Methodological Quality of National Guidelines for Pediatric Inpatient Conditions

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BACKGROUND: Guidelines help inform standardization of care for quality improvement (QI). The Pediatric Research in Inpatient Settings network published a prioritization list of inpatient conditions with high prevalence, cost, and variation in resource utilization across children’s hospitals. The methodological quality of guidelines for priority conditions is unknown.

OBJECTIVE: To rate the methodological quality of national guidelines for 20 priority pediatric inpatient conditions.

DESIGN: We searched sources including PubMed for national guidelines published from 2002 to 2012. Guidelines specific to 1 organism, test or treatment, or institution were excluded. Guidelines were rated by 2 raters using a validated tool (Appraisal of Guidelines for Research and Evaluation) with an overall rating on a 7-point scale (7 = the highest). Inter-rater reliability was measured with a weighted kappa coefficient.

RESULTS: Seventeen guidelines met inclusion criteria for 13 conditions; 7 conditions yielded no relevant national guidelines. The highest methodological-quality guidelines were for asthma, tonsillectomy, and bronchiolitis (mean overall rating 7, 6.5, and 6.5, respectively); the lowest were for sickle cell disease (2 guidelines) and dental caries (mean overall rating 4, 3.5, and 3, respectively). The overall weighted kappa was 0.83 (95% confidence interval 0.78–0.87).


Researchers from the Pediatric Research in Inpatient Settings (PRIS) network, an open pediatric hospitalist research network,\textsuperscript{1} have identified inpatient pediatric medical and surgical conditions considered high priority for quality improvement (QI) initiatives and/or comparative effectiveness research based on prevalence, cost, and interhospital variation in resource utilization.\textsuperscript{2} One approach for improving the quality of care within hospitals is to operationalize evidence-based guidelines into practice.\textsuperscript{3} Although guidelines may be used by individual clinicians, systematic adoption by hospitals into clinical workflow has the potential to influence providers to adhere to evidence-based care, reduce unwarranted variation, and ultimately improve patient outcomes.\textsuperscript{3–6}

There are critical appraisal tools to measure the methodological quality, as defined by the Institute of Medicine (IOM) and others in their guidelines.\textsuperscript{7–12} One such validated tool is the AGREE II instrument, created by the AGREE (Appraisal of Guidelines for REsearch and Evaluation) collaboration.\textsuperscript{13,14} It defines methodological quality as “the confidence that the biases linked to the rigor of development, presentation, and applicability of a clinical practice guideline have been minimized and that each step of the development process is clearly reported.”\textsuperscript{13}

The objective of our study was to rate the methodological quality of national guidelines for 20 of the PRIS priority pediatric inpatient conditions.\textsuperscript{2} Our intent in pursuing this project was 2-fold: first, to inform pediatric inpatient QI initiatives, and second, to call out priority pediatric inpatient conditions for which high methodological-quality guidelines are currently lacking.

METHODS
The study methods involved (1) prioritizing pediatric inpatient conditions, (2) identifying national guidelines for the priority conditions, and (3) rating the methodological quality of available guidelines. This study was considered non–human-subject research (A. Johnson, personal e-mail communication, November 14, 2012), and the original prioritization study was deemed exempt from review by the institutional review board of the Children’s Hospital of Philadelphia under 45 CFR 46.102(f).\textsuperscript{2}
Prioritizing Pediatric Inpatient Conditions

Methods for developing the prioritization list are published elsewhere in detail and briefly described here. An International Classification of Diseases, 9th Revision, Clinical Modification-based clinical condition grouper was created for primary discharge diagnosis codes for inpatient, ambulatory surgery, and observation unit encounters accounting for either 80% of all encounters or 80% of all charges for over 3.4 million discharges from 2004 to 2009 for 38 children’s hospitals in the Pediatric Health Information Systems (PHIS) database, which includes administrative and billing data. A standardized cost master index was created to assign the same unit cost for each billable item (calculated as the median of median hospital unit costs) to allow for comparisons of resource utilization across hospitals (eg, the cost of a chest x-ray was set to be the same across all hospitals in 2009 dollars). Total hospital costs were then recalculated for every admission by multiplying the standardized cost master index by the number of units for each item in the hospital bill, and then summing the standardized costs of each line item in every bill. Conditions were ranked based on prevalence and total cost across all hospitals in the study period. The variation in standardized costs across hospitals for each condition was determined.

