MAJOR ARTICLE

Quality and Strength of Evidence of the Infectious Diseases Society of America Clinical Practice Guidelines

Abdur Rahman Khan,[1] Sobia Khan, Valerie Zimmerman, Larry M. Baddour,[3] and Imad M. Tleyjeh[1,2,3,4]

[1]Division of Infectious Diseases, Department of Medicine, and [2]Research Centre, King Fahd Medical City, Riyadh, Saudi Arabia; and [3]Division of Infectious Diseases, Department of Medicine, and [4]Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota

(See the editorial commentary by Deresinski, on pages 1157–1159.)

Objective. To describe the distribution and temporal trends of the quality and strength of evidence supporting recommendations in the Infectious Diseases Society of America (IDSA) clinical practice guidelines.

Methods. Guidelines either issued or endorsed by IDSA from March 1994 to July 2009 were evaluated using the IDSA–US Public Health Service Grading System. In this system, the letters A–E signify the strength of the recommendation, and numerals I–III indicate the quality of evidence supporting these recommendations. The distribution of the guideline recommendations among strength of recommendation and quality of evidence classes was quantified. Temporal changes between the first and current guideline version were evaluated.

Results. Approximately one-half (median, 50.0%; interquartile range [IQR], 38.1%–58.6%) of the recommendations in the current guidelines are supported by level III evidence (derived from expert opinion). Evidence from observational studies (level II) supports 31% of recommendations (median, 30.9%; IQR, 23.3%–43.2%), whereas evidence based on ⩾1 randomized clinical trial (level I) constitutes 16% of the recommendations (median, 15.8%; IQR, 5.8%–28.3%). The strength of recommendation was mainly distributed among classes A (median, 41.5%; IQR, 28.7%–55.6%) and B (median, 40.3%; IQR, 27.1%–47.9%). Among guidelines with ⩾1 revised version, the recommendations moved proportionately toward more level I evidence (+12.4%). Consequently, there was a proportional increase in class A recommendations (+11.1%) with a decrease in class C recommendations (–23.5%).

Conclusions. The IDSA guideline recommendations are primarily based on low-quality evidence derived from nonrandomized studies or expert opinion. These findings highlight the limitations of current clinical infectious diseases research that can provide high-quality evidence. There is an urgent need to support high-quality research to strengthen the evidence available for the formulation of guidelines.

Clinical practice guidelines, considered to be the essence of evidence-based medicine, were defined by the Institute of Medicine in 1990 as "systematically developed statements to assist practitioners and patients in making decisions about appropriate health care for specific clinical circumstances" [1, p 38]. Since then, hundreds of organizations have promulgated thousands of guidelines, with more than 2000 guidelines currently registered with the National Guideline Clearinghouse [2].

The Infectious Diseases Society of America (IDSA) has issued or endorsed clinical practice guidelines since 1994 to assist physicians and other health care providers in the prevention, diagnosis, and management of patients infected with infectious diseases. Few studies have evaluated the impact and effectiveness of these published guidelines [3–10]; however, it is equally as important to determine whether the recommendations are, indeed, based on high-quality evidence. Moreover, the recent focus on improving research suggests that recommendation quality and the strength of evidence should have improved over time. This article describes the distribution and temporal trends of the quality and strength of evidence supporting recommendations in the IDSA guidelines.

Received 2 March 2010; accepted 15 June 2010; electronically published 14 October 2010.

Presented in part: Late Breaker Session of the 47th Annual Meeting of the Infectious Diseases Society of America, 29 October to 1 November 2009, Philadelphia, Pennsylvania (abstract LB-31).

Reprints or correspondence: Dr Imad Tleyjeh, Research Center, PO Box 59046, King Fahd Medical City, Riyadh, Saudi Arabia (itleyjeh@kfmc.med.sa).

Clinical Infectious Diseases 2010; 51(10):1147–1156

1058-4838/2010/5110-0005$15.00
DOI: 10.1086/656735

METHODS

All guidelines issued or endorsed by the IDSA from March 1994 to July 2009 and posted on the IDSA Web site (http://www.idsociety.org) were retrieved. Guidelines were divided into 3 categories similar to those used by the IDSA: (1) infections by organ system; (2) infections by organism, subdivided into bacterial, fungal, and viral infections; and (3) other, combining antimicrobial agent use and guidelines related to fever and infection.

Most of the IDSA guidelines were graded according to the IDSA–US Public Health Service Grading System (USPHS) for ranking recommendations in clinical guidelines [11]. In this system, the letters A–E signify the strength of the recommendation for or against a preventive or therapeutic measure, and Roman numerals I–III indicate the quality of evidence supporting the recommendation (Table 1). Three guidelines followed a grading system similar to IDSA-USPHS with minor differences that did not preclude their inclusion in the analysis (community-acquired pneumonia [CAP] [12], cystitis/pyelonephritis [13], and *Clostridium difficile*–associated diarrhea [14]). Guidelines that followed a different grading method (hepatitis [15, 16] and infective endocarditis [IE] [17]) were regraded per the IDSA-USPHS grading system for our analysis.

The number of recommendations and their distributions among strength of recommendation and quality of evidence classes were quantified. Temporal grade changes between the first and current versions of guidelines were evaluated. Data were summarized as the percentage distribution among ranks within each guideline. Median and interquartile ranges (IQRs) for all guidelines and for the categories and their subdivisions were calculated. Accordingly, unless otherwise noted, summary percentage data are presented as medians. Because the number of recommendations in each guideline version may vary, proportional changes in the level of evidence and the strength of recommendation between guideline versions are expressed as the relative change between current and old versions of the guidelines ([percentage from current version − percentage from old version] / percentage from old version).

