

- fections, and development of bacterial resistance in esophageal resection. *Intensive Care Med* 1990;16 Suppl 3:S224–228.
28. van der Voort PH, van Roon EN, Kampinga GA, Boerma EC, Gerritsen RT, Egbers PH, Kuiper MA. A before-after study of multi-resistance and cost of selective decontamination of the digestive tract. *Infection* 2004; 32(5):271–277.
  29. Diez-Roux AV. Bringing context back into epidemiology: variables and fallacies in multilevel analysis. *Am J Public Health* 1998;88(2):216–222.
  30. Gastinne H, Wolff M, Delatour F, Faurisson F, Chevret S. A controlled trial in intensive care units of selective decontamination of the digestive tract with nonabsorbable antibiotics. The French Study Group on Selective Decontamination of the Digestive Tract. *N Engl J Med* 1992; 326(9):594–599.
  31. Kollef MH. Opinion: the clinical use of selective digestive decontamination. *Crit Care* 2000;4(6):327–332.
  32. Monnet DL, MacKenzie FM, Lopez-Lozano JM, Beyaert A, Camacho M, Wilson R, et al. Antimicrobial drug use and methicillin-resistant *Staphylococcus aureus*, Aberdeen, 1996–2000. *Emerg Infect Dis* 2004;10(8):1432–1441.
  33. Morgenstern H. Ecologic studies. In: Rothman KJ, Greenland S, editors. *Modern epidemiology*. Philadelphia: Lippincott-Raven; 1998:459–480.
  34. Klein BS, Perloff WH, Maki DG. Reduction of nosocomial infection during pediatric intensive care by protective isolation. *N Engl J Med* 1989;320(26):1714–1721.
  35. Johnson S, Gerding DN, Olson MM, Weiler MD, Hughes RA, Clabots CR, Peterson LR. Prospective, controlled study of vinyl glove use to interrupt *Clostridium difficile* nosocomial transmission. *Am J Med* 1990;88(2): 137–140.
  36. Maki DG, Zilz MA, McCormick R. The effectiveness of using preemptive barrier precautions routinely (protective isolation) in all high-risk patients to prevent nosocomial infection with resistant organisms, especially MRSA, VRE, and *C. difficile* (abstract). Proceedings and abstracts of the Thirty-fourth Annual Meeting of the Infectious Disease Society of America, New Orleans, Louisiana, September 1996. *Clin Infect Dis* 1996;23:43.
  37. Montecalvo MA, Jarvis WR, Uman J, Shay DK, Petrullo C, Rodney K, et al. Infection-control measures reduce transmission of vancomycin-resistant enterococci in an endemic setting. *Ann Intern Med* 1999;131(4): 269–272.
  38. Srinivasan A, Song X, Ross T, Merz W, Brower R, Perl TM. A prospective study to determine whether cover gowns in addition to gloves decrease nosocomial transmission of vancomycin-resistant enterococci in an intensive care unit. *Infect Control Hosp Epidemiol* 2002;23(8):424–428.
  39. Safdar N, Marx J, Meyer N, Maki DG. The effectiveness of preemptive enhanced barrier precautions for controlling MRSA in a burn unit (abstract). Proceedings and abstracts of the 43rd InterScience Conference on Antimicrobial Agents and Chemotherapy, 2003; Chicago, Illinois.
  40. Paterson DL, Singh N, Rihs JD, Squier C, Rihs BL, Muder RR. Control of an outbreak of infection due to extended-spectrum beta-lactamase-producing *Escherichia coli* in a liver transplantation unit. *Clin Infect Dis* 2001;33(1):126–128.
  41. Bonten MJ, Hayden MK, Nathan C, van Voorhis J, Matushek M, Slaughter S, et al. Epidemiology of colonisation of patients and environment with vancomycin-resistant enterococci. *Lancet* 1996;348(9042):1615–1619.
  42. Bonten MJ, Slaughter S, Ambergen AW, Hayden MK, van Voorhis J, Nathan C, Weinstein RA. The role of “colonization pressure” in the spread of vancomycin-resistant enterococci: an important infection control variable. *Arch Intern Med* 1998; 158(10):1127–1132.
  43. Maki DG. Nosocomial infection in the intensive care unit. In: Parrillo J, Bone R, editors. *Critical care medicine*. St Louis: Mosby; 1994:893–954.
  44. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet* 1999; 354(9193):1851–1858.
  45. Valles J, Artigas A, Rello J, Bonsoms N, Fontanals D, Blanch L, et al. Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. *Ann Intern Med* 1995;122(3):179–186.