For the current study, conditions were considered if they had a top 20 prevalence rank, a top 20 cost rank, high variation (intraclass correlation coefficient >0.1) in standardized costs across hospitals, a minimum number of PHIS hospitals with annualized overexpenditures (using the standardized cost master) of at least $50,000 when compared to the mean, or a minimum median of 200 cases per hospital over the 6-year study period to assure sufficient hospital volume for future interventions. This resulted in 29 conditions; the selected 20 conditions matched the top 20 prevalence rank (see Supporting Information, Table 1, in the online version of this article).

Identifying National Guidelines

We developed a search protocol (see Supporting Information, Table 2, in the online version of this article) using condition-specific keywords and the following criteria: guideline, pediatric, 2002 to 2012. A medical librarian (E.E.) used the protocol to search PubMed, National Guidelines Clearing House, and the American Academy of Pediatrics website for guidelines for the 20 selected conditions.

We limited our study to US national guidelines published or updated from 2002 to 2012 to be most relevant to the 38 US children’s hospitals in the original study. Guidelines had to address either medical or surgical or both types of inpatient management for the condition, depending on how the condition was categorized on the PRIS prioritization list. For example, to target inpatient issues, otitis media was treated as a surgical condition when the prioritization list was created, therefore guidelines included in our study needed to address surgical management (ie, myringotomy or tympanostomy tubes). Guidelines specific to 1 organism, test, or treatment were a priori excluded, as they would not map well to the prioritization list, and would be difficult to interpret. Guidelines focusing exclusively on condition prevention were also excluded. Guidelines with a broad subject matter (eg, abdominal infection) or unclear age were included if they contained a significant focus on the condition of interest (eg, appendicitis without peritonitis), such that the course of pediatric inpatient care was described for that condition. Retracted or outdated (superseded by a more current version) guidelines were excluded.

An investigator (G.H.) reviewed potentially relevant results from the librarian’s search. For example, the search for tonsillectomy guidelines retrieved a guideline on the use of polysomnography prior to tonsillectomy in children but did not cover the inpatient management or tonsillectomy procedure. This guideline was excluded from our study, as it focused on a specific test and did not discuss surgical management of the condition.

Rating Methodological Quality of Guidelines

Methodological quality of guidelines was rated with the AGREE II tool by 2 investigators (G.H. and K.N.). This tool has 2 overall guideline assessments and 23 subcomponents within 6 domains, reflecting many of the IOM’s recommendations for methodological quality in guidelines: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence.

The AGREE II tool rates each of the 23 subcomponent questions using a 7-point scale (1=strongly disagree–7=strongly agree). We followed the AGREE II user’s manual suggestion in rating subcomponents as 1, indicating an absence of information for that question if the question was not addressed within the guideline. The AGREE II user’s manual describes the option of creating standardized domain scores; however, as the objective of our study was to assess the overall methodological quality of the guideline and not to highlight particular areas of strengths/weaknesses in the domains, we elected to present raw scores only.

For the overall guideline rating item 1 (“Rate the overall quality of this guideline.”) the AGREE II tool instructs that a score of 1 indicates lowest possible quality and 7 indicates highest possible quality. As these score anchors are far apart with no guide for interpretation of intermediate results, we modified the descriptive terms on the tool to define scores <3 as low quality, scores 3 to 5 as moderate quality, and scores >5 as high quality to allow for easier interpretation of our results. We also modified the final overall recommendation score (on a 3-point scale) from...
“I would recommend this guideline for use” to “I
would recommend this guideline for use in the pedi-
atric inpatient setting.” A score of 1 indicated to
not recommend, 2 indicated to recommend with
modifications, and 3 indicated to recommend without
modification.

