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Severity Assessment Tools for Patients With Community-Acquired Pneumonia: A Rapid Review

Health Quality Ontario

November 2013

Evidence Development and Standards Branch at Health Quality Ontario

Severity Assessment Tools for Patients With Community-Acquired Pneumonia: A Rapid Review.
November 2013; pp. 1–27

Suggested Citation

This report should be cited as follows:

Health Quality Ontario. Severity assessment tools for patients with community-acquired pneumonia: a rapid review. Toronto, Ontario; 2013 November. 27 p. Available from: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/rapid-reviews.

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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.

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List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
CAP	Community-acquired pneumonia
CRB-65	Confusion, respiratory rate, blood pressure, and age ≥ 65 years
CURB-65	Confusion, urea, respiratory rate, blood pressure, and age ≥ 65 years
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HQO	Health Quality Ontario
ICU	Intensive care unit
PSI	Pneumonia Severity Index

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

This rapid review aims to determine which severity assessment tool is the most accurate for patients with community-acquired pneumonia.

Clinical Need and Target Population

Community-acquired pneumonia (CAP) is a common cause of hospitalization and one of the leading causes of death in Canada. (1) Evidence suggests that patients with CAP are frequently over- and underestimated for their risk of complication, leading to inappropriate hospitalizations. (2) An objective scoring system that assesses the severity of pneumonia has the potential to improve the management of CAP by guiding antibiotic prescribing and by more appropriately identifying patients requiring hospitalization and admission into an intensive care unit (ICU). (3)

Three severity assessment scales are most commonly used:

- Pneumonia Severity Index (PSI) calculates a score using several parameters, including age, gender, coexisting illnesses, and physical, laboratory and radiographic findings. Based on the overall PSI score, patients are stratified into 1 of 5 risk categories, with categories IV and V being the most severe.
- CURB-65 bases its score on the level of a patient's confusion, urea nitrogen, respiratory rate, blood pressure, and age (for an overall score out of 5, with 4 to 5 being the most severe).
- CRB-65 is the same as CURB-65 except that it does not include urea nitrogen levels. (4)

These scales are frequently used in emergency departments to establish the severity of a patient's condition. However, international guidelines on the diagnosis and management of adults with CAP have inconsistent recommendations regarding which tool to use when determining hospital and ICU admission. Table 1 lists the recommendations according to various guidelines.

Table 1. Guideline Recommendations for Severity Assessment Tools to Determine ICU Admission for Patients With Community-Acquired Pneumonia

Guideline	Severity Assessment Tool		
	PSI	CURB-65	CRB-65
Canadian Thoracic Society (CTS) (1)	✓		
British Thoracic Society (BTS) (5)		✓	✓
Infectious Disease Society of America / American Thoracic Society (IDSA/ATS) (6)	✓	✓	
South African Pulmonology Society / Antibiotic Study Group of South Africa (SAPS/ ASGSA) (7)		✓	
Dutch Working Party on Antibiotic Policy / Dutch Association of Chest Physicians (SWAB/NVALT) (8)	✓	✓	✓
Swedish Society of Infectious Diseases (SSID) (9)			✓
European Respiratory Society / European Society for Clinical Microbiology and Infection Diseases (ERS/ESCMID) (10)			✓

Abbreviations: CRB-65, confusion, respiratory rate, blood pressure, and age ≥ 65 years; CURB-65, confusion, urea, respiratory rate, blood pressure, and age ≥ 65 years; PSI, Pneumonia Severity Index.

It was unclear if the more comprehensive PSI scale was more accurate at predicting ICU admission than either CURB-65 or CRB-65, which are shorter and easier to implement. This rapid review was designed to answer this question.

Rapid Review

Research Question

Which severity assessment tool most accurately predicts ICU admission and mortality in patients with community-acquired pneumonia?