### Selective Decontamination of the Digestive Tract and Ventilator-Associated Pneumonia (Part 2)

We read with interest the article “The Gastrointestinal Tract and Ventilator-Associated Pneumonia,” by Kallet and Quinn.<sup>1</sup> We are delighted that for the first time since the introduction of SDD in Europe over 20 years ago, American respiratory and infectious-disease physicians acknowledge that SDD is an evidence-based-medicine manoeuvre. SDD using parenteral and enteral antimicrobials, a prophylactic method that costs \$7 a day, reduces pneumonia by 65% and mortality by 22%, without antimicrobial resistance emerging in unselected critically ill patients.

The authors agree that “by the customs of evidence-based-medicine, the findings normally would warrant a recommendation favoring SDD.” Remarkably, the next sentence reads as follows: “Yet we are not prepared to endorse SDD to reduce the risk of VAP.” The authors put forward 2 reasons: (1) level-I evidence does not consistently suggest a clear mortality benefit, and (2) SDD increases resistance. To impress the reader, Kallet and Quinn make a mountain out of the second argument, as they split the resistance issue into 3 subheadings that amount to 4 major reasons why American colleagues prefer to behave in an “abnormal” way. Their conclusion against the use of SDD is not based on evidence from RCTs and meta-analyses, but on the opinion of the experts (ie, the lowest level of evidence).

Although a trend toward improved survival in SDD-treated patients was found in most studies, the majority were too small to show a significant effect. In a recent German study<sup>2</sup> by Krueger and co-authors, mortality was lower in a subgroup of 237 surgical patients who had Acute Physiology and Chronic Health Evaluation (APACHE II) scores in the mid-range stratum (ICU-admission score of 20–29). In those patients ICU mortality was 33% in the placebo group versus 16.4% in the SDD group ( $p = 0.01$ ). Interestingly, had they analyzed their data on a strict intention-to-treat basis, the reduction in mortality would have been significant, with a relative risk of 0.69 (95% CI 0.51–0.95). In that study, the incidence of both Gram-negative and Gram-positive infections was lower in SDD-treated patients. Strikingly, the authors dismiss the mortality data of that German trial, but refer to it only for secondary end points, such as antibiotic use. Recently, the results of the largest SDD study to date were published.<sup>3</sup> This Dutch study included 934 medical and surgical ICU patients. A significant reduction in hospital mortality, from 31% in the control group to 24% in the SDD group, was found. The reduction in mortality in SDD-treated patients was found in medical as well as in surgical patients. The evidence of the effectiveness of SDD in reducing mortality has been “consistently” confirmed in all 6 meta-analyses of RCTs so far conducted (ie, when the analysis had adequate statistical power).<sup>4</sup> For example, the most recent Cochrane Library meta-analysis, published in 2004, reports reduced mortality in SDD-treated patients, with an odds ratio of 0.78 (95% CI 0.68–0.89).<sup>5</sup>

The parenteral and enteral antimicrobials of the SDD protocol mainly target AGNB. Two RCTs evaluated the impact of SDD on resistance among AGNB as the primary end point. The Dutch study<sup>3</sup> demonstrated that carriage of AGNB resistant to imipenem, ceftazidime, ciprofloxacin, tobramycin, and polymyxins occurred in 16% of the SDD patients, compared with 26% of the control patients, with a relative risk of 0.6 (95% CI 0.5–0.8). This is in line with an earlier French RCT, which showed that the addition of enteral to the parenteral antimicrobials controlled carriage and infection due to extended-spectrum  $\beta$ -lactamase-producing *Klebsiella*.<sup>6</sup> Kallet and Quinn write in their summary that SDD reduced morbidity, mortality, and resistance only in RCTs from countries where drug-resistant Gram-positive bacteria such as VRE and MRSA are not endemic. Fair enough; the SDD prophylaxis, being not active against VRE and MRSA, may promote gut overgrowth of these intrinsically resistant Gram-positive bacteria.