Significant discrepancies (>2-point difference on over-
all rating) between the 2 raters were to be settled by con-
sensus scoring by 3 senior investigators blinded to
previous reviews, using a modified Delphi technique.

Inter-rater reliability was measured using a
weighted kappa coefficient and reported using a boot-
strapped method with 95% confidence intervals. Inter-
pretation of kappa is such that 0 is the amount of
agreement that would be expected by chance, and 1 is
perfect agreement, with previous researchers stating
scores >0.81 indicate almost perfect agreement.

RESULTS
The librarian’s search retrieved 2869 potential results
(Figure 1). Seventeen guidelines met inclusion criteria
for 13 of the 20 priority conditions. Seven conditions
did not have national guidelines meeting inclusion cri-
teria. Table 1 displays the 20 medical and surgical
conditions on the modified PRIS prioritization list,
including overall guideline scoring, recommendation
scores, and kappa results for each guideline. The high-
est methodological-quality guidelines were for
asthma, tonsillectomy, and bronchiolitis (mean
overall rating 7, 6.5, and 6.5, respectively). The low-
est methodological-quality guidelines were for 2 sickle
cell disease guidelines and 1 dental caries guide-
line (mean overall rating 4, 3.5, and 3, respectively).
Seven guidelines were rated as high overall quality,
and 10 guidelines were rated as moderate overall
quality. Eight of the 17 guidelines were recom-
manded for use in the pediatric inpatient setting
without modification by both reviewers. Two guide-
lines (for dental caries and sickle cell) were not
recommended for use by 1 reviewer.

As an example of scoring, a national guideline for
asthma had high overall scores (7 from each reviewer)
and high scores across most AGREE II subcomponents.
The guideline was found by both reviewers to be system-
atic in describing guideline development with clearly
stated recommendations linked to the available evidence
(including strengths and limitations) and implementation
considerations. Conversely, a national guideline for
sickle cell disease had moderate overall scores (scores
of 3 and 4) and low-moderate scores across the majority of
the subcomponent items. The reviewers believe that
this guideline would have been strengthened by
increased transparency in guideline development, discus-
sion of the evidence surrounding recommendations, and
discussion of implementation factors. A table with
detailed scoring of each guideline is available (see Sup-
porting Information, Table 3, in the online version of
this article).

Agreement between the 2 raters was almost perfect, with
an overall boot-strapped weighted kappa of 0.83
(95% confidence interval 0.78–0.87) across 850 scores.
There were no discrepancies between reviewers in over-
all scoring requiring consensus scoring.

DISCUSSION
Using a modified version of a published prioritization
list for inpatient pediatric conditions, we found
national guidelines for 13 of 20 conditions with high
prevalence, cost, and interhospital variation in
resource utilization. Seven conditions had no national
guidelines published within the past 10 years applica-
ble for use in the pediatric inpatient setting. Of 17
guidelines for 13 conditions, 10 had moderate and 7
had high methodological quality.

Our findings add to the literature describing meth-
odological quality of guidelines. Many publications
focus on the methodological quality of guidelines as a
group and use a standardized instrument (eg, the
AGREE II tool) to rate within domains (eg, domain 1:
scope and purpose) across guidelines in an effort to
courage improvement in developing and reporting
in guidelines. Our study differs in that we chose
to focus on the overall quality rating of individual
guidelines for specific prioritized conditions to allow
hospitals to guide QI initiatives. One study that had a
similar aim to ours surveyed Dutch pediatricians to
select priority conditions and used the AGREE II tool
to rate 17 guidelines, recommending 14 for use in the
Netherlands.33