Research Methods

Literature Search

A literature search was performed on June 24, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2008, until June 24, 2013. 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 reports
- published between January 1, 2008, and June 24, 2013
- health technology assessments, systematic reviews, and meta-analyses
- hospitalized adult patients with CAP
- studies comparing PSI, CURB-65, and CRB-65 as severity assessment tools

Exclusion Criteria

- primary studies (randomized controlled trials [RCTs], observational studies, case series, and other primary study types)
- children (patients aged < 18 years)
- outpatients with CAP
- patients with hospital-acquired and ventilator-associated pneumonia
- studies where outcomes of interest cannot be extracted

Outcomes of Interest

- mortality
- ability to predict ICU admission

Expert Panel

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

The role of the expert advisory panel was to contextualize the evidence produced by HQO 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 panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of the selected systematic reviews. (11)

Details on the outcomes of interest were abstracted from the selected reviews, 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. (12) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural method.

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. (12) For more detailed information, please refer to the latest series of GRADE articles. (12)

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 Literature Search

The database search yielded 62 citations published between January 1, 2008, and June 24, 2013 (with duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Three articles were identified that met the inclusion criteria. (2;3;13) A systematic review and meta-analysis by Chalmers et al published in 2011 assessed the outcome of ICU admission (3). Loke et al (13) and Chalmers et al (2) each published systematic reviews and meta-analyses in 2010 that assessed the outcome of mortality.

On assessment using the AMSTAR tool, the two systematic reviews by Chalmers et al (3) on ICU admission and mortality each received a score of 9 and the systematic review by Loke et al (13) on mortality received a score of 8. (Appendix 2, Table A1). The systematic reviews are summarized in Table 2.

Table 2. Summary of Included Systematic Reviews

Author, Year	Search Dates	Inclusion Criteria	Outcomes Studied	Number of Studies	AMSTAR Score[a]
Chalmers et al, 2011 (3)	January 1980 to October 2010	English-language only Patients with radiographic confirmation of CAP Patients presenting to the hospital with CAP (no outpatients included)	ICU admission	**PSI**: 28 **CURB-65**: 12 **CRB-65:** 4	9
Chalmers et al, 2010 (2)	January 1980 to August 2009	English-language only Patients with radiographic confirmation of CAP	Mortality	**PSI:** 31 **CURB-65:** 17 **CRB-65:** 11	9
Loke et al, 2010 (13)	January 1999 to October 2009	English-language only At least 100 participants Prospective studies Patients with confirmed diagnosis of CAP	Mortality	**PSI:** 16 **CURB-65**: 12 **CRB-65:** 10	8

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; CAP, community-acquired pneumonia; CRB-65, confusion, respiratory rate, blood pressure, and age ≥ 65 years; CURB-65, confusion, urea, respiratory rate, blood pressure, and age ≥ 65 years; PSI, Pneumonia Severity Index.
[a]Maximum possible score is 11. See Appendix 2, Table A1 for details on these AMSTAR scores.

Results for Outcomes of Interest

The systematic review by Chalmers et al (3) reports on how well PSI, CURB-65 and CRB-65 predict ICU admission, and the systematic reviews by Loke et al (13) and Chalmers et al (2) report on how well the three severity assessment scores identify patients at risk of death. None of these articles provides the GRADE level of evidence; therefore, their included individual studies were reviewed and the GRADE for each outcome was assessed.

Prediction of ICU Admission

Chalmers et al (3) identified 26 studies that evaluated the sensitivity and specificity of the PSI score for predicting ICU admission using the PSI score, 12 studies that used CURB-65, and 4 studies using CRB-

65. Based on these studies, the authors conducted a meta-analysis for the severity assessment tools (Table 3). The meta-analysis found that for the prediction of ICU admission, PSI has higher sensitivity but lower specificity than either CURB-65 or CRB-65. The diagnostic odds ratio was highest for CRB-65: however, all of the ratios were greater than 1.0, indicating that all the assessment scales have some utility for the prediction of ICU admission.

The quality assessment of evidence for this outcome was conducted based on details published in the systematic review by Chalmers et al (3). A number of sources of risk of bias were identified; most notably only 2 of the 30 studies clearly stated the criteria for ICU admission. As well, the mean age in the studies varied largely, from 59 to 78 years. Finally, all studies were observational, with no RCTs available. As a result, the effect estimate for the outcome of ICU admission is based on very low GRADE quality of evidence (Appendix 2, Table A2 and Table A3).