VRE carriage and infection were the primary end points of SDD RCTs in 2 American ICUs with endemic VRE.<sup>7,8</sup> There were no differences between the test and control groups. Seven RCTs have been conducted in ICUs where MRSA was endemic at the time of the trial, so they report a trend towards higher MRSA carriage and infection rates in patients receiving SDD.<sup>9–15</sup> The addition of enteral vancomycin to the classical SDD is required to control MRSA in ICUs with endemic MRSA.<sup>16,17</sup> VRE did not emerge in any of the studies that used enteral vancomycin.<sup>3,16–22</sup> The authors' assertion that there is strong contravening evidence that SDD promotes infection due to Gram-positive bacteria is expert opinion and is unsupported by facts. This makes their claim about resistance during SDD a poor Grade-E recommendation in evidence-based-medicine terms. Kallet and Quinn maintain that the efficacy of SDD depends on the country, but that does not make sense, as all RCTs that have used the patient as the denominator invariably demonstrated control of (multi-resistant) AGNB, regardless of the global position. There are 4 possible explanations why SDD reduces resistance amongst the target bacteria: (1) in eradicating overgrowth, SDD prevents spontaneous mutation, (2) very high topical bactericidal levels in throat and gut eradicate resistant mutants already present, (3) polymyxin E

and tobramycin are a synergistic mixture, and (4) the administration of parenteral antimicrobials is lower in successfully decontaminated patients.<sup>3</sup>

Antimicrobial resistance, being a long-term issue, has been evaluated in 10 SDD studies, which monitored it between 2 and 9 years, and bacterial resistance associated with SDD has not been a clinical problem.<sup>23–32</sup> The authors have serious concerns about the long-term use of SDD; however, to answer their concerns they should endorse the use of SDD, not reject it.

The emerging public health crisis from the steady rise in drug-resistant Gram-positive bacteria prohibits the recommendation of SDD. We hope that Kallet and Quinn appreciate that the public health crisis in America, where SDD is discouraged, developed during a policy of parenteral antimicrobials only. We assume that the continuation of only systemic antibiotics is one of the less radical alternatives proposed by the authors. Can we respectfully suggest that surveillance cultures of throat and gut are the unique method to fully evaluate the disastrous impact of systemic agents such as piperacillin/tazobactam?<sup>33,34</sup>

Kallet and Quinn's summary and recommendations are expert opinion, but, sadly, are based on a fundamental misunderstanding of the SDD philosophy. SDD is based on the realization that the abnormal carrier state, only detectable by surveillance cultures of throat and rectum, harms the critically ill. Disease influences carriage; that is, illness severity is the major risk factor for abnormal carriage of AGNB, and drugs, including antimicrobials, that disregard "colonization resistance" may promote subsequent overgrowth of these abnormal bacteria.<sup>35</sup> The conversion of "abnormal" into "normal" carriage (ie, a critically ill patient who is successfully decontaminated should be free from AGNB in throat and gut) is pivotal in the management of the critically ill, as this type of patient is unable to clear abnormal flora because of the underlying disease. Surveillance cultures are also required to classify pneumonia into primary and secondary endogenous, and exogenous.<sup>36</sup> The immediate administration of adequate parenteral antimicrobials aims to control primary endogenous pneumonia, secondary endogenous pneumonia is prevented by the enteral decontaminating agents, and a high level of hygiene prevents exogenous pneumonia. This full SDD reg-

imen is required to significantly reduce pneumonia and mortality without antimicrobial resistance emerging. Surveillance cultures supported by molecular techniques have shown that oropharyngeal rather than gastric carriage promotes pneumonia in the critically ill, making the "gastropulmonary hypothesis" expert opinion, the lowest level of evidence.<sup>37,38</sup> Nevertheless, the gut component of SDD is crucial in the control of secondary carriage and infection, of translocation, lowering of gut endotoxin to restore the immunosuppression, and minimizing of antimicrobial resistance, resulting in overall mortality reduction.<sup>39</sup>

Finally, can we remind Kallet and Quinn and their followers that, on average, for every 5 patients who do not receive SDD, one extra patient develops a pneumonia, and that there is one extra death every 21 patients in units that do not administer SDD?<sup>5</sup> Twenty years of clinical research into SDD show that the addition of enteral to parenteral antimicrobials prevents mutation and eradicates mutants; therefore, it is not surprising that the pre-1980s antibiotics are still active, as long as they are combined with the eradication of AGNB from the gut.<sup>23–32</sup> Furthermore, it can be anticipated that in SDD units the antibiotic era will be prolonged.<sup>40</sup> We believe that the answer lies not in the development of single, new, more potent and expensive systemic antimicrobials, but in a radical rethinking of the philosophy by which antimicrobials are used.<sup>39</sup>