Identifying high methodological-quality guidelines is
only 1 in a series of steps prior to successful guideline
implementation in hospitals. Other aspects of guide-
lines, including the strength of the evidence (eg, from
randomized controlled trials) and subsequent force
and clarity (eg, use of “must” instead of “consider”)
<table>
<thead>
<tr>
<th>Condition by PRIS Priority Rank</th>
<th>Guidelines Meeting Inclusion Criteria*</th>
<th>Guidelines Citation</th>
<th>Mean Overall Reviewer Methodological Quality Rating (Rater 1, Rater 2)†</th>
<th>Recommended for Use in the Pediatric Inpatient Setting, Mean (Rater 1, Rater 2)‡</th>
<th>Weighted Kappa(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otitis media, unspecified, s</td>
<td>1</td>
<td>American Academy of Family Physicians; American Academy of Otolaryngology-Head and Neck Surgery; American Academy of Pediatrics Subcommittee on Otitis Media With Effusion. Clinical Practice Guidelines. Otitis media with effusion. Pediatrics. 2004 May;113(5):1412-29.</td>
<td>6 (6, 6)</td>
<td>3 (3, 3)</td>
<td>0.76 (0.49–0.93)</td>
</tr>
<tr>
<td>Hypertrophy of tonsils and adenoids, s</td>
<td>1</td>
<td>Baugh RF et al. Clinical practice guideline: tonsillectomy in children. Otolaryngol Head Neck Surg. 2011;144(1 suppl):S1–S30.</td>
<td>6.5 (7, 6)</td>
<td>3 (3, 3)</td>
<td>0.49 (0.05–0.81)</td>
</tr>
<tr>
<td>Asthma, m</td>
<td>1</td>
<td>National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. Expert panel report 3 (EPR-3): guidelines for the diagnosis and management of asthma-full report 2007. Pages 1-440. Available at: <a href="http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf">http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf</a> Accessed: 8/24/2012</td>
<td>7 (7, 7)</td>
<td>3 (3, 3)</td>
<td>0.62 (0.21–0.87)</td>
</tr>
<tr>
<td>Bronchiolitis, m</td>
<td>1</td>
<td>American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. Pediatrics. 2006;118:1774-1793.</td>
<td>6.5 (6, 7)</td>
<td>3 (3, 3)</td>
<td>0.95 (0.87–1.00)</td>
</tr>
<tr>
<td>Pneumonia, m</td>
<td>1</td>
<td>Bradley JS et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011;53(7):e25–e76.</td>
<td>6 (6, 6)</td>
<td>3 (3, 3)</td>
<td>0.82 (0.64–0.96)</td>
</tr>
<tr>
<td>Dental caries, s</td>
<td>1</td>
<td>American Academy on Pediatric Dentistry Clinical Affairs Committee–Pulp Therapy Subcommittee; American Academy on Pediatric Dentistry Council on Clinical Affairs. Guideline on pulp therapy for primary and young permanent teeth. Pediatr Dent. 2008;30:170–174.</td>
<td>3 (3, 3)</td>
<td>1.5 (1, 2)</td>
<td>0.51 (0.14–0.83)</td>
</tr>
<tr>
<td>Chemotherapy, m</td>
<td>0</td>
<td>Stevens DL et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis. 2005;41:1373–146.</td>
<td>4.5 (4, 5)</td>
<td>2.5 (2, 3)</td>
<td>0.52 (0.15–0.79)</td>
</tr>
<tr>
<td>Cellulitis, m</td>
<td>1</td>
<td>Vardenplas Y et al. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of NASPGHAN and ESPGHAN. J Pediatr Gastroenterol Nut. 2009;49(4):486–547.</td>
<td>5 (5, 5)</td>
<td>3 (3, 3)</td>
<td>0.69 (0.45–0.87)</td>
</tr>
<tr>
<td>Inguinal hernia, s</td>
<td>0</td>
<td>Furuta GT et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. Gastroenterology. 2007;133:1342–1363.</td>
<td>5 (5, 5)</td>
<td>2.5 (2, 3)</td>
<td>0.93 (0.85–0.98)</td>
</tr>
<tr>
<td>Gastroesophageal reflux and esophagitis, m, s</td>
<td>2</td>
<td>American Academy of Pediatrics Task Force on Circumcision. Male circumcision. Pediatrics. 2012;130(3):e756-e785.</td>
<td>6 (6, 6)</td>
<td>3 (3, 3)</td>
<td>0.66 (0.25–0.89)</td>
</tr>
<tr>
<td>Dehydration, m</td>
<td>0</td>
<td>Roberts KB et al. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128:595–610.</td>
<td>5.5 (5, 6)</td>
<td>2.5 (2, 3)</td>
<td>0.62 (0.23–0.84)</td>
</tr>
<tr>
<td>Redundant prepuce and phimosis, s</td>
<td>1</td>
<td>Roberts KB et al. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128:595–610.</td>
<td>5.5 (5, 6)</td>
<td>2.5 (2, 3)</td>
<td>0.62 (0.23–0.84)</td>
</tr>
<tr>
<td>Abdominal pain, m</td>
<td>0</td>
<td>Solotkin JS et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Clin Infect Dis. 2010;50:133–164.</td>
<td>4.5 (5, 4)</td>
<td>2.5 (2, 3)</td>
<td>0.37 (–0.11–0.81)</td>
</tr>
</tbody>
</table>
of recommendations, may affect clinician or patient adherence, work processes, and ultimately patient outcomes. Strong evidence should translate into forceful and clear recommendations. Authors with the Yale Guideline Recommendation Corpus describe significant variation in reporting of guideline recommendations, and further studies have shown that the force and clarity of a recommendation is associated with adherence rates.34–37 Unfortunately, current guideline appraisal tools lack the means to score the strength of evidence, and force and clarity of recommendations as additional reasons why evidence for the impact of guidelines on patient outcomes remains mixed in the literature.38 One recent study found that adherence to antibiotics recommended within a national pediatric community-acquired pneumonia guideline, which had a high methodological-quality score in our study, did not change hospital length of stay or readmissions.29,39 There are several possible interpretations for this. Recommendations may not have been based upon strong evidence, research methodology assessing how adherence to recommendations impacts patient outcomes may have been limited, or the outcomes measured in current studies (such as readmission) are not the outcomes that may be improved by adherence to these recommendations (such as decreasing antimicrobial resistance). These are important considerations when hospitals are incorporating recommendations from guidelines into practice. Hospitals should assess the multiple aspects of guidelines, including methodological quality, which our study helps to identify, strength of evidence, and force and clarity of recommendations, as well as adherence, patient preferences, work processes, and key outcome measures when implementing guidelines into clinical practice. A study

