Should Committees That Write Guidelines and Recommendations Publish Dissenting Opinions?

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Abstract

Medical guidelines tend to convey a sense of unanimity of opinion that may not reflect the deliberations of the experts who wrote them. Using, as an example, an analysis of the recently published recommendations on administering pneumococcal conjugate vaccine to adults, the present article raises the question of whether official recommendations and guidelines should include dissenting opinions, analogous to decisions issued by the US Supreme Court. The argument that such a policy would lead to confusion in our profession is addressed in 2 ways: (1) the current system, in which different professional societies publish conflicting recommendations, as in the case of breast or prostate cancer screening, can be far more confusing, and (2) in the long run, greater transparency will lead to more thoughtful and higher-quality medical care. Perhaps the most important point of this paper is the suggestion that it is far better to bring dissent into the recommendation process than to act as if it is not there.

When the Supreme Court of the United States issues a decision, it publishes separate concurring opinions from justices in the majority and dissenting opinions from those in the minority. Medical committees that write guidelines or make official recommendations may have heated debates and substantial internal disagreement, but only the conclusions are published. As citizens of the United States, we are as much bound by a 5-4 decision of the High Court as a 9-0 vote (although closely passed decisions are more likely to be overturned in future cases). Similarly, as practitioners of medicine, until new guidelines are written, we are seriously constrained by, if not actually bound by, existing ones, without regard to the unanimity of opinion in the recommending committee. Nevertheless, there is much to gain from studying dissenting opinions, as was famously shown by the writings of Justices Holmes and Brandeis, many of whose minority opinions, in time, became the law of the land. I propose that the failure to publish differing or dissenting views in medical guidelines presents our profession with an inappropriately monolithic view—one that is studied as gospel by physicians-in-training and forced on practitioners by incorporation into a variety of performance measures.

I propose to examine the subject of dissenting opinions using, as a case in point, the recent recommendations by the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention regarding a dual vaccine approach to pneumococcal vaccination for adults. The 2 vaccines are 23-valent pneumococcal polysaccharide vaccine (PPSV23), marketed in the United States as Pneumovax 23 (Merck & Co Inc) and 13-valent pneumococcal conjugate vaccine (PCV13), marketed as Prevnar 13 (Wyeth LLC). The essence of the recommendation is that (1) vaccine-naïve adults (≥19 years old) with immunocompromising conditions receive both vaccines, with PCV13 given first followed by PPSV23 (those who have already received PPSV23 should be given PCV13 alone) and (2) this same approach be applied to all adults 65 years and older.

I served on the working group that recommended the use of PCV13 to the ACIP, and I strongly disagreed with the final recommendation. I had ample opportunity during multiple telephone conferences to express my dissenting opinion. Although we used the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) system, the final grading did not average the grading by individual members but was determined by consensus. Thus, if the
majority agreed on a grade, this was not affected by a strong dissent. In other words, dissenting minority opinions had essentially no voice, and the recommendations went forward to the ACIP, which accepted them by a majority vote.5

In this brief communication, I summarize the reasons why I regard the final ACIP recommendations on pneumococcal vaccination for adults 65 years and older to be inappropriate. My purpose is neither to criticize the ACIP, which has played a central role in promoting public health in the United States, nor to encourage failure to comply with the recommendations, which are already being implemented. (Interestingly, PCV13 for adults ≥65 years old was recommended with the understanding7 that the subject will be revisited in 2018, suggesting that the issues are, in fact, far more fluid and complex than is indicated by reading the final document.) Rather, I use this issue to raise the general question of whether medical guidelines should follow the example of the Supreme Court by publishing separate concurring and dissenting opinions. Dissenting opinions are rarely published in these circumstances,6 and, until very recently,7 no one has, to my knowledge, addressed this problem in the medical literature. I contend that a great deal of transparency would result from publishing dissenting opinions, and the result would be greatly beneficial to our profession and to the public. For full disclosure, the reader should note that I adhere to vaccination recommendations and urge my students to do the same, although I lecture on the underlying controversy because those of us who teach should be showing learners how to think about problems, present and future, not just how to follow guidelines.

Ample evidence shows that PPSV23 protects adults against noninvasive pneumococcal pneumonia (NIPP; pneumonia without a positive blood culture) and invasive pneumococcal disease (IPD; infection with Streptococcus pneumoniae grown from any sterile site).8 A Cochrane review by Moberley et al in 20089 documented 73% protection against vaccine-type specific NIPP and 82% protection against IPD by PPSV23; a more recent Cochrane review10 presented similar findings. The working group and the ACIP misinterpreted the Cochrane review by Moberley et al10 interpreting the results as showing no protection against NIPP and instead accepting a meta-analysis by Huss et al,11 which I have critiqued elsewhere.12 Incorrectly assuming the inadequacy of PPSV23 greatly lowered the threshold for approving another vaccine strategy.

