Updating Professional Society Guidelines for Bacterial Infections

Cynthia L. Sears, M.D.
Immediate Past President, IDSA
Professor of Medicine, Infectious Diseases
Johns Hopkins University School of Medicine

FDA-IDSA-Pew Public Workshop
Enhancing the Clinical Trial Enterprise for Antibacterial Drug Development
in the United States
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Disclosures

Bristol Myers Squibb (research grant, microbiome & cancer immunotherapy)
Janssen (research grant, microbiome & colorectal cancer)
Past President, IDSA
UpToDate (reviewer, author)
The Digital and Trustworthy Evidence Ecosystem

**Synthesize evidence**
Relevant, timely, and living systematic reviews and health technology assessments incorporating new data within existing knowledge

**Produce evidence**
Relevant and high-quality primary research, real world evidence, and big data

**Produce and disseminate guidance**
Trustworthy decision aids, clinical practice guidelines and health technology assessments for patients, clinicians and policy-makers

**Implement and evaluate**
Clinical decision support and quality improvement initiatives, linked to evaluation of practice and patient outcomes in dynamic registries

**Tools and platforms**

**Trusted methodology**

**Digitally structured data**

**Culture for sharing**

**Universal standards**

**Coordination and support**

**Data**

What is the purpose and promise of clinical guidelines?

**Purpose**
To provide evidence-based—‘trustworthy’—recommendations to support patient care.
To develop a framework for determining acceptable clinical care.

**Action**
Systematically synthesize typically complex data into a format readily used by physicians and other health care providers to inform patient care decisions.

‘Promise’/’Hope’
To support more uniform care for patients, yielding better patient outcomes.
Diminish health disparities.

Physicians/health care providers must be able to judge the quality of the evidence & whether the recommendations apply to their patient or populations in care.
Multisite retrospective comparison of 28 day all-cause mortality in 1675 patients with MRSA bacteremia before & after UK National MRSA Treatment Guidelines.

Richard Brindle* on behalf of Wessex Microbiologists†

Table 1. Characteristics of the three patient groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Years during which data were collected</th>
<th>No. of patients</th>
<th>Mean age (SD)</th>
<th>Deaths within 28 days</th>
<th>28 day survival (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>&lt;2000–2003</td>
<td>535</td>
<td>70.1 (17.8)</td>
<td>191</td>
<td>64.3% (60.1%–68.4%)</td>
</tr>
<tr>
<td>B</td>
<td>2004–2005</td>
<td>589</td>
<td>69.3 (18.6)</td>
<td>219</td>
<td>62.8% (58.8%–66.7%)</td>
</tr>
<tr>
<td>C</td>
<td>2006–2008</td>
<td>551</td>
<td>69.9 (19.3)</td>
<td>205</td>
<td>62.8% (58.6%–66.8%)</td>
</tr>
</tbody>
</table>

Data only adjusted for age
Failed to adjust for: time to diagnosis
time to appropriate therapy
patient co-morbidities
hospital or practice setting

This paper & others have questioned clinical acceptance of guidelines, impact of guidelines on care & veracity of guideline processes. Guideline approaches highly variable.
Impact of IDSA/SHEA *C. difficile* Guidelines on Fidaxomicin and Vancomycin Therapeutic Use

Are physicians aware of the drugs and do they know when to use them?

*Estimated Number of Courses (qvia)*

**FDX**

**VAN**

- Tolevamer PACT Trial Published
- IDSA *C. diff* Guidelines Published

March 2018

*PACT Phase 3 data initially presented 2007 ICAAC and 2008 ECCMID: IDSA Guidelines 2010*
In stages, IDSA has sought to implement IOM standards in its guideline process.
IDSA Guidelines are:

Highest-rated IDSA member product

Critical to member satisfaction

In parallel, member and guideline panel member dissatisfaction with long timelines for development and updates of IDSA guidelines.
ID Guidelines Published in CID to Date

<table>
<thead>
<tr>
<th>Year</th>
<th># Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-2000</td>
<td>12</td>
</tr>
<tr>
<td>2000-2005</td>
<td>19</td>
</tr>
<tr>
<td>2006-2011</td>
<td>20</td>
</tr>
<tr>
<td>2011-2015</td>
<td>16</td>
</tr>
<tr>
<td>2016-Present</td>
<td>19</td>
</tr>
</tbody>
</table>
What constitutes the guideline process?