RESULTS

From March 1994 to July 2009, the IDSA issued 6643 recommendations in 65 guidelines [18–61]. At the time of our review, there were 52 guidelines posted on the IDSA Web site, 44 of which qualified for inclusion in the analysis. Two guidelines that lacked recommendations (outpatient parenteral antiinfective therapy and international standards for care of tuberculosis) and 6 guidelines that were under development at the 30 July 2009 retrieval deadline (complicated urinary tract infections, rhinosinusitis, prosthetic joint infections, clinical microbiology, immunization for the compromised host, and immunizations of infants, children, adolescents, and adults) were not included. Forty-two guidelines reported both the level of evidence and strength of recommendations, whereas hospital-acquired pneumonia [19] and hepatitis B [25] guidelines reported only level of evidence.

Level of evidence. Approximately one-half of the total number of recommendations were based on level III evidence (median, 50.0%; IQR, 38.1%–58.6%), almost one-third were based on level II evidence (median, 30.9%; IQR, 23.3%–43.2%), and less than one-sixth were based on level I evidence (median, 15.8%; IQR, 5.8%–28.3%) (Table 2; Appendix [which appears only in the electronic version of the journal], Tables A1 and A2). The predominance of level III evidence was greatest in the fungi guidelines (median, 73.1%; IQR, 65.0%–84.2%), whereas streptococcal pharyngitis and influenza guidelines had the least

Table 1. Infectious Diseases Society of America–US Public Health Service Grading System for Ranking Recommendations in Clinical Guidelines.

Category, grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use
Quality of evidence	
I	Evidence from ⩾1 properly randomized, controlled trial
II	Evidence from ⩾1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

NOTE. From [11].

Table 2. Summary of All Current Guidelines

Variable	No. (%) of recommendations	Median percentage (interquartile range)
Level of evidence (total recommendations, 4182)		
I	617 (14.8)	15.8 (5.8–28.3)
II	1240 (29.7)	30.9 (23.3–43.2)
III	2325 (55.5)	50.0 (38.1–58.6)
Class of recommendation (total recommendations, 3998[a])		
A	1606 (40.2)	41.5 (28.7–55.6)
B	1509 (37.7)	40.3 (27.1–47.9)
C	561 (14.0)	8.1 (1.8–14.7)
Other (classes D and E)	322 (8.1)	0 (0–6.7)
None[a]	184	…
Classes of recommendation across levels of evidence (total recommendations, 3998[b,c])		
I–A	407 (10.2)	11.3 (3.8–18.2)
I–B	113 (2.8)	0.7 (0–3.8)
I–C	17 (0.4)	0 (0–0)
I–Other	30 (0.8)	…
II–A	596 (14.9)	14.0 (5.7–20.8)
II–B	416 (10.4)	10.0 (4.9–15.2)
II–C	45 (1.1)	0 (0–1.8)
II–Other	95 (2.4)	…
III–A	603 (15.1)	10.2 (0–18.4)
III–B	980 (24.5)	20.5 (10.3–32.9)
III–C	499 (12.5)	5.4 (0–12.6)
III–Other	197 (4.9)	…

[a] No class (strength) of recommendations were issued for guidelines pertaining to hospital-acquired pneumonia and hepatitis B; not included in the denominator of class of recommendations.
[b] Total number of recommendations is excluding the guidelines that do not have any assigned class of recommendations (ie, hospital-acquired pneumonia and hepatitis B guidelines).
[c] Category "other" constitutes classes D and E.

recommendations with level III evidence (17.6% and 17.5%, respectively) (Appendix, Tables A1 and A2).

Strength of recommendation. The strength of recommendations were evenly distributed among classes A (median, 41.5%; IQR, 28.7%–55.6%) and B (median, 40.3%; IQR, 27.1%–47.9%), which accounted for ~80% of the recommendations. Classes D and E accounted for ~8.1% of the total recommendations (class D, $n = 238$ [6%; median, 0%]; class E, $n = 84$ [2.1%; median, 0%]) (Table 2; Appendix, Tables A1 and A2). The most common class-level designation overall was III–B, accounting for 24.5% of recommendations (median, 20.5%; IQR, 10.3%–32.9%) (Appendix, Tables A3 and A4). Level I evidence was most frequently associated with class A recommendations. The association between strength of recommendation and quality of evidence categories, however, was inconsistent. For example, recommendations based on level III evidence (median, 50.0%; IQR, 38.1%–58.6%) did not correlate with the class C recommendations (median, 8.1%; IQR, 1.8%–14.7%). Similarly, more class A recommendations were based on level II and III rather than I evidence (Table 2; Appendix, Tables A3 and A4; Figures 1 and 2).

Temporal trends. Twelve of 14 guidelines with >1 version qualified for analysis of the temporal changes in the IDSA guidelines. The hepatitis C and new fever in critically ill patients guidelines lacked strength of recommendations and were not included. The number of recommendations increased from 1025 to 1431 (+39.6%) from the first through the current ver-

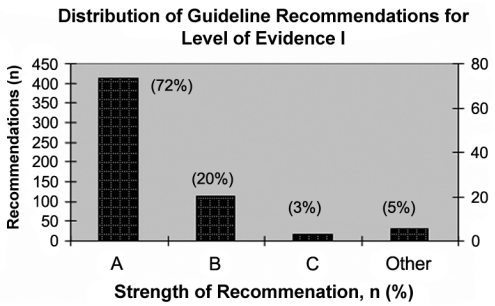

Figure 1. Distribution of the strength (classes) of recommendations across the level of evidence I.

