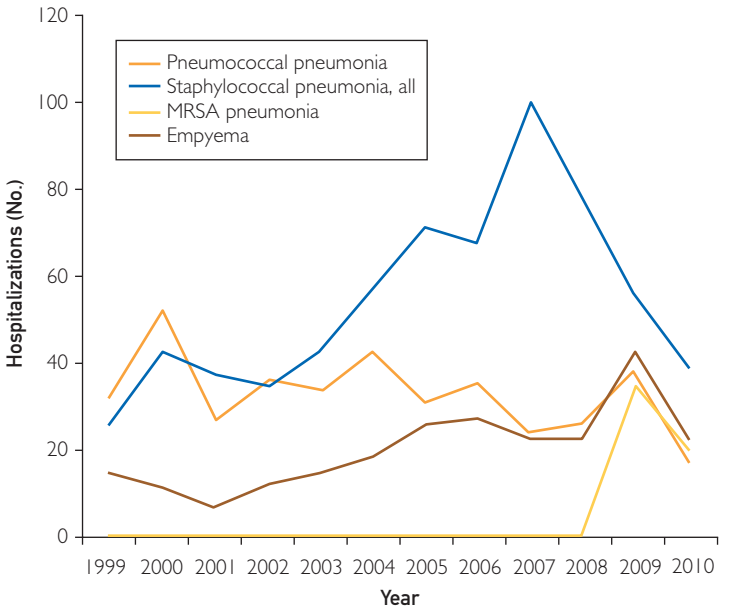

FIGURE. Hospitalizations during the study period for *International Classification of Diseases, Ninth Revision* codes for pneumococcal, staphylococcal, and methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia and empyema.

serotypes and replacement by *S aureus*. However, while all staphylococcal pneumonia diagnoses significantly increased from the pre-PCV7 era to the early post-PCV7 era (P=.049), a nonsignificant decrease was observed in the late post-PCV7 era (P=.10), which includes the 2009-2010 influenza pandemic that was associated with an increase in secondary bacterial pneumonia.[6] We also examined whether empyema diagnoses increased during this period, which has been noted in other studies in the last post-PCV7 era,[4] but no statistically significant trend was evident in our data.

Study Limitations. One must be wary of drawing too specific a conclusion from our findings because the trends were based solely on *ICD-9* codes, which can be inaccurately recorded by clinicians. Furthermore, most of the *ICD-9* code diagnoses were pneumonia and bacterial pneumonia and were not pathogen specific; hence, we could have potentially increased the number of confirmed pathogens if we did an in-depth chart review. We did not abstract the clinical, radiologic, and microbiological data to confirm the diagnosis. Statistically, we did not perform multiple comparison adjustment. Appropriately controlling for multiple comparisons is difficult in this case due to the correlation between end points, but none of the trends would have been significant with a conservative Bonferroni adjustment.

Conclusion. This study provides preliminary findings that indicate, in a state where a high percentage of children are vaccinated with PCV7, the possible impact of childhood immunization with pneumococcal conjugate vaccination on pneumonia hospitalizations of adults and children and a possible correlation with staphylococcal pneumonia hospitalizations.

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Reversal of Medical Practices

To the Editor: We recently read with great interest "A Decade of Reversal: An Analysis of 146 Contradicted Medical Practices" by Prasad et al,[1] along with the accompanying editorial by Ioannidis.[2] The authors have done an admirable job of quantitatively analyzing the number of reversals published over a decade in one high-impact journal, of course begging the question of how many reversals might be found across the medical literature. We would like to raise 2 important points. The first is about dissemination of the finding of reversal. It is well known that a new practice or device takes years to promulgate from published evidence of effectiveness to actual routine clinical use;

how long does it take for a replaced practice to disappear from clinical use? One can imagine Rogers' technology adoption lifecycle working in reverse, in which a core of "early abandoners" are followed by the early and late majorities and finally by the laggards.[3] As with the adoption of new interventions, there is also likely to be a substantial minority who persist with the use of a reversed idea, either through ignorance or conviction (or both).

The second point relates to treatments that were standard of care before the now reversed treatment came along. Do such historical treatments regain prominence when an intermediary is replaced? In order to attempt to answer such a question, we recently published a network meta-analysis of all randomized controlled trials in the first-line treatment of chronic myelogenous leukemia published between 1968 and 2012.[4] We found 5 distinct epochs, each of which represents a replacement of the preceding epoch, for the treatment of this disease: (1) the busulfan era (1968-1992), (2) the hydroxyurea era (1993-1994), (3) the interferon era (1994-2002), (4) the imatinib era (2003-2009), and (5) the second-generation tyrosine kinase inhibitor (TKI) era (2010 to the present). What we found notable is that even though imatinib was "replaced" in 2010 (in terms of efficacy; toxicities and cost of the second-generation TKIs are considerable, and thus imatinib is still routinely used and recommended), the historical standard (interferon) has never been compared directly to the newest standard (second-generation TKIs). In fact, one might conclude that the "third-generation" drug (interferon) should be carefully reconsidered as a viable option for the treatment of this disease. This and many other examples illustrate the need for systematic and quantitative "medical archeology"—a need that should be prompted by the publication of high-impact reversals such as those found by Prasad et al. [1] It is our hope that such analysis of the medical literature will become routine and that a centralized knowledge base will be established to quickly disseminate important findings of reversal.

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In reply I—Reversal of Medical Practices

Warner et al raise 2 important issues regarding our investigation of 146 medical reversals.[1] First, how long do contradicted practices persist in clinical practice? One of the reversals we noted informs this point. The use of percutaneous coronary intervention for patients with stable angina was a widespread practice that was largely contracted in 2007 with the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial.[2] Although initial evidence suggested decreased use of stenting in the wake of the COURAGE study, more recent data suggest a resurgence of this practice to pre-COURAGE levels.[3] An empirical investigation suggests that citations to contradicted practices decrease only a decade after a reversal study.[4] Thus, Warner et al are correct to note that contradicted practices are not immediately withdrawn, and future patients are subjected to reversed interventions. As Hall[5] noted with respect to the pulmonary artery catheter over a decade ago, "the extrication from widespread use of a technology that has not been adequately assessed is difficult and painful, and should be made unnecessary by the prospective testing of all technology introduced into critical care in the future."

The authors' second point is whether new therapies that replace older ones—based on superiority in well-done trials—should be tested against therapies that have fallen out of favor several generations ago. In effect, the authors ask whether the *transitive property* is true for trials. If nilotinib is better than imatinib and imatinib is better than interferon, can we safely conclude that nilotinib is better than interferon? There are 2 points here worth making. First, it is always difficult to draw lessons from the case of chronic myelogenous leukemia, in which an exquisitely targeted agent inhibits a key driver mutation and has revolutionized outcomes for an illness. Second, although second-generation tyrosine kinase inhibitors (nilotinib, dasatinib) have improved response rates compared with imatinib, overall survival benefits from using these agents as first-line treatment has yet to be documented, and thus, there remains genuine uncertainty regarding the best first-line therapy,[6] as the authors note. That said, in general, we think it is important to study the history of medical practices, and we generally trust the transitive property in medicine.

Finally, we wish to clarify the terms we use. *Reversal* refers to a medical practice that is actually no better or worse than a lesser standard; *replacement* occurs when a new practice