Online Supplement

Methods

Panel composition

This guideline was developed by a multidisciplinary panel that consisted of 14 members including pulmonary, critical care and infectious disease specialists, 1 medical librarian (AM) and 3 methodologists with expertise in evidence synthesis and guideline development (ALJ, EO, and LCM). The panel was chaired by SE and CD.

Conflict of interest declaration and management

Panel members disclosed all potential conflicts of interest according to ATS policies. Declarations were reviewed by panel chairs, along with staff of the ATS conflict-of-interest committees and classified as: 1) no potential conflict; 2) the interest is irrelevant or insignificant; 3) manageable conflict of interest; or 4) disqualifying conflict of interest. During the process, 2 members (BC and RGW) recused themselves from voting on the final recommendation due to conflicts of interest. A summary of the declarations of actual, potential or perceived conflicts of interest is provided at the end of this document. Methodologists were non-voting members of the panel but were involved in developing the initial direction of the recommendation.

Meetings

This guideline was developed using electronic communication, including conference calls and email correspondence. These mechanisms of interaction were used to develop and refine the PICO question, analyze and grade evidence, and draft and finalize recommendations. During the inaugural conference call, ALJ presented the panel with an overview of the guideline development process as well as the GRADE approach to making recommendations. ATS provided financial support for expenses resulting from conference calls. The views and interests of the ATS, as well as of any commercial entity that provided external funding for professional societies, had no influence on topics discussed and recommendations made.

Clinical questions and outcomes of interest

The scope of the guideline and the PICO question of interest were identified by panel members, using the 2019 ATS/IDSA CAP guideline document as a starting point. Potential outcomes of interest were generated by the panel members using an online survey developed by the methodology team, and then rated by each panel member. Ratings provided by panel members were used to categorize outcomes as critical or as important, but not critical. Critical outcomes included: duration of antibiotic therapy, time to antibiotic de-escalation, antibiotic treatment rate, and hospital length of stay. Important but not critical outcomes included: hospital mortality, 30-day mortality, antiviral treatment rate, intensive care unit admission rate, mechanical ventilation, time to clinical stability, hospitalization rate and rate of *Clostridium difficile* infection. Consensus was achieved for all final outcomes.

Evidence review and development of clinical recommendations

With the assistance of a medical librarian (AM), the methodology team conducted a pragmatic systematic review and performed evidence synthesis, including preparation of the evidence summaries following the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach (1). Our search strategy was developed using medical subject heading keywords and text words and used the PubMed platform to search MEDLINE for relevant literature. Search results were obtained in July 2019 and organized using Rayyan online application for systematic reviews (2). The process of reviewing search results, as outlined below, ended in November 2019.

Prior to screening of titles and abstracts, we delineated specific exclusion and inclusion criteria to inform study selection. We included published studies on adults (≥18 years) without restriction on study design (i.e. we did not look exclusively for randomized controlled trials). Our patient population of interest included those with suspected community-acquired

pneumonia. We prespecified that if an insufficient number of studies were found that enrolled patients with suspected community-acquired pneumonia, then we would select studies that enrolled patients with confirmed CAP. The primary intervention/exposure of interest was nucleic acid-based testing for pathogens other than influenza and the comparison no nucleic acid-based testing. Only studies published in English were included. We did not consider studies looking solely at pediatric patients (age <18 years), nor did we include case reports, case series, comments, conference abstracts, editorials, letters to the editor, narrative reviews, workgroup proceedings, society guidelines, unpublished trial data or dissertation/thesis papers.

Our search yielded an initial 12,255 papers for screening. ACL and LCM completed title and abstract screening and EO provided additional review of articles which were potentially relevant to the question of interest. Title and abstract screening led to exclusion of 11,942 papers and additional review of full texts led to exclusion of another 287 studies. In addition to those studies not meeting the criteria outlined above, exclusions occurred for the following reasons: article not relevant to the topic (e.g. testing related to tuberculosis or fungal infection), epidemiologic surveillance (e.g. describing the incidence or prevalence of a particular infection with no comparisons relative to testing), focus on assay development, or comparison of specific tests (e.g. studies comparing molecular test to conventional methods OR studies comparing commercial molecular assays to in-house molecular assays OR studies comparing commercial molecular assays to other commercial molecular assays, all done to determine sensitivity and specificity, but not assessing patient-centered outcomes). For the remaining studies, the methodologists reviewed the full text for each papers and generated a list of final papers for evidence synthesis (n=10) as well as a list of papers for inclusion as supporting, albeit indirect evidence for the PICO question (n=16). During this process, panel members were asked to confirm completeness of the body of evidence and suggest additional articles that might have been missed.

For articles selected as evidence, data abstraction was performed by EO and LCM using a pre-designed data abstraction form. Following completion of data abstraction, ALJ reviewed and provided feedback on abstracted data. The identified evidence was not amenable to meta-analysis due to heterogeneity of study design and classification of outcomes; thus, we summarized the evidence in a narrative form. We prepared evidence summaries for following the GRADE approach (3, 4) using the GRADEpro Guideline Development Tool online application (www.gradepro.org). We assessed the quality of the evidence for each of the outcomes of interest following the GRADE approach (5), based on the following criteria: risk of bias in primary studies, precision, consistency, directness of the evidence, magnitude of effect, risk of publication bias, presence of dose-effect relationship, and an assessment of the effect of residual confounding. Quality of the evidence was categorized using 4 levels: high, moderate, low and very low. Evidence summaries were provided to all panel members for review. The panel developed recommendations based on GRADE evidence summaries as well as additional information from studies included in non-GRADE tables (e.g. studies including patient populations with both CAP and non-CAP illnesses). Final recommendations and their strengths were decided by consensus. We labeled recommendations as either “strong” or “conditional” according to the GRADE approach and used the words “we recommend” for strong recommendations and “we suggest” for conditional recommendations.

Manuscript preparation

Following finalization of recommendations, the chairs and panel members drafted the guideline document. The complete manuscript was then reviewed by the entire panel as well as the methodologists, and feedback was provided by electronic communication until consensus on the final document was achieved. The final approved version was submitted to the sponsoring professional society for peer review.

References

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5. Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011; 64: 401-406.

Search Strategy	Results	Date
(community-acquired pneumonia*) OR respiratory tract infections/diagnosis[majr]) OR (respiratory tract infection* OR respiratory infection* OR respiratory illness* OR respiratory virus*)) AND (Molecular Diagnostic Techniques[mh] OR Point-of-Care Testing[mh] OR Nucleic Acid Amplification Techniques[mh] OR molecular[tiab] OR amplification[tiab] OR "polymerase chain reaction"[tiab] OR nucleic acid[tiab] OR PCR[tiab] OR hybrid*[tiab] OR film*[tiab] OR microarray[tiab] OR array[tiab] OR assay[tiab] OR biochip[tiab] OR chip[tiab] OR multiplex[tiab] OR "respiratory panel"[tiab] OR "rapid diagnostic"[tiab] OR "point of care"[tiab])) AND english[la] NOT (animals[mh] NOT humans[mh])	12,255	July 2019