Meeting IOM standards
Grading of Recommendation Assessment, Development & Evaluation (GRADE)

*Pre-development:*
Compose panel, methodologist, COI, agreements

*Development:*
Define scope of topic
Frame clinical questions*
Select patient-important outcomes
Systematic literature search
Literature screen, risk of bias assessment
Evidence synthesis and grading
Development & grading of recommendations**
Writing manuscript

*Post-development:*
Review process and approval
Guideline dissemination & implementation

*Overall timeline: 1.5-2 years*

*Issues:*
Time of member volunteers
Paucity of methodologists
& librarians
Poorly understood process

*Common clinical questions that typically apply to a large proportion of patients; termed PICO questions (Patient, Intervention, Comparator, Outcome)*

** Recommendations—designed to answer a focused, sensible clinical question
## IDSA-Led Guidelines

<table>
<thead>
<tr>
<th>Guideline Name</th>
<th>Estimated Publication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Babesiosis</td>
<td>Winter 2020</td>
</tr>
<tr>
<td>Bone &amp; Joint Infections Osteomyelitis - Joint w/PIDS</td>
<td>Winter 2020</td>
</tr>
<tr>
<td>Bone &amp; Joint Infections Septic Arthritis - Joint w/PIDS</td>
<td>Spring 2020</td>
</tr>
<tr>
<td>Lyme Disease - Joint w/AAN &amp; ACR</td>
<td>Spring 2020</td>
</tr>
<tr>
<td>IV Catheter Infections</td>
<td>Fall 2019</td>
</tr>
<tr>
<td>C-diff Rapid Update</td>
<td>Spring 2020</td>
</tr>
<tr>
<td>Intra-abdominal Infections</td>
<td>Spring 2020</td>
</tr>
<tr>
<td>Staphylococcus aureus Bacteremia - Joint w/ESCMID</td>
<td>Spring 2020</td>
</tr>
<tr>
<td>Community-Acquired Pneumonia (CAP) in Children</td>
<td>Summer 2020</td>
</tr>
<tr>
<td>Cystitis UTI</td>
<td>Winter 2021</td>
</tr>
<tr>
<td>Cryptococcal Disease</td>
<td>TBD</td>
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</tbody>
</table>

*Designates IDSA guideline involving anti-bacterial therapy*
<table>
<thead>
<tr>
<th>Name</th>
<th>Lead Organization</th>
<th>Estimated Publication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin, Dosing and Monitoring of - Joint w/ASHP, SIDP &amp; PIDS</td>
<td>ASHP</td>
<td>Fall 2019</td>
</tr>
<tr>
<td>Community-Acquired (CAP) - Joint w/ATS</td>
<td>ATS</td>
<td>Fall 2019</td>
</tr>
<tr>
<td>NTM Statement - Joint w/ATS, ERS &amp; ESCMID</td>
<td>ATS</td>
<td>Fall 2019</td>
</tr>
<tr>
<td>MDR-TB - Joint w/ATS, ERS &amp; CDC</td>
<td>ATS</td>
<td>Fall 2019</td>
</tr>
<tr>
<td>Critically Ill Patients - Joint w/SCCM</td>
<td>SCCM</td>
<td>Winter 2021</td>
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<tr>
<td>Antimicrobial prophylaxis in surgery update - Joint w/ASHP, SIS, SHEA</td>
<td>ASHP</td>
<td>Winter 2021</td>
</tr>
<tr>
<td>Name</td>
<td>Lead Organization</td>
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</tr>
<tr>
<td>----------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Diagnosis of Periprosthetic Joint Infections w/AAOS</td>
<td>AAOS</td>
<td>TBD</td>
</tr>
<tr>
<td>Initiation of Abx in LTC w/SHEA</td>
<td>SHEA</td>
<td>Fall 2019</td>
</tr>
<tr>
<td>Appropriateness Criteria Suspected Spine Infection</td>
<td>ACR</td>
<td>Fall 2020</td>
</tr>
<tr>
<td>Sepsis in Emergency Medicine w/ACEP</td>
<td>ACEP</td>
<td>Spring 2020</td>
</tr>
<tr>
<td>Appropriateness Criteria Osteomyelitis, Septic Arthritis-Child</td>
<td>ACR</td>
<td>Spring 2021</td>
</tr>
<tr>
<td>Infection Prevention and Control in LTC w/SHEA</td>
<td>SHEA</td>
<td>Fall 2021</td>
</tr>
<tr>
<td>White Paper on Healthcare Workers Infected with Hepatitis/HIV w/SHEA</td>
<td>SHEA</td>
<td>Winter 2021</td>
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<tr>
<td>Sterilization and High-Level Disinfection Expert Guidance w/SHEA</td>
<td>SHEA</td>
<td>Winter 2021</td>
</tr>
<tr>
<td>Sepsis in Adults w/SCCM</td>
<td>SCCM</td>
<td>Winter 2021</td>
</tr>
<tr>
<td>Pediatric Sepsis Definition w/SCCM</td>
<td>SCCM</td>
<td>Winter 2021</td>
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What are other options for conveying science-derived, actionable bedside advice to clinicians?