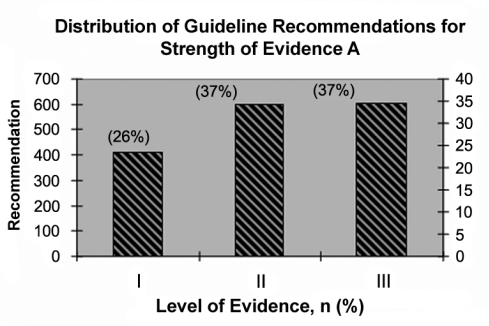

Figure 2. Distribution of the levels of evidence across the strength (classes) of recommendation A.

sions. Although absolute increases in the number of recommendations per category were greatest in level III (+197/577) and classes A (+184/333) and B (+183/387), the guidelines moved proportionately toward more level I (percentage change, +12.4%) and II evidence (percentage change, +2.0%). Similarly, there was an overall proportional increase in class A (percentage change, +11.1%) and B (percentage change, +5.3%) recommendations, whereas class C recommendations underwent a proportional decrease (percentage change, −23.5%) (Table 3; Appendix, Tables A5–A9; Figures 3 and 4).

The increase in level I evidence was accompanied by a corresponding increase in class B and C recommendations (percentage change: I–A, −2.1%; I–B, +54.2%; I–C, +100.0%), whereas an increase in class A strength of recommendation was accompanied by level III evidence (percentage change: I–A, −2.1%; II–A, −17.0%; III–A, +68.9%) (Table 3; Appendix, Tables A5–A9; Figures 3 and 4).

DISCUSSION

Findings. Approximately one-half of the recommendations in the current IDSA guidelines are supported by level III evidence, that is, by opinions of respected authorities or based on clinical experience, descriptive studies, or reports of expert committees. Evidence from observational studies (level II) supports 31% of recommendations, whereas level I evidence based on at least 1 randomized, controlled trial (RCT) constitutes only 16% of the recommendations. The level of evidence varies across categories of guidelines and across individual guidelines. Moreover, only 26% of strong (class A) recommendations were supported by strong (level I) evidence. Conversely, with recommendations having level I evidence, ~25% of the recommendations were less than class A strength.

Three-fourths of class A recommendations have no supporting RCT data, which might lead to greater use of diagnostic or treatment modalities with uncertain benefit. This raises concern that conflict of interest, real or perceived, may have influenced selection of guideline recommendations that are based on less robust, objective evidence [62, 63].

Overall, the IDSA guidelines are moving toward a more robust evidence base, and consequently the strength of recommendations is also improving. However, the increase in the

Table 3. Summary of the Change in the Number of Recommendations and Distribution Across the Levels of Evidence and Classes of Recommendation between First Guideline Version and Current Version

Variable	No. (%) of guidelines		Change in recommendations, no. (%)
	Old (n = 1025)	New (n = 1431)	
Level of evidence			
I	132 (12.9)	208 (14.5)	+76 (+12.4)
II	316 (30.8)	449 (31.4)	+133 (+2.0)
III	577 (56.3)	774 (54.1)	+197 (−3.9)
Strength of recommendation			
Class A	333 (32.5)	517 (36.1)	+184 (+11.1)
Class B	387 (37.8)	570 (39.8)	+183 (+5.3)
Class C	205 (20.0)	219 (15.3)	+14 (−23.5)
Level of evidence across strength of recommendation			
I-A	96 (9.4)	131 (9.2)	+35 (−2.1)
II-A	145 (14.1)	168 (11.7)	+23 (−17.0)
III-A	92 (9.0)	218 (15.2)	+126 (+68.9)
I-B	25 (2.4)	53 (3.7)	+28 (+54.2)
II-B	138 (13.5)	153 (10.7)	+15 (−20.7)
III-B	224 (21.9)	364 (25.4)	+140 (+16.0)
I-C	03 (0.3)	09 (0.6)	+6 (+100)
II-C	05 (0.5)	13 (0.9)	+8 (+80.0)
III-C	197 (19.2)	197 (13.8)	0 (−28.1)

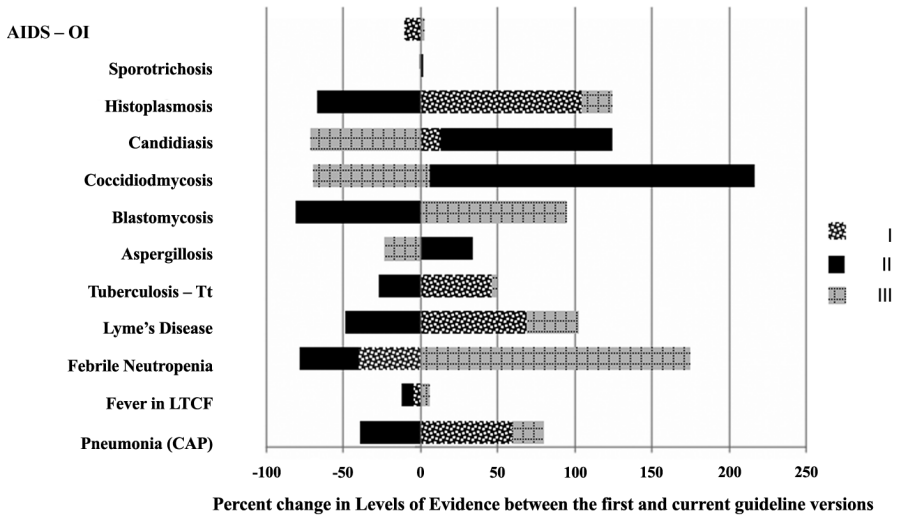

Figure 3. Percentage change in levels of evidence between the first and current guideline version.

strength of recommendations is not concordant with the level of evidence. The increase in level I evidence was accompanied by a corresponding increase in class B and C recommendations, whereas an increase in class A strength of recommendation was accompanied by level III evidence.

Comparison with other studies. Our findings agree with a recent study by Tricoci et al [64], who found that the guidelines developed by the American College of Cardiology and American Heart Association are based largely on lower levels of evidence. Harpole et al [65] also discovered that most of the recommendations for guidelines pertaining to lung cancer were not evidence based. A study performed to evaluate the quality of guidelines for breast and colorectal cancers found out the overall quality of these guidelines was modest [66]. This implies that deficiency of high-quality evidence is not a limitation of only IDSA guidelines but also of guidelines issued by other professional organizations.