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## REFERENCES

- Kallet RH, Quinn TE. The gastrointestinal tract and ventilator-associated pneumonia. *Respir Care* 2005;50(7):910–923.
- Krueger WA, Lenhart FP, Neeser G, Ruckdeschel G, Schreckhase H, Eissner HJ, et al. Influence of combined intravenous and topical antibiotic prophylaxis on the incidence of infections, organ dysfunctions, and mortality in critically ill surgical patients: a prospective, stratified, randomized, double-blind, placebo-controlled clinical trial. *Am J Respir Crit Care Med* 2002;166(8):1029–1037.
- de Jonge E, Schultz MJ, Spanjaard L, Bossuyt PM, Vroom MB, Dankert J, Kescioglu J. Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. *Lancet* 2003;362(9389):1011–1016.
- Liberati A, D'Amico R, Brazzi L, Pifferi S. Influence of methodological quality on study conclusions. *JAMA* 2001;286(20):2544–2547.
- Liberati A, D'Amico R, Pifferi, Torri V, Brazzi L. Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care. *Cochrane Database Syst Rev* 2004;(1):CD000022.
- Brun-Buisson C, Legrand P, Rauss A, Richard C, Montravers F, Besbes M, et al. Intestinal decontamination for control of nosocomial multi-resistant Gram-negative bacilli: study of an outbreak in an intensive care unit. *Ann Intern Med* 1989;110(11):873–881.
- Arnou PM, Carandang GC, Zabner R, Irwin ME. Randomised controlled trial of selective bowel decontamination for prevention of infections following liver transplantation. *Clin Infect Dis* 1996;22(6):997–1003.
- Hellinger WC, Yao JD, Alvarez S, Blair JE, Cawley JJ, Paya CV, et al. A randomised, prospective, double-blind evaluation of selective bowel decontamination in liver transplantation. *Transplantation* 2002;73(12):1904–1909.
- Ferrer M, Torres A, Gonzalez J, Puig de la Bellacasa J, el-Ebiary M, Roca M, et al. Utility of selective digestive decontamination in mechanically ventilated patients. *Ann Intern Med* 1994;120(5):389–395.
- Gastinne H, Wolff M, Delatour F, Faurisson F, Chevret S. A controlled trial in intensive care units of selective decontamination of the digestive tract with nonabsorbable antibiotics. The French Study Group on Selective Decontamination of the Digestive Tract. *N Engl J Med* 1992;326(9):594–599.
- Hammond JM, Potgieter PD, Saunders GL, Forder AA. Double-blind study of selective decontamination of the digestive tract in intensive care. *Lancet* 1992;340(8810):5–9.
- Lingnau W, Berger J, Javorsky F, Lejeune P, Mutz N, Benzer H. Selective intestinal decontamination in multiple trauma patients: prospective, controlled trial. *J Trauma* 1997;42(4):687–694.
- Verwaest C, Verhaegen J, Ferdinande P, Schetz M, Van den Bergh G, Verbist L, Lauwers P. Randomised, controlled trial of selective digestive decontamination in 600 mechanically ventilated patients in a multi disciplinary intensive care unit. *Crit Care Med* 1997;25(1):63–71.
- Wiener J, Itokazu G, Nathan C, Kabins SA, Weinstein RA. A randomized, double-blind, placebo-controlled trial of selective digestive decontamination in a medical-surgical intensive care unit. *Clin Infect Dis* 1995;20(4):861–867.
- de La Cal MA, Cerda E, Garcia-Hierro P, van Saene HK, Gomez-Santos D, Negro E, Lorente JA. Survival benefit in critically ill burned patients receiving selective decontamination of the digestive tract: a randomised, placebo-controlled, double-blind trial. *Ann Surg* 2005;241(3):424–430.
- Sanchez M, Mir N, Canton R et al. The effect of topical vancomycin on acquisition, carriage and infection with methicillin-resistant *Staphylococcus aureus* in critically ill patients: a double-blind, randomized, placebo-controlled study (abstract). 37th ICAAC, 1997 Toronto, Canada. ASM Press. 1997;J-119:310.