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<th>Weighted Kappa(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eso- exo- hetero-, and hypertropia, s</td>
<td>0</td>
<td>Brophy GM et al; Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. Neurocrit Care. 2012;17:3-23.</td>
<td>5 (5, 5)</td>
<td>3 (3, 3)</td>
<td>0.95 (0.87–0.99)</td>
</tr>
<tr>
<td>Fever, m</td>
<td>0</td>
<td>Hetz D et al. Practice parameter: treatment of the child with a first unprovoked seizure: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2003;60:166–175.</td>
<td>5 (5, 5)</td>
<td>2.5 (2, 3)</td>
<td>0.73 (0.41–0.94)</td>
</tr>
<tr>
<td>Seizures with and without intractable epilepsy, m</td>
<td>3</td>
<td>Rivello JJ Jr et al. Practice parameter: diagnostic assessment of the child with status epilepticus (an evidence-based review); report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2006;67:1542–1550.</td>
<td>5 (4, 6)</td>
<td>2.5 (2, 3)</td>
<td>0.80 (0.63–0.94)</td>
</tr>
<tr>
<td>Sickle cell disease with crisis, m</td>
<td>2</td>
<td>Section on Hematology/Oncology Committee on Genetics; American Academy of Pediatrics. Health supervision for children with sickle cell disease. Pediatrics. 2002;109:526–535. National Heart, Lung, and Blood Institute, National Institutes of Health. The management of sickle cell disease. National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD. Available at: <a href="http://www.nhlbi.nih.gov/health/prof/blood/sickle/sc_mngt.pdf">http://www.nhlbi.nih.gov/health/prof/blood/sickle/sc_mngt.pdf</a>. Revised June 2002.</td>
<td>3.5 (3, 4)</td>
<td>1.5 (1, 2)</td>
<td>0.92 (0.80–0.98)</td>
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<td>NOTE: Abbreviations: m, medical; PRIS, Pediatric Research in Inpatient Settings; s, surgical.</td>
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<td>*Inclusion criteria include national guideline published 2002–2012, describing pediatric inpatient medical or surgical management for given condition. Guidelines specific to an organism, test, or treatment or condition prevention alone were excluded.</td>
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<td>†Overall methodological quality rating on the AGREE II instrument, using a 7-point scale: 1 = lowest, 7 = highest.</td>
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<td>‡Recommended for use scoring on a 3-point scale: 1 = not recommended, 2 = recommended with modifications, 3 = recommended.</td>
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</table>
utilizing a robust QI methodology demonstrated that clinician adherence to several elements in an asthma guideline, which also had a high methodological-quality score in our study, led to a significant decrease in 6-month hospital and emergency department readmission for asthma.\(^6,20\)