Explanations. Our findings highlight an important deficiency of high-quality evidence in clinical infectious disease guidelines. The quality of a guideline is mainly dependent on the evidence available to formulate the guideline.

The paucity of recommendations based on RCT evidence can be attributed to several factors. Many infectious diseases present in myriad fashion, complicating the formulation of a discrete disease definition that can be incorporated into a feasible research protocol. In addition, RCT finance, time, and

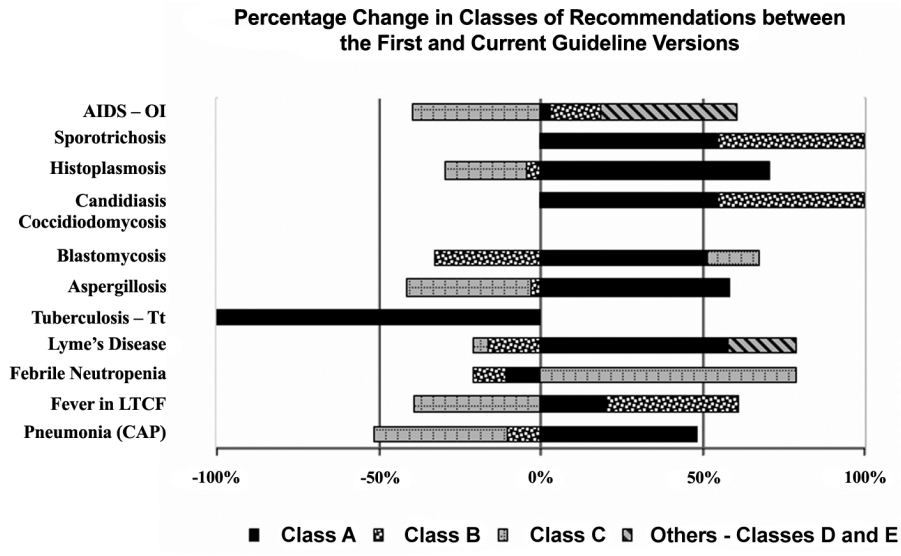

Figure 4. Percentage change in the strength of recommendations between the first and current guideline versions.

resource commitments can be substantial, and even when clinically feasible, the inefficiency of the current research system discourages researchers from conducting randomized trials [67]. The IDSA guidelines with <5% level I evidence exemplify infections and situations where it is a demanding task to enroll patients in trials because of difficulty in diagnosis and management. For example, a recent, randomized, unblinded trial of patients with proven or probable invasive aspergillosis required >4 years to enroll and follow up 391 subjects in 95 medical centers in 19 countries [68]. The rarity of some infectious diseases precluding the conduct of RCTs was reflected by 3 (42.9%) of the 7 IDSA fungi guidelines having no recommendations based on level I evidence. The increase in level I evidence in diseases with a higher prevalence is most likely associated with greater feasibility in designing and conducting studies. In addition, it may not be ethical to perform randomized studies in some disease circumstances. Random allocation of patients with IE to valve surgery or medical management, for example, would be ethically unacceptable. Accordingly, although surgery is considered the standard of care in certain patients with IE, management remains controversial, and the efficacy of surgery is challenged by recent observational evidence [69].

Lower strength of recommendations associated with level I evidence may be attributable to many factors. For example, the quality of the RCT supporting the recommendation on the role of adjunctive dexamethasone in the management of bacterial meningitis in neonates prompted the guideline authors to ascribe a lower strength of recommendation despite qualifying for level I evidence [20, 70]. Moreover, if there are contradictory results among studies, the recommendation may also be of lower strength. In addition, if >1 treatment regimen has been evaluated in controlled studies, 1 alternative may be given a lower strength of recommendation—for example, use of isoniazid and rifampin versus isoniazid and rifapentine in the treatment of culture-positive pulmonary tuberculosis [71].

Optimizing the evidence from RCTs. RCTs are the gold standard of evidence-based medicine; however, to consider all controlled studies as reflective of high-quality evidence irrespective of the quality of the studies and their internal and external validity is not only simplistic but also inappropriate [72]. This has also been shown in the IDSA guidelines where RCT-derived evidence was not accorded strong recommendation strength.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system has been suggested to provide a better approach to synthesize guidelines. The GRADE system recommends conducting a systematic review, preparing evidence profiles, and grading the quality of evidence after considering 4 elements: study design, study quality, consistency, and directness. The balance between benefits and harms, quality of evidence, applicability, and the certainty of the baseline risk are then considered in judgments about the strength of recommendations [73].

A study by McAlister et al [74] evaluated the quality of evidence of cardiovascular risk management guidelines. Considering 3 of the 4 GRADE criteria (study design, quality, and directness), they found that only 45% of RCT-based recommendations provided high-quality evidence. Similarly, applying the GRADE system to IDSA guidelines would likely reveal that a large proportion of level I evidence supporting IDSA guidelines were not of high quality.

Although the GRADE system has been adopted as is, or with minor modifications, by many professional organizations, it has been criticized for being inconsistent and lacking proof of effectiveness [75]. Because, the GRADE system disassociates the strength of recommendations from the level of evidence, it may lead to inconsistency in the translation of evidence into recommendations. This may well lead to interobserver variation between guideline development groups evaluating the same evidence. Others may consider this to be a strength of the GRADE system because it allows value judgments to be incorporated into the guideline development process in a transparent manner. Another criticism of the GRADE system cautions that it could stifle further research if it labels a recommendation as strong [76], but this would hold true for any classification system. In the recent IDSA CAP guidelines, the guideline authors, in response to reviewers' comments, state, "More extensive and validated criteria, such as GRADE, were impractical for use at this stage" [18, p S33]. Despite its limitations, the GRADE system is an important tool for synthesizing evidence and guideline development. It is a major step in moving toward an international standard for grading evidence.