Table 3. Results of Meta-analysis for Prediction of ICU Admission

	Severity Assessment Scale		
	PSI (26 studies)	**CURB-65 (11 studies)**	**CRB-65 (4 studies)**
Pooled number of patients	25,609	11,602	3,096
Pooled number of patients admitted to ICU[a]	2,410	1,149	271
Pooled sensitivity (95% CI)	74.1% (72.3–75.8)	48.8% (45.9–51.7)	41.7% (35.8–47.8)
Pooled specificity (95% CI)	47.9% (47.3–48.6)	74.0% (73.2–74.9)	85.1% (83.8–86.4)
Diagnostic odds ratio (95% CI)	2.83 (2.34–3.42)	2.40 (1.63–3.53)	5.72 (3.79–8.63)

Abbreviations: CRB-65, confusion, respiratory rate, blood pressure, and age ≥ 65 years; CURB-65, confusion, urea, respiratory rate, blood pressure, and age ≥ 65 years; ICU, intensive care unit; PSI, Pneumonia Severity Index.
[a]The cut-off for admission to ICU was ≥ IV for PSI, ≥ 3 for CURB-65, and ≥ 3 for CRB-65.
Source: Chalmers et al, 2011. (3)

Prediction of Mortality

The 2 systematic reviews that assessed the tools' ability to predict risk of death found consistent results (Table 4). They found that PSI had the highest sensitivity compared to CURB-65 and CRB-65, and that CRB-65 had the highest specificity compared to PSI and CURB-65. The diagnostic odds ratios were also relatively consistent across both systematic reviews. PSI had the highest diagnostic odds ratio, followed by CURB-65 and then CRB-65. All of the pooled diagnostic odds ratios were well over 1.0, suggesting that each tool can predict the risk of death.

Assessment of the quality of evidence was conducted based on details published in the systematic reviews by Loke et al (13) and Chalmers et al. (2) The authors state that there is considerable heterogeneity in the populations from the different studies, as well as differences in microbiological spectrum and antibiotic sensitivity. As a result of these limitations, the effect estimate for the outcome of mortality is based on very low GRADE quality of evidence (Appendix 2, Table A2 and Table A3).

Table 4. Results of Meta-Analyses for Prediction of Risk of Death Using PSI, CURB-65, and CRB-65 for High-Risk Patients

Author, Year		Severity Assessment Scale		
		PSI	CURB-65	CRB-65
Chalmers et al, 2010 (2)	Pooled number of patients[a] (number of studies)	81,797 (31)	15,596 (17)	397,211 (11)
	Pooled sensitivity (95% CI)	91.4% (90.8–92.1)	62.0% (59.3–64.6)	29.1% (28.8–29.5)
	Pooled specificity (95% CI)	49.5% (49.2–49.9)	80.8% (80.2–81.4)	90.9% (90.8–91.0)
	Diagnostic odds ratio (95% CI)	9.6 (8.0–11.6)	7.0 (5.8–8.3)	6.9 (4.9–9.5)
Loke et al, 2010 (13)	Pooled number of patients[a] (number of studies)	16,519 (16)	11,199 (12)	8,143 (10)
	Pooled sensitivity (95% CI)	90% (87–92)	62% (54–70)	33% (24–44)
	Pooled specificity (95% CI)	53% (46–59)	79% (75–83)	92% (86–96)
	Diagnostic odds ratio (95% CI)	10.8 (8.3–14.0)	6.4 (5.1–8.1)	6.0 (3.4–10.4)

Abbreviations: CRB-65, confusion, respiratory rate, blood pressure, and age ≥ 65 years; CURB-65, confusion, urea, respiratory rate, blood pressure, and age ≥ 65 years; ICU, intensive care unit; PSI, Pneumonia Severity Index.
[a]The cut-off for high risk (defined as requiring admission to ICU) was ≥ IV for PSI, ≥3 for CURB-65, an ≥3 for CRB-65.

Limitations

There is significant heterogeneity in the inclusion and exclusion criteria applied in the individual studies included in the systematic reviews, resulting in very large heterogeneity in the pooled results. For the outcome of mortality, many studies in the meta-analysis do not have any deaths, and the low sample size of deaths may impact the validity of the summary statistic.

Conclusions

Based on **very low** quality of evidence, the systematic reviews evaluating the performance of PSI, CURB-65 and CRB-65 as severity assessment tools for patients with community-acquired pneumonia reached the following conclusions:

- The diagnostic odds ratios for the prediction of ICU admission and prediction of death are not significantly different between PSI, CURB-65, and CRB-65.
- PSI had a higher sensitivity and lower specificity compared to both CURB-65 and CRB-65 for the prediction of ICU admission and prediction of death.