Our study also highlights that several pediatric conditions with high prevalence, cost, and interhospital resource utilization variation lack recent national pediat- rie guidelines applicable to the inpatient setting. If strong evidence exists for these priority conditions, professional societies should create high methodological-quality guidelines with strong and clear recommenda- tions. If evidence is lacking for these priority conditions, then investigators should focus on generat- ing research in these areas.

There are several limitations to this study. The AGREE II tool does not have a mechanism to measure the strength of evidence used in a guideline. Methodo- logical quality of a guideline alone may not translate into improved outcomes. Conditions may have national guidelines published before 2002, institution-specific or interhospital guidelines, or adult guidelines that might be amenable to use in the pediatric inpatient setting but were not included in this study. Several conditions on the prioritization list are broad in nature (eg, dehy- dration) and may not be amenable to the creation of guidelines. Other conditions on the prioritization list (eg, chemotherapy or cellulitis) may have useful guidelines within the context of specific conditions (eg, acute lymphoblastic leukemia) or for specific organisms (eg, methicillin-resistant \textit{Staphylococcus aureus}). We elected to exclude these narrower guidelines to focus on broad and comprehensive guidelines applicable to a wider range of clinical situations. Additionally, although use of a validated tool attempts to objectively guide rat- ings, the rating of quality is to some degree subjective. Finally, our study used a previously published prioritization list using data from children’s hospitals, and the list likely under-represents conditions commonly managed in community hospitals (eg, hyperbilirubinemia).\(^2\) Exclusion of these conditions was not reflective of importance or quality of available national guidelines.

**CONCLUSIONS**

Our study adds to recent publications on the need to prioritize conditions for QI in children’s hospitals. We identified a group of moderate to high methodological-quality national guidelines for pediat- rie inpatient conditions with high prevalence, cost, and variation in interhospital resource utilization. Not all prioritized conditions have national high methodological-quality guidelines available. Hospitals should prioritize conditions with high methodological-quality guidelines to allocate resources for QI initia- tives. Professional societies should focus their efforts on producing methodologically sound guidelines for prioritized conditions currently lacking high-quality guidelines if sufficient evidence exists.

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