Optimizing the evidence from observational research: the real-world data. Recommendations based on level II evidence should not automatically be considered a failure of the guideline development process. Different questions are best answered using different study designs. High-quality observational studies of data in registries and other real-world databases can provide valuable information to fill gaps in areas where RCTs are not feasible or where external validity of RCTs is circumspect [77, 78]. Observational studies are being used increasingly in the formulation of guidelines. The 2007 CAP guidelines released jointly by IDSA and the American Thoracic Society were derived from multiple large retrospective cohort studies [79, 80]. The recommendations were supported by cohort studies that found benefit when these guidelines were followed [3, 4]. Observational studies can also be used to evaluate patient safety data and for comparative effectiveness research (CER).

CER has been known to researchers for a long time but has recently been given priority with stimulus funds allocated for it. CER has been defined as "the conduct and synthesis of research comparing the benefits and harms of different inter-

Table 4. Priority Topics for Comparative Effectiveness Research Funding in Infectious Diseases

Compare the effectiveness of various screening, prophylaxis, and treatment interventions in eradicating methicillin-resistant *Staphylococcus aureus* in communities, institutions, and hospitals.
Compare the effectiveness of strategies (e.g., bio-patches, reducing central catheter entry, chlorhexidine for all catheter entries, antibiotic impregnated catheters, treating all line entries via a sterile field) for reducing health care–associated infections, including catheter-associated bloodstream infection, ventilator-associated pneumonia, and surgical site infections in children and adults.
Compare the effectiveness of human immunodeficiency virus screening strategies based on recent Centers for Disease Control and Prevention recommendations and traditional screening in primary care settings with significant prevention counseling.
Compare the effectiveness of alternative clinical management strategies for hepatitis C, including alternative duration of therapy for patients based on viral genomic profile and patient risk factors (eg, behavior-related risk factors).

NOTE. From [82].

ventions and strategies to prevent, diagnose, treat, and monitor health conditions in real-world settings" [81, p 5].

Observational research with its large electronic databases and registries will play a major role in CER. The use of electronic health records with its extensive data will need sophisticated analyses like data mining techniques to extract meaningful information from the voluminous observational data. The need for adequate electronic health records for CER is recognized by the Institute of Medicine: "The CER Program should help to develop large-scale, clinical and administrative data networks to facilitate better use of data and more efficient ways to collect new data to inform CER" [82, p 154].

This real-world data derived from registries, observational studies, and other electronic health databases has been criticized for being susceptible to multiple biases and confounders. These can be mitigated by ensuring that appropriate design, data collection, and analytical procedures are used. Tleyjeh et al, for example, suggested criteria that can be used to design cohort studies to assess the role of surgery in IE [83]. Many of these recommendations need not be limited to IE and should be considered by infectious disease clinician scientists when designing observational research. Moreover, the Strengthening the Reporting of Observational Studies in Epidemiology guidelines can be used for reporting observational studies [84].

We do not suggest making observational research on a par with RCTs, which will remain the benchmark of evidence-based medicine, but observational research can be used to strengthen the evidence base (improve the evidence base from level III to level II).

Expert opinions. There is a growing belief that expert opinions are important because many recommendations are based on sound clinical judgment that will never be tested in an RCT. Moreover, expert opinion can help to guide patient care in areas with relative paucity of adequate evidence because physicians may need expert opinion in the areas that lack prior research. This opinion can then be further validated by controlled or observational studies. It has been suggested that it may be preferable for guideline committees to develop 2 parallel reports, one presenting guidelines for which evidence is available and another identifying issues that need more data and for which only expert opinion can be given [85]. The US Preventive Task Force, for example, does not issue recommendations without supporting evidence [86].

Allocation of funds. There should be adequate funds available to optimize and expand the existing evidence base—support RCTs where needed, develop registries and databases to strengthen observational research, and support CER. There is a need to identify other sources of funds besides the traditional ones and to support research in areas that may lack apparent commercial value or have a long gestation period from the bench to the bedside. Public-private partnerships and private philanthropy could step in to facilitate translational research [67], which frequently does not attract investment by the private sector. Thus, public resources can bridge the gap between discovery and clinical testing so that more efficient translation of promising discoveries may take place. There have been many new initiatives to fund and encourage translational research: the National Institutes of Health Rapid Access to Interventional Development Program [87] and Microscope to Marketplace, a collaboration between the National Institutes of Health and the US Food and Drug Administration under the Cures Acceleration Network [88].

The American Recovery and Reinvestment Act of 2009 funding reflects the recognition of the potential of CER to improve and strengthen existing "best practices" [81]. CER funds offer an extraordinary opportunity to complement ongoing research in the public and private sectors by establishing a solid infrastructure for future CER. Some priority areas in infectious diseases have been identified for CER, to be undertaken with American Recovery and Reinvestment Act funding (Table 4) [82].

Thus, adequate resources directed toward priority areas in infectious diseases, such as those identified, as initial national priorities in CER and as areas lacking in high-quality evidence highlighted by IDSA guidelines and translational research, can potentially strengthen the evidence base of IDSA clinical practice guidelines.

Conclusions. The IDSA guideline recommendations are primarily based on low-quality evidence derived from nonrandomized studies or expert opinion. These findings highlight a serious deficiency in clinical infectious diseases research that can provide high-quality evidence. There is an urgent need to close these knowledge gaps by performing RCTs as appropriate, to optimize the conduct and reporting of observational studies,

and to perform CER, which can potentially strengthen the evidence. This will not be achieved without ensuring adequate funding is available to support high-quality research. Our findings should not be considered a call to ignore practice guidelines. Studies have shown improvement in patient care with better clinical outcomes when IDSA guidelines are followed. However, physicians must always rely on their clinical judgment during the application of practice guidelines.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