‘Guidance’  Marquis examples:

- Clinical consensus statements
- Practice guidance
- Provisional clinical opinions

Most applicable when evidence base is insufficient for a clinical practice guideline, but significant practice variations and quality improvement opportunities exist.

In general, recommendations based on expert consensus utilize a less formal process (non-GRADE)

*Potential hazards: accuracy, completeness, COI, transparency*
The Challenge: Upholding methodological rigor while meeting a reduced development timeframe

Potential Solution: Rapid Guidelines*

Rationale:
Response to emergencies, rapid increases in cases of a condition or disease severity, or new evidence regarding treatment

Examples:
• Interim Guidelines (CDC)
• Short Clinical Guidelines (UK National Institute for Health and Care Excellence)
• Rapid Advice (WHO)

Limitation:
It requires a high concentration of skilled resources to be rigorous and rapid.

STRATEGIC PLANNING FOR IDSA:
2018-2019

- Stakeholder interviews
- Member survey
- Task Force for Strategic Planning
- IDSA leadership staff
- IDSA Board of Directors
- Vigorous Debate
A Strategic Model: R-G-T

**Run:** Continual process and quality improvements focused adding value to existing programs and functions.

**Grow:** Targeted, meaningful investments to extend, adapt, reposition, reimagine, or innovate within priority areas.

**Transform:** Long-term, high-impact efforts to bring about profound, lasting change within the association, profession, or society at large.
2019 IDSA STRATEGIC PLAN:
TRANSFORMING
THE SOCIETY AND THE PROFESSION

Charting the Path Forward: Development, Goals and Initiatives of the 2019 Infectious Diseases of America Strategic Plan


Clinical Infectious Diseases

Optimize Guidelines

Communicate ID Value, Advance Professional Fulfillment and Ensure Appropriate Compensation

Grow the ID Workforce

Invest in and Lead Efforts to Decrease AMR
Gap

Trustworthy, real-time, focused guideline/guidance on treatment of antimicrobial resistant infections.
Moment of Opportunity

Completion of the 2019 Strategic Plan means IDSA intends to invest significant staff and financial resources beginning in 2020.
Expanding IDSA’s Guideline Program to Meet the Needs of the Clinical ID Community

**Development**
- Guideline Methodology – continuous quality improvement
- Prioritization & Harmonization
- Expand the Portfolio of Guidance Products
  - Interim recommendations supplementing standard clinical guidelines

**Dissemination & Implementation**
- Format
- Connect guidelines and measures
- Technology- EHR integration to allow for data capture and clinical decision support
Proposal:
Antimicrobial Treatment Alert & Clinical Commentary from IDSA

• Rapid dissemination of emerging trial and drug data on antimicrobials
• New drug/innovation placed in context by clinical experts – clinical expert recommendations
• Comparison charts of new versus current treatments for bacteria involved
• ‘In progress’ antibiotics?
• Delineation of questions in need of further research
Provide your suggestions and input for action.

Questions for consideration:

What should be the format and components of real-time AMR treatment advice?
What is/are the clinical audiences?
What is the requirements & standards for data inclusion & changes in treatment advice provided?
How should dissemination of this information be approached?
What are the concerns about such a process & approach?