- Silvestri L, van Saene HK, Milanese M, Fontana F, Gregori D, Oblach L, et al. Prevention of MRSA pneumonia by oral vancomycin decontamination: a randomised trial. *Eur Respir J* 2004;23(6):921–926.
- Bergmans DC, Bonten MJ, Gaillard CA, Paling JC, van der Geest S, van Tiel FH, et al. Prevention of ventilator-associated pneumonia by oral decontamination: a prospective, randomized, double-blind, placebo-controlled study. *Am J Respir Crit Care Med* 2001;164(3):382–388.
- Gaussorgues Ph, Salord F, Sirodot M, Tigaud S, Cagnin S, Gerard M et al. Efficacité de la décontamination digestive sur la survenue des bactériémies nosocomiales chez les patients sous ventilation mécanique et recevant des bêta-lactamiques. *Réanimation Soins Intensif Médecine d'Urgence* 1991;7:169–174. (Article in French)
- Korinek AM, Laisne MJ, Nicolas MH, Raskine L, Deroin V, Sanson-Lepors MJ. Selective decontamination of the digestive tract in neuro-surgical intensive care unit patients: a double-blind, randomized, placebo-controlled study. *Crit Care Med* 1993;21(10):1466–1473.
- Pugin J, Auckenthaler R, Lew DP, Suter PM. Oropharyngeal decontamination decreases incidence of ventilator-associated pneumonia: a randomized, placebo-controlled, double-blind clinical trials. *JAMA* 1991;265(20):2704–2710.
- Schardey HM, Joosten U, Finke U, Staubach KH, Schauer R, Heiss A, et al. The prevention of anastomotic leakage after total gastrectomy with local decontamination: a prospective, randomized, double-blind, placebo-controlled multicenter trial. *Ann Surg* 1997;225(2):172–180.
- Hammond JM, Potgieter PD. Long-term effects of selective decontamination on antimicrobial resistance. *Crit Care Med* 1995;23(4):637–645.
- van der Voort PH, van Roon EN, Kampinga GA, Boerma EC, Gerritsen RT, Egbers PH, Kuiper MA. A before-after study of multi-resistance and cost of selective decontamination of the digestive tract. *Infection* 2004;32(5):271–277.
- Viviani M, van Saene HK, Dezzoni R, Silvestri L, Di Lenarda R, Berlot G, Gullo A. Control of imported and acquired methicillin-resistant *Staphylococcus aureus* (MRSA) in mechanically ventilated patients: a dose-response study of enteral vancomycin to reduce absolute carriage and infection. *Anaesth Intensive Care* 2005;33(3):361–372.
- Stoutenbeek CP, van Saene HK, Zandstra DF. The effect of oral non-absorbable antibiotics on the emergence of resistant bacteria in patients in an intensive care unit. *J Antimicrob Chemother* 1987;19(4):513–520.
- Sarginson RE, Taylor N, Reilly N, Baines PB, van Saene HK. Infection in prolonged pediatric critical illness: a prospective four-year study based on knowledge of the carrier state. *Crit Care Med* 2004;32(3):839–847.
- Lingnau W, Berger J, Javorsky F, Fille M, Allerberger F, Benzer H. Changing bacterial ecology during a five year period of selective intestinal decontamination. *J Hosp Infect* 1998;39(3):195–206.
- Leone M, Albanese J, Antonini F, Nguyen-Michel A, Martin C. Long-term [6 year] effect of selective digestive decontamination on antimicrobial resistance in intensive care, multitrauma patients. *Crit Care Med* 2003;31(8):2090–2095.
- de la Cal MA, Cerda E, van Saene HK, Garcia-Hierro P, Negro E, Parra ML, et al. Effectiveness and safety of enteral vancomycin to control endemicity of methicillin-resistant *Staphylococcus aureus* in a medical/surgical intensive care unit. *J Hosp Infect* 2004;56(3):175–183.
- Tetteroo GW, Wagenvoort JH, Bruining HA. Bacteriology of selective decontamination: efficacy and rebound colonization. *J Antimicrob Chemother* 1994;34(1):139–148.