References

1. Field MJ, Lohr KN, eds; Committee to Advise the Public Health Service on Clinical Practice Guidelines, Institute of Medicine. Clinical practice guidelines: directions of a new program. Washington, DC: National Academy Press, **1990**.
2. National Guideline Clearinghouse Web site. http://www.guideline.gov. Updated 24 August 2009. Accessed 30 August 2009.
3. Forest WA, Scott AL, Guy NB, et al. Improving outcomes in elderly patients with community-acquired pneumonia by adhering to national guidelines: Community-Acquired Pneumonia Organization international cohort study results. Arch Intern Med **2009**; 169:1515–1524.
4. Caitlin M, Cheryl K, Huiling Z, Jennifer D, David NF. Guideline-concordant therapy and reduced mortality and length of stay in adults with community-acquired pneumonia: playing by the rules. Arch Intern Med **2009**; 169:1525–1531.
5. Wu JH, Howard DH, McGowan JE Jr, Turpin RS, Henry Hu X. Adherence to infectious diseases society of America guidelines for empiric therapy for patients with community- acquired pneumonia in a commercially insured cohort. Clin Ther **2006**; 28:1451–1461.
6. Bodi M, Rodríguez A, Solé-Violán J, et al. Antibiotic prescription for community-acquired pneumonia in the intensive care unit: impact of adherence to Infectious Diseases Society of America guidelines on survival. Clin Infect Dis **2005**; 41:1709–1716.
7. Orrick JJ, Segal R, Johns TE, Russell W, Wang F, Yin DD. Resource use and cost of care for patients hospitalised with community acquired pneumonia: impact of adherence to Infectious Diseases Society of America guidelines. Pharmacoeconomics **2004**; 22:751–757.
8. Nucci M, Landau M, Silveira F, Spector N, Pulcheri W. Application of the IDSA guidelines for the use of antimicrobial agents in neutropenic patients: impact on reducing the use of glycopeptides. Infect Control Hosp Epidemiol **2001**; 22:651–623.
9. Lawton RM, Fridkin SK, Gaynes RP, McGowan JE Jr. Practices to improve antimicrobial use at 47 US hospitals: the status of the 1997 SHEA/IDSA position paper recommendations: Society for Healthcare Epidemiology of America/Infectious Diseases Society of America. Infect Control Hosp Epidemiol **2000**; 21:256–259.
10. Kawada Y, Ishihara S. Adequacy of the new guidelines on clinical evaluation of drug efficacy in acute uncomplicated cystitis. Int J Antimicrob Agents **1999**; 11:185–187.
11. Canadian Task Force on the Periodic Health Examination. The periodic health examination. Can Med Assoc J 1979; 121:1193–1254.
12. Kish MA. Guide to development of practice guidelines. Clin Infect Dis **2001**; 32:851–854.
13. McGowan JE Jr, Chesney PJ, Crossley KB, LaForce FM. Guidelines for the use of systemic glucocorticosteroids in the management of selected infections. J Infect Dis **1992**; 165:1–13.
14. Gross PA, Barret TL, Dellinger EP, et al. Consensus development of quality standards. Infect Control Hosp Epidemiol **1994**; 15:18–181.
15. American Gastroenterogical Association policy statement on the use of medical practice guidelines by managed care organizations and insurance carriers. Gastroenterology **1995**; 108:925–926.
16. Shiffman RN, Shekelle P, Overhage JM, Slutsky J, Grimshaw J, Deshpande AM. Standardized reporting of clinical practice guidelines: a proposal from the Conference on Guideline Standardization. Ann Intern Med **2003**; 139:493–498.
17. Manual for ACC/AHA Guideline Writing Committees. Section II: tools and methods for creating guidelines. **2010**. http://circ.ahajournals.org/manual/manual_IIstep6.shtml.
18. Mandell LA, Wunderink RA, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis **2007**; 44:S27–S72.
19. Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia (Official statement of the American Thoracic Society and the Infectious Diseases Society of America). Am J Respir Crit Care Med **2005**; 171:388–416.
20. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis **2004**; 39:1267–1284.
21. Tunkel AR, Glaser CA, Bloch KC, et al. The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis **2008**; 47:303–327.
22. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Clin Infect Dis **1999**; 29:745–758.
23. Lindsay EN, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis **2005**; 40:643–654.
24. Lipsky BA, Berendt AR, Deery HG, et al. Diagnosis and treatment of diabetic foot infections. Clin Infect Dis **2004**; 39:885–910.
25. Anna S., Lok F, McMahon BJ. AASLD practice guidelines: chronic hepatitis B. Hepatology **2007**; 45: 507–539.
26. Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update (AASLD practice guidelines, endorsed by IDSA). Hepatology **2009**; 49:1335–1374.
27. Guerrant RL, Gilder TV, Steiner TS, et al. Practice guidelines for the management of infectious diarrhea. Clin Infect Dis **2001**; 32:331–350.
28. Gerding DN, Johnson S, Peterson LR, Mulligan ME, Silva J Jr. *Clostridium difficile*–associated diarrhea and colitis (SHEA Position Paper). Infect Control Hosp Epidemiol **1995**; 16:459–477.
29. Solomkin JS, Mazuski JE, Baron EJ, et al. Guidelines for the selection of anti-infective agents for complicated intra-abdominal infections. Clin Infect Dis **2003**; 37:997–1005.
30. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis 2005; 41:1373–1406.
31. Bisno AL, Gerber MA, Gwaltney JM Jr, Kaplan EL, Schwartz RH. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. Clin Infect Dis **2002**; 35:113–125.
32. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: Endorsed by the Infectious Diseases Society of America. Circulation **2005**; 111:e394–e433.
33. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care

