Despite numerous technological advances in the delivery of intravenous (IV) therapy over the past 3 decades, infection remains a major cause of morbidity and mortality among its recipients. Furthermore, IV-therapy-related infection is the single leading cause of nosocomial bacteremia. Approximately 90% of IV-therapy-related bacteremias are associated with catheter colonization. Most infections of this type are caused by gram-positive cocci, in particular staphylococci. Appropriately, most recent clinical investigations aimed at reducing the risk of IV-related infection are centered on reducing colonization of the catheter or surrounding skin by these organisms. Bacteremia caused by the infusion of contaminated fluids is less common, but nevertheless is a potentially serious problem that can affect single patients or dozens of patients, depending on the circumstances of contamination. Unlike catheter-related bacteremia, bacteremia due to contaminated infusate is often due to gram-negative bacilli such as Klebsiella, Enterobacter, and Serratia species, which, unlike staphylococci, can multiply in glucose-containing IV solutions. Staphylococci can, however, multiply in blood products and lipid emulsions.

Contamination of the infusate can occur through several routes. Intrinsic contamination occurs at the time of manufacture of the fluid. This type of contamination fortunately is rare, but has the potential to cause a large number of episodes of infection. In what is perhaps the best studied outbreak due to intrinsic contamination, 378 cases of bacteremia due to Enterobacter aerogenes or Enterobacter agglomerans were documented in 25 different US hospitals. The cases were traced to contamination of the cap used in IV-fluid bottles; bacteria were readily transferred from the cap to the fluid during manipulation of the bottle. The low numbers of bacteria present were able to multiply within the fluid; there was an association between the occurrence of bacteremia and duration of time that the bottle and administration set were in use. The clinical features of bacteremia in this outbreak were notable in that patients often had no conditions predisposing to gram-negative bacteremia; the mortality rate was 13.4%. The outbreak was terminated by discontinuing use of the implicated product.

More common, and perhaps more insidious, is extrinsic contamination, which occurs during subsequent admixture of IV fluids or during manipulation of the infusion apparatus. Breaks in sterile technique can introduce organisms into the infusate, where they may multiply to high concentrations. Repeated manipulation of infusion sets is a potential means of introduction of bacteria into IV fluids. Prolonged "hang time" of the fluid or components of the administration set may permit the multiplication of these organisms to relatively high concentration. Infusion of such fluids can lead to the abrupt onset of fever and hypotension in a previously stable patient. Because single patients or a very limited number of patients may be affected, such contamination may be difficult to recognize.

The Centers for Disease Control and Prevention has developed a comprehensive set of guidelines for the prevention of intravascular-device–related infections. With regard to replacement of administration sets, the current recommendation is that replacement should occur "... no more frequently than at 72-hour intervals. ..." An exception is made for administration of blood or lipid emulsion, which requires change of the administration set at 24 hours.

The current recommendations evolved over a 25-year period, beginning with an initial recommendation of change at 24 hours that was based on observations made during the nationwide epidemic of Enterobacter septicemia. Subsequent studies showed that changes at 48 hours and then 72 hours were not associated with an increased risk of infection. The impetus for increasing the interval is, of
Thus, I believe that the changing of IV administration sets was a decreasing frequency of change at each subsequent teremia may be as high as $40,000, in the anticipated surveillance, since infusion-related bacteremia typically represent only a small percentage of bloodstream infections. Furthermore, as the cost of an episode of IV-related bacteremia may be as high as $40,000, the anticipated savings may fail to materialize if the rate of infection increases. Thus, I believe that the changing of IV administration sets every 4 to 7 days should be considered comparable with the current practice of change at 72 hours only if the respective risk estimates are demonstrated to lie within a fairly narrow confidence interval.

The authors are appropriately conservative in calling for a randomized, multicenter trial to confirm their observations. In addition to providing the necessary power to assure equivalency of a longer IV administration set change interval, such a study would have the merit of assessing it in diverse institutions and patient populations. Standards of IV care in an academically affiliated oncology center with a long history of research into nosocomial infection may be more meticulous than that provided in other facilities.

Evaluation of changes in practice aimed at reducing healthcare expenditure is an appropriate area of clinical investigation. Dollars available for healthcare are not limitless; money saved by eliminating unneeded equipment changes can and should be diverted into expenditures that actually benefit patients. However, since individual patients cannot expect any benefit from such trials, protection of patient safety is essential. The trial reported by Raad and colleagues in this issue offers an example of how such trials can be conducted in a responsible manner. They used an incremental approach to the intervention that was based on the results of previous trials. Informed consent was obtained from all participants. In addition, they provided a mechanism for interim analysis that could terminate the study early if a trend toward increased adverse events was noted in the experimental group. Although the authors were not able to settle the question they set out to answer definitively, their report should serve as a model for future investigations.

REFERENCES