included Systematic Review[a]

Author, Year	AMSTAR Score	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Athanassa et al, 2008 (10)	7	▯	▯	▯	▯	▯	▯	▯	▯	▯	▯	▯

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews.
[a]Maximum possible score is 11. Details of AMSTAR method are described in Shea et al. (8)

Table A2: GRADE Evidence Profile for Comparison of Criteria for Switching From IV to Oral Antibiotics

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Length of Stay							
6 (RCTs)	No serious limitations	No serious limitations	Very serious limitations (–2)[a]	No serious limitations	Undetected	None	⊕⊕ Low
Clinical Cure							
6 (RCTs)	No serious limitations	No serious limitations	Very serious limitations (–2)[a]	No serious limitations	Undetected	None	⊕⊕ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IV, intravenous; RCT, randomized controlled trial.
[a]Studies presented evidence indirectly related to the research question.

Table A3: Risk of Bias Among Randomized Controlled Trials for Comparison of Criteria for Switching From IV to Oral Antibiotics

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Castro-Guardiola et al, 2001 (12)	No limitations	Limitations[a]	No limitations	No limitations	No limitations
Omidvari et al, 1998 (13)	No limitations	Limitations[a]	Serious limitations[b]	No limitations	No limitations
Siegel et al, 1996 (14)	Limitations[c]	Limitations[a]	Limitations[d]	No limitations	No limitations
Norrby et al, 1998 (15)	No limitations	Limitations[a]	No limitations	No limitations	No limitations
Oosterheert et al, 2006 (16)	No limitations	Limitations[a]	No limitations	No limitations	No limitations
Yakub et al, 2005 (17)	Limitations[c]	Limitations[a]	No limitations	No limitations	No limitations

Abbreviation: IV, intravenous.

[a]No blinding of participants or investigators was reported; however, this was not considered a serious limitation, since objective outcomes were used.

[b]A large proportion of patients dropped out of the study.

[c]Randomization process not described in detail.

[d]A considerable number of patients were excluded from the study.

References

(1) Ramirez JA, Vargas S, Ritter GW, Brier ME, Wright A, Smith S, et al. Early switch from intravenous to oral antibiotics and early hospital discharge: a prospective observational study of 200 consecutive patients with community-acquired pneumonia. Arch Intern Med. 1999 Nov 8;159(20):2449-54.

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