and Outcomes Research Interdisciplinary Working Group. Circulation **2007**; 116:1736–1154.
34. Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. MMWR Morb Mortal Wkly Rep **2000**; 49(RR-10):1–125.
35. Hill DR, Ericsson CD, Pearson RD, et al. The practice of travel medicine: guidelines by the Infectious Diseases Society of America. Clin Infect Dis **2006**; 43:1499–1539.
36. Mermel LA, Farr BM, Sherertz RJ, et al. Guidelines for the management of intravascular catheter–related infections. Clin Infect Dis **2001**; 32:1249–1272.
37. High KP, Bradley SF, Gravenstein S, et al. Clinical practice guideline for the evaluation of fever and infection in older adult residents of long-term care facilities: 2008 update by the Infectious Diseases Society of America. Clin Infect Dis **2009**; 48:149–171.
38. Hughes WT, Armstrong D, Bodey GP, et al. 2002 Guidelines for the use of antimicrobial agents in neutropenic patients with cancer. Clin Infect Dis **2002**; 34:730–751.
39. Yokoe DS, Mermel LA, Anderson DJ, et al. A compendium of strategies to prevent healthcare associated infections in acute care hospitals. Infect Control Hosp Epidemiol **2008**; 29:S12–S21.
40. Dellinger EP, Gross PA, Barrett TL, et al. Quality standard for antimicrobial prophylaxis in surgical procedures. Clin Infect Dis **1994**; 18:422–427.
41. Shlaes DM, Gerding DN, John JF Jr, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. Clin Infect Dis **1997**; 25:584–599.
42. Dellit TH, Owens RC, McGowan JE Jr, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis **2007**; 44:159–177.
43. Rybak M, Lomaestro B, Crotschafer J, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm **2009**; 66:82–98.
44. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis **2006**; 43:1089–134.
45. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An Official ATS/IDSA Statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med **2007**; 175:367–416.
46. Centers for Disease Control and Prevention, American Thoracic Society, and Infectious Diseases Society of America. Treatment of tuberculosis. MMWR Morb Mortal Wkly Rep **2003**; 52(RR-11):1–77.
47. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America. Controlling tuberculosis in the United States. Am J Respir Crit Care Med **2005**; 172:1169–1227.
48. Walsh TJ, Anaissie EJ, Denning DW, et al. Treatment of aspergillosis: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis **2008**; 46:327–360.
49. Chapman SW, Dismukes WE, Proia LA, et al. Clinical practice guidelines for the management of blastomycosis: 2008 update by the Infectious Diseases Society of America. Clin Infect Dis **2008**; 46:1801–1812.
50. Galgiani JN, Ampel NM, Blair JE, et al. Coccidioidomycosis. Clin Infect Dis **2005**; 41:1217–1223.
51. Saag MS, Graybill RJ, Larsen RA, et al. Practice guidelines for the management of cryptococcal disease. Clin Infect Dis **2000**; 30: 710–718.
52. Pappas PG, Kauffman CA, Andes D, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis **2009**; 48:503–535.
53. Wheat LJ, Freifeld AG, Kleiman MB, et al. Clinical practice guidelines for the management of patients with histoplasmosis: 2007 update by the Infectious Diseases Society of America. Clin Infect Dis 2007; 45: 807–825.
54. Kauffman CA, Bustamante B, Chapman SW, Pappas PG. Clinical practice guidelines for the management of sporotrichosis: 2007 update by the Infectious Diseases Society of America. Clin Infect Dis **2007**; 45:1255–1265.
55. Aberg JA, Gallant JE, Anderson J, et al. Primary care guidelines for the management of persons infected with human immunodeficiency virus: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis **2004**; 39:609–629.
56. Gupta SK, Eustace JA, Winston JA, et al. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis **2005**; 40:1559–1585.
57. Dube MP, Stein JH, Aberg JA, et al. Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)–infected adults receiving antiretroviral therapy: recommendations of the HIV Medicine Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group. Clin Infect Dis **2003**; 37:613–627.
58. Centers for Disease Control and Prevention. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Morb Mortal Wkly Rep **2009**; 58(RR-4):1–207.
59. Guidelines for prevention and treatment of opportunistic infections among HIV-exposed and HIV-infected children: recommendations from Centers for Disease Control and Prevention, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, and the Pediatric Infectious Diseases Society. http://AIDSinfo.nih.gov. Accessed 20 June 2008.
60. Centers for Disease Control and Prevention. Incorporating HIV prevention into the medical care of persons living with HIV: recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Morb Mortal Wkly Rep **2003**; 52(RR-12):1–24.
61. Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults and children—diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis **2009**; 48:1003–1032.
62. Grol R. Has guideline development gone astray? yes. BMJ **2010**; 340: c306.
63. Choudhry NK, Stelfox TH, Detsky AS. Relationships between authors of clinical practice guidelines and the pharmaceutical industry. JAMA **2002**; 287:612–617.
64. Tricoci P, Allen JM, Kramer JM, et al. Scientific evidence underlying the ACC/AHA clinical practice guidelines. JAMA **2009**; 301:831–841.
65. Harpole LH, Kelley MJ, Schreiber G, Toloza EM, Kolimaga J, McCrory DC. Assessment of the scope and quality of clinical practice guidelines in lung cancer. Chest **2003**; 123(1 suppl):7S-20S.
66. Vigna-Taglianti F, Vineis P, Liberati A, Faggiano F. Quality of systematic reviews used in guidelines for oncology practice. Ann Oncol **2006**; 17:691–701.
67. Crowley WF Jr, Sherwood L, Salber P, et al. Clinical research in the United States at a crossroads: proposal for a novel public-private partnership to establish a national clinical research enterprise. JAMA **2004**; 291:1120–1126.
68. Herbrecht R, Denning DW, Patterson TF, et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N Engl J Med **2002**; 347:408–415.