Capsular polysaccharides (CPSs) do not interact with helper T cells but, rather, directly stimulate B cells by cross-linking receptors on their cell surfaces. The immature immune system does not respond to polysaccharides. As a result, PPSV23 is not immunogenic in infants. Chemical conjugation of pneumococcal CPSs to immunogenic proteins yields PCVs that evoke T-cell responses, effectively stimulating protective antibody responses in infants. Revaccination after initial sensitization with a protein antigen generally leads to a booster response, whereas repeated vaccination with a polysaccharide antigen is suppressive, especially if given at close intervals.13

From these basic principles, but with slender supporting evidence, the working group assumed that (1) PCV13 stimulates higher levels of anti-CPS antibody than PPSV23, (2) this antibody persists for longer intervals, (3) PCV13 primes the immune system for a booster response by PPSV23, and (4) PCV13 more effectively protects immunocompromised and elderly adults than does PPSV23.

Published data available at the time the ACIP made these recommendations did not support these conclusions.14 Many earlier studies showed that PCV7 was equivalent, but not clearly superior, to PPSV23 in stimulating antibody activity.14 It required a study of nearly 900 older adults to show that 1 month after vaccination, antibody activity was significantly greater against 8 of 12 CPSs in recipients of PCV13 vs PPSV23. Whether this difference is meaningful is unknown because a protective level of antibody against each serotype in adults has not been determined. These data were presented to the working group before publication, a practice to which I was strongly opposed. However, the published document15 showed (and, then, only in the supplementary materials) that by 1 year after vaccination, antibody activity for vaccine serotypes was identical in recipients of PPSV23 or PCV13.15 Ridda et al16 reached a similar conclusion in frail, elderly people.

The medical literature also did not support the concept that PCV13 would prime for a booster effect by PPSV23. In one large study,17...
a booster effect was shown for 6 of 12 serotypes, but the effect was measured only 1 month after the boosting dose. A small-scale experiment in my laboratory found a suggestive booster effect after 1 month, but differences were no longer apparent 6 months later, and a recent study in immunocompromised hosts showed no booster effect from PPSV23 after 3 doses of PCV13.

No clinical trial has directly compared the clinical efficacy of PPSV23 vs PCV13. French et al showed that PPSV23 provided no protection in Ugandan patients who had untreated acquired immunodeficiency syndrome. A subsequent study in Malawi by the same group of investigators found that PCV13 reduced IPD by 74% in the first year; no protection was observed after that. However, 12% of the Malawi participants did not have human immunodeficiency virus infection, and 42% of those who did received antiretroviral drug treatment during the study period. Although the use of antiretroviral agents in the Malawi trial clearly renders these studies noncomparable, the working group and the ACIP regarded them as sufficiently similar to conclude that PCV protects patients with acquired immunodeficiency syndrome and PPSV does not.

The final recommendations for vaccination of adults 65 years and older placed undue emphasis on the results of the Community-Acquired Pneumonia Immunization Trial in Adults (CAPiTA), a well-designed study of 83,000 Dutch adults 65 years and older randomized to receive PCV13 or placebo. Of note, this study excluded adults who had any known immunocompromising condition. PCV13 reduced IPD due to vaccine-type pneumococci by 75%, a result similar to that previously reported for PPSV23, and was less effective in protecting against NIBP than was PPSV23 (46% vs 72%, respectively). The CAPiTA did not compare PCV13 with PPSV23, so any conclusion about the relative benefits of either vaccine could be inferential only.

Again, despite my strong objection, the working group made its recommendation before the results of the CAPiTA met editorial scrutiny and were published. This practice has been followed in the past when there was a clear need for a vaccine and no alternative was available, but this was not the case here. When the paper finally appeared, an analysis of individuals who, during the study, developed a condition or were begun on a treatment that rendered them immunocompromised failed to show protection by PCV13. Twenty-five cases of IPD occurred in such immunocompromised persons: 14 in the vaccinated group and 11 in the placebo group. In other words, immunocompromised persons—the group for whom the ACIP has strongly urged the use of PCV13—were not shown to be protected in the CAPiTA study.

The ACIP’s interpretation of cost analysis studies was also problematic. The Delphi expert panel studies assumed that PPSV23 protects against IPD but not against NIPP. The Cochrane reviews by Moberley et al did not support this assumption, but, as noted previously herein, the working group and most of the Delphi expert panel accepted the conclusions of Huss et al while rejecting those of Moberley et al. If, in comparing PCV13 with PPSV23, the latter is assumed to provide no protection against NIPP (~75% of all pneumococcal pneumonia is thought to be noninvasive), the use of PCV13 becomes economically feasible. However, when cost analyses calculated protection by PPSV23 based on only 45% efficacy against NIPP, the cost of adding PCV13 per quality-adjusted life-year rose well in excess of $100,000. These studies also assumed that S pneumoniae causes 30% of community-acquired pneumonia; more recent estimates based on studies in the Netherlands are closer to 13% and in the United States are 8% to 12%, which would even further increase the cost per quality-adjusted life-year. Subsequent analyses have shown that PCV13 is not more cost-effective than the existing PPSV23.