Acknowledgements

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

Panel Members	Affiliation(s)	Appointment(s)
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Dr Michael Miletin	William Osler Health Centre	Director of Critical Care
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Dr John Jordan	Byron Family Medical Centre Western University	Professor of Family Medicine
Dr Frank Martino	William Osler Health Centre McMaster University Ontario College of Family Physicians	Lead Physician President, OCFP
Hospitalist		
Dr Robert Maloney	Sault Area Hospital	Chief Hospitalist
Dr Cary Shafir	Guelph General Hospital	Chief Hospitalist
Dr Warren Wilkins	Peterborough Regional Health Centre	Medical Director, Internal Medicine Program Acting Lead Hospitalist
Hospitalist/Geriatrician		
Dr Mireille Norris	Sunnybrook Health Sciences	Education Director of Hospitalist Training Program

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Geriatrician		
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Clinical Pharmacist		
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Pharmacotherapy Specialist		
Miranda So, PharmD	University Health Network Mount Sinai Antimicrobial Stewardship Program	Pharmacotherapy Specialist
Antimicrobial Pharmacy Specialist		
Rosemary Zvonar	The Ottawa Hospital	Antimicrobial Pharmacy Specialist
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Registered Nurse		
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Physiotherapist		
Cathy Relf	Trillium Health Partners – Mississauga Hospital	Physiotherapist
Intensive Care Physiotherapist		
Tania Larsen	London Health Sciences	Intensive Care Physiotherapist
Decision Support and Case Costing Specialist		

Panel Members	Affiliation(s)	Appointment(s)
Linda Welham	Southlake Regional Health Centre	Decision Support and Case Costing Specialist

Appendices

Appendix 1: Literature Search Strategies

Search date: June 24, 2013
Databases searched: Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase; Ovid All EBM Reviews

Q: Which CAP severity assessment tool has the highest accuracy for predicting ICU admission and mortality?

Limits: 2008-current; English
Filters: Meta-analyses, systematic reviews, health technology assessments

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 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 <May 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 25>, Ovid MEDLINE(R) <1946 to June Week 2 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 21, 2013>

Search Strategy:

#	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 "Severity of Illness Index"/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	174962
5	exp pneumonia severity index/ use emez	356
6	(pneumonia severity index or PSI or CURB-65 or CRB-65).ti,ab.	21119
7	(severity adj2 (scale* or index* or indice* or tool* or assessment*or evaluation*)).ti,ab.	24674
8	or/4-7	215185
9	3 and 8	4712
10	limit 9 to (english language and yr="2008 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	2243
11	Meta Analysis.pt.	43474
12	Meta-Analysis/ use mesz or exp Technology Assessment, Biomedical/ use mesz	51972
13	Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez	83182
14	(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
15	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	4816
16	or/11-15	414598
17	10 and 16	70
18	remove duplicates from 17	57

CINAHL

#	Query	Results
S13	S9 AND S12	22
S12	S10 OR S11	Display
S11	((health technology N2 assess*) or meta analy* or metaanaly* or pooled analysis or (systematic* N2 review*) or published studies or medline or embase or data synthesis or data extraction or cochrane)	Display
S10	(MH "Meta Analysis") or (MH "Systematic Review")	Display
S9	S3 AND S7 Limiters - Published Date from: 20080101-20131231; English Language	629
S8	S3 AND S7	1,117
S7	S4 OR S5 OR S6	39,200
S6	severity N2 (scale* or index* or indice* or tool* or assessment*or evaluation*)	36,647
S5	pneumonia severity index or PSI or CURB-65 or CRB-65	516
S4	(MH "Severity of Illness Indices+")	32,296
S3	S1 OR S2	18,548
S2	(pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) N1 inflammation*))	18,487
S1	(MH "Pneumonia+")	11,193