69. Tleyjeh IM, Ghomrawi HMK, Steckelberg JM, et al. The impact of valve surgery on 6-month mortality in left-sided infective endocarditis. Circulation **2007**; 115:1721–1728.
70. Daoud AS, Baticha A, Al-Sheyyab M, et al. Lack of effectiveness of dexamethasone in neonatal bacterial meningitis. Eur J Pediatr 1999; 158:230–233.
71. Benator D, Bhattacharya M, Bozeman L, et al. Rifapentine and isoniazid once a week versus rifampicin and isoniazid twice a week for treatment of drug-susceptible pulmonary tuberculosis in HIV-negative patients: a randomized clinical trial. Lancet **2002**; 360:528–534.
72. Norris SL. Clinical Practice Guidelines and Scientific Evidence [letter]. JAMA **2009**; 302:142–147.
73. Atkins D, Best D, Briss PA, et al. GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ **2004**; 328: 1490–1497.
74. McAlister FA, van Diepen S, Padwal RS, Johnson JA, Majumdar SR. How evidence-based are the recommendations in evidence-based guidelines? PLoS Med **2007**; 4:e250.
75. Atkins D, Briss PA, Eccles M, et al. Systems for grading the quality of evidence and the strength of recommendations II: pilot study of a new system. BMC Health Serv Res **2005**; 5:25.
76. Kavanagh B. The GRADE System for Rating Clinical Guidelines. PLoS Med **2009**; 6(9):e1000094.
77. Gliklich RE, Dreyer NA, eds. Registries for evaluating patient outcomes: a user's guide [AHRQ publication No. 07-EHC001–1, April 2007]. Agency for Healthcare Research and Quality. http://effectivehealthcare.ahrq.gov/repFiles/DEcIDEs_Registries.html. Accessed 6 July 2009.
78. Dreyer NA, Garner S. Registries for robust evidence. JAMA**2009**; 302: 790–91.
79. Gleason PP, Meehan TP, Fine JM, Galusha DH, Fine MJ. Associations between initial antimicrobial therapy and medical outcomes for hospitalized elderly patients with pneumonia. Arch Intern Med **1999**; 159:2562–2572.
80. Dudas V, Hopefl A, Jacobs R, Guglielmo BJ. Antimicrobial selection for hospitalized patients with presumed community-acquired pneumonia: a survey of non-teaching US community hospitals. Ann Pharmacother **2000**; 34:446–452.
81. US Department of Health and Human Services Federal Coordinating Council for Comparative Effectiveness Research. Report to the President and Congress. Washington, DC: Dept of Health and Human Services; June 2009. http://www.hhs.gov/recovery/programs/cer/cerannualrpt.pdf. Accessed 20 June 2009.
82. Ratner R, Eden J, Wolman D, Greenfield S, Sox H, eds. Institute of Medicine: initial national priorities for comparative effectiveness research. Washington, DC: National Academies Press, **2009**.
83. Tleyjeh IM, Kashour T, Zimmerman V, Steckelberg JM, Wilson WR, Baddour LM. The role of valve surgery in infective endocarditis management: a systematic review of observational studies that included propensity score analysis. Am Heart J **2008**; 156:901–909.
84. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Prev Med **2007**; 45:247–251.
85. Shaneyfelt TM. Clinical practice guidelines and scientific evidence [letter]. JAMA **2009**; 302:146–147.
86. Sawaya GF, Guirguis-Blake J, LeFevre M, Harris R, Petitti D; US Preventive Services Task Force. Update on the methods of the US Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med **2007**; 147:871–875.
87. NIH Common Fund. http://nihroadmap.nih.gov/clinicalresearch/overview-translational.asp. Accessed 25 June 2010.
88. Foley Hoag. Healthcare Law and Policy Blog. http://www.healthcarelawandpolicy.com/2010/04/articles/health-reform/the-cures-acceleration-network-developing-and-approving-high-need-cures/. Accessed 25 June 2010.
89. Bartlett JG, Breiman RF, Mandell LA, File TM Jr. Community-acquired pneumonia in adults: guidelines for management. Clin Infect Dis **1998**; 26:811–838.
90. Bentley DW, Bradley S, High K, Schoenbaum S, Taler G, Yoshikawa TT. Practice guideline for evaluation of fever and infection in long-term care facilities. Clin Infect Dis **2000**; 31:640–653.
91. Hughes WT, Armstrong D, Bodey GP, et al. 1997 Guidelines for the use of antimicrobial agents in neutropenic patients with unexplained fever. Clin Infect Dis **1997**; 25:551–573.
92. Wormser GP, Nadelman RB, Dattwyler RJ, et al. Practice guidelines for the treatment of Lyme disease. Clin Infect Dis **2000**; 31(suppl 1): S1–S14.
93. Horsburgh CR Jr, Feldman S, Ridzon R. Practice guidelines for the treatment of tuberculosis. Clin Infect Dis **2000**; 31:633–639.
94. Stevens DA, Kan VL, Judson MA, et al. Practice guidelines for diseases caused by aspergillus. Clin Infect Dis **2000**; 30:696–709.
95. Chapman SW, Bradsher RW Jr, Campbell GW Jr, Pappas PG, Kauffman CA. Practice guidelines for the management of patients with blastomycosis. Clin Infect Dis **2000**; 30:679–683.
96. Galgiani JN, Ampel NM, Catanzaro A, Johnson RH, Stevens DA, Williams PL. Practice guidelines for the treatment of coccidioidomycosis. Clin Infect Dis **2000**; 30:658–661.
97. Rex JH, Walsh TJ, Sobel JD, et al. Practice guidelines for the treatment of candidiasis. Clin Infect Dis **2000**; 30:662–678.
98. Wheat J, Sarosi G, McKinsey D, et al. Practice guidelines for the management of patients with histoplasmosis. Clin Infect Dis **2000**; 30:688–695.
99. Kauffman CA, Hajjeh R, Chapman SW, for the Mycoses Study Group; Practice guidelines for the management of patients with sporotrichosis. Clin Infect Dis **2000**; 30:684–687.
100. Centers for Disease Control and Prevention. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. MMWR Morb Mortal Wkly Rep **1995**; 44(RR-8):1–34.
101. Centers for Disease Control and Prevention. Treating opportunistic infections among HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/Infectious Diseases Society of America. MMWR Morb Mortal Wkly Rep **2004**; 53(RR-15):1–112.