The most compelling reason not to use PCV13 routinely in adults is that disease caused by vaccine strains is rapidly disappearing. PCV stimulates mucosal immunity and prevents nasopharyngeal colonization, thereby reducing the dissemination of pneumococci in the community. Historically, adults most often acquire contagious respiratory diseases from children. After routine adoption of PCV7 for infants, infection of adults due to vaccine types declined by nearly 95%, lagging eradication in children by 4 to 5 years (Figure). There was no reason to believe that the same effect would not be seen with PCV13. By 2013, only 3 years...
after the adoption of PCV13 for children, the incidence of adult disease caused by serotypes present in PCV13 but not in PCV7 had already declined by 58% to 72%,32 and no more than 10% of IPD was caused by serotypes contained in PCV13.33 Thus, just as the PCV13 vaccine program is ramping up in the adult population, this vaccine has become increasingly irrelevant.

Despite strong minority objections, the ACIP recommendations to use PCV13 in adults have become the standard of care—the law of the land, to return to the Supreme Court analogy. Current ACIP recommendations will lead to the widespread administration of PCV13 to all adults 65 years and older and all immunocompromised persons older than 19 years, followed by PPSV23, an approach that may minimally enhance protection (compared with PPSV23 alone) against a rapidly vanishing set of pneumococcal serotypes.

The perceived problems with publishing dissenting opinions are that this practice would (1) cause confusion within the medical community and (2) diminish the force of the recommendations. Regarding the former, the current situation, in which dissent is not included but in which subsequent articles dispute the formal recommendations,12,34–38 or different professional societies publish divergent guidelines, is amply confusing—witness the differing guidelines for screening for breast, lung, or prostate cancer. It defies reason to believe that every member of the American Cancer Society’s committee thought that breast cancer screening should begin at age 40 years, whereas all who participated in the US Preventive Services Task Force agreed that screening should wait until age 50 years. Inclusion of dissenting opinions in the final version of published guidelines may well have reduced polarization and confusion by bringing dissent into the recommendation process. This would also greatly increase transparency in the process. Interestingly, instead of issuing its own guidelines, the American College of Physicians recently suggested an individualized, patient-directed approach to prostate cancer screening (https://www.acponline.org/newsroom/prostate_cancer_screening.htm),39 an approach that will encourage more thoughtful and relevant medical care; admittedly, this works much better for practice guidelines than for vaccination guidelines.

Regarding the question of whether publishing dissenting opinions will reduce the force or the prestige of the recommending body, this issue greatly concerned Chief Justice John Marshall in the early years of the US Supreme Court. At the time the Court was established, the practice was, in fact, for each justice to issue his own opinion, a process called seriatim. Marshall strongly opposed this, believing that seriatim decisions diminished the prestige and

![Image](https://www.mayoclinicproceedings.org)

### FIGURE

Decline in vaccine-type specific cases of invasive pneumococcal disease in children younger than 5 years (A) and adults older than 65 years (B).31 *PCV7 was introduced in the second half of 2000. PCV7 = 7-valent pneumococcal protein—conjugate vaccine.
authority of the court. In fact, as Melvin Urofsky recently reported, 1 during Marshall’s tenure as Chief Justice, only 87 of 1187 decisions (7.3%) included either concurring or dissenting opinions. Urofsky emphasizes, however, that certain court decisions were deeply flawed. One notorious example was Chief Justice Taney’s Dred Scott decision, and the lesser-known dissents by Justices McLean and Curtis, served to guide legislators as they later established the law of the land. My concept for medical guidelines, especially for treatment guidelines, is that if they are published together with dissenting and concurring opinions, physicians will adhere to them anyway, but there will be greater impetus for revision and change. Recommendations related to pediatric vaccines simply need to be followed because there is no room for individualization, although vaccine recommendations for adults might be open to some question, as noted in the present article.

Finally, a striking recent trend in medical education has been the increasing emphasis on practice guidelines. Our very capable residents and fellows can often recite them verbatim. Unfortunately, few have read the references that underlie them, and even fewer have thought about their validity, the uniformity of opinion underlying them, or the universality with which they can or should be applied. Dissenting opinions are valuable, and they should be published for their learning value for all of us and, in the case of practice guidelines, for their application to patient care.

**Abbreviations and Acronyms.** ACIP = Advisory Committee on Immunization Practices; CAPITA = Community-Acquired Pneumonia Immunization Trial in Adults; CPS = capsular polysaccharide; IPD = invasive pneumococcal disease; NIPP = noninvasive pneumococcal pneumonia; PCV7 = 7-valent pneumococcal conjugate vaccine; PCV13 = 13-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine

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**REFERENCES**