Appendix 2: Quality Assessment Tables

Table A1: AMSTAR Scores of Included Systematic Reviews

Author, Year	AMSTAR Score[a]	(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
Chalmers et al, 2011 (3)	9	✓	✓	✓	✓		✓	✓	✓	✓		✓
Chalmers et al, 2010 (2)	9	✓	✓	✓	✓		✓	✓	✓	✓		✓
Loke et al, 2010 (13)	8	✓	✓	✓	✓		✓		✓	✓		✓

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews

[a] Maximum possible score is 11. Details of AMSTAR method are described in Shea et al. (11)

Table A2: Risk of Bias Among Studies Included in Systematic Reviews Comparing Severity Assessment Tools for Patients with Community-Acquired Pneumonia

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Ewig et al, 2004 (14)	Very serious limitations[a]	Very serious limitations[a]	Serious limitations[c]	No serious limitations	Serious limitations[b]
Feagan et al, 2000 (15)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Lim et al, 2003 (16)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Roson et al, 2001 (17)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Angus et al, 2002 (18)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Capelaslegui et al, 2006 (19)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Lamy et al, 2004 (20)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Riley et al, 2004 (21)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
van der Eerden et al, 2004 (22)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]
Aujesky et al, 2005 (23)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]
Gutierrez et al, 2005 (24)	Very serious limitations[a]	Very serious limitations[a]	Serious limitations[c]	No serious limitations	No serious limitations
Spindler et al, 2006 (25)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Migliorati et al, 2006 (26)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Myint et al, 2006 (27)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]

Barlow et al, 2007 (28)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Buising et al, 2007 (29)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Man et al, 2007 (30)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Etzion et al, 2007 (31)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]
Marrie et al, 2007 (32)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Renaud et al, 2007a (33)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]
Renaud et al, 2007b (34)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Reyes-Calzada et al, 2007 (35)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Chalmers et al, 2008 (36)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Charles et al, 2008 (37)	Very serious limitations[a]	Very serious limitations[a]	Serious limitations[c]	No serious limitations	Serious limitations[b]
Restrepo et al, 2008 (38)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Garau et al, 2008 (39)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Ananda-Rajah et al, 2008 (40)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Johnstone et al, 2008 (41)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Schuetz et al, 2008 (42)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Zuberi et al, 2008 (43)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Yandiola et al, 2009 (44)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Liapikou et al, 2009 (45)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Feldman et al, 2009 (46)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Kontou et al, 2009 (47)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Phua et al, 2009 (48)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Brown et al, 2009 (49)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	No serious limitations
Menendez et al, 2009 (50)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]
Myint et al, 2009 (51)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]
Pilotto et al, 2009 (52)	Very serious limitations[a]	Very serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[b]

[a] Due to the nature of the research question, blinding was not possible in the studies.
[b]Treatment regimen was not mentioned in the study's methods.
[c]Authors failed to provide information on follow-up and outcome ascertainment.
Source: All studies included in the systematic reviews by Chalmers et al, 2011 (3) and Loke et al, 2010 (13).

Table A3: GRADE Evidence Profile for Comparison of CAP Severity Assessment Tools

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
PSI for prediction of ICU admission							
28 (Observational)	Very serious limitations (-2)[a]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
CURB-65 for prediction of ICU admission							
12 (Observational)	Very serious limitations (-2)[a]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
CRB-65 for prediction of ICU admission							
4 (Observational)	Very serious limitations (-2)[a]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
PSI for prediction of risk of death							
16 (Observational)	Very serious limitations (-2)[a]	No serious limitations	No serious limitations	Serious limitations[b]	Undetected	None	⊕Very low
CURB-65 for prediction of risk of death							
12 (Observational)	Very serious limitations (-2)[a]	No serious limitations	No serious limitations	Serious limitations[b]	Undetected	None	⊕Very low
CURB-65 for prediction of risk of death							
10 (Observational)	Very serious limitations (-2)[a]	No serious limitations	No serious limitations	Serious limitations[b]	Undetected	None	⊕Very low

Abbreviations: CAP, community-acquired pneumonia; CRB, confusion, respiratory rate, blood pressure, and age ≥ 65; CURB-65, confusion, urea, respiratory rate, blood pressure, and age ≥ 65; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICU, intensive care unit; PSI, pneumonia severity index.

[a]All studies are observational, leading to no allocation concealment, blinding, or adequate sequence generation.

[b]Several studies had zero deaths, leading to potentially misleading summary statistics.

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