32. Abella A, de la Cal MA, Cerda E, Lopez L, Alia I, Garcia-Hierro P, et al. Control of MRSA endemicity with enteral vancomycin in a burn intensive care unit (abstract). *Intensive Care Med* 2004;30(Suppl 1):556:S145.
33. Toltzis P, Yamashita T, Vilt L, Green M, Morrissey A, Spinner-Block S, Blumer J. Antibiotic restriction does not alter endemic colonization with resistant Gram-negative rods in a pediatric intensive care unit. *Crit Care Med* 1998;26(11):1893-1899.
34. Donskey CJ, Chowdhry TK, Hecker MT, Hoyer CK, Hanrahan JA, Hujer AM, et al. Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients. *N Engl J Med* 2000;343(26):1925-1932.
35. van Saene HK, Zandstra DF. Selective decontamination of the digestive tract: rationale behind evidence-based use in liver transplantation. *Liver Transpl* 2004;10(7):828-833.
36. de La Cal MA, Cerda E, Garcia-Hierro P, Lorente L, Sanchez-Concheiro M, Diaz C, van Saene HK. Pneumonia in patients with severe burns: a classification according to the concept of the carrier state. *Chest* 2001;119(4):1160-1165.
37. Bonten MJ, Gaillard CA, van Tiel FH, Smeets HG, van der Geest S, Stobberingh EE. The stomach is not a source for colonization of the upper respiratory tract and pneumonia in ICU patients. *Chest* 1994;105(3):878-884.
38. Garrouste-Orgeas M, Chevret S, Arlet G, Marie O, Rouveau M, Popoff N, Schlemmer B. Oropharyngeal or gastric colonization and nosocomial pneumonia in adult intensive care unit patients: a prospective study based on genomic DNA analysis. *Am J Respir Crit Care Med* 1997;156(5):1647-1655.
39. van Saene HK, Petros AJ, Ramsay G, Baxby D. All great truths are iconoclastic: selective decontamination of the digestive tract moves from heresy to level 1 truth. *Intensive Care Med* 2003;29(5):677-690.
40. Baines PB, Meyer J, de la Cal MA. Antimicrobial resistance in the intensive care unit: the use of oral non-absorbable antimicrobials may prolong the antibiotic era. *Curr Anaesth Crit Care* 2001;12(1):41-47.

#### *The authors reply:*

Perhaps the most telling aspect of van Saene and colleagues' letter is the passage, "To impress the reader, Kallet and Quinn make a mountain out of the second argument" (increased microbial resistance). Of course, the complete expression is "*making a mountain out of a mole hill*."—clearly, a statement meant to dismiss valid concerns over what the established medical and scientific communities consider an impending crisis.<sup>1-3</sup> SDD is based upon the theories that impaired colonization resistance and the gastropulmonary route are important factors in the development of VAP. Contrary to the impression conveyed by van Saene and colleagues (and as we pointed-out in our paper), neither theory has been proven beyond question, and in fact plausible alternative explanations exist.<sup>4</sup>

It is particularly noteworthy that other participants in the conference on VAP elucidated several problems and concerns regarding SDD, such as (1) the important role of oral decontamination; (2) that some of the efficacy of SDD is predicated upon the concomitant use of parental antibiotics; (3) the effectiveness of concomitant, stringent, ancillary infection-control practices on microbial resistance at Dutch hospitals that routinely use SDD; (4) SDD requires prolonged antibiotic therapy, and increased microbial resistance is intimately related to the *duration* of antibiotic use; and (5) a small subgroup of severely debilitated patients may benefit from SDD, but the overall medical value of the therapy is diminished by misapplying antibiotic prophylaxis to patients who do not need it.<sup>4</sup>

The relationship between SDD and the selection for resistant Gram-positive microorganisms is unclear and requires extensive research. van Saene suggests that we should endorse SDD *because of* our concerns about antimicrobial resistance, not *in spite of* these concerns. We respectfully point out that none of the randomized trials used the emergence of antimicrobial resistance as a primary out-

come measure. To date, no sufficiently large, temporally-appropriate, prospective, randomized clinical trials clarifying this issue exist. Just because currently there is a higher level of evidence supporting SDD (compared to that which links SDD to promoting drug-resistant microorganisms) does not, by itself, constitute an unambiguous recommendation for *general clinical use*. Evidence-based medicine is not an epistemological game whereby a particular viewpoint is argued regardless of the larger context in which that evidence exists. Increased microbial resistance has profound ecological consequences, not all of which can be predicted.<sup>5</sup> The very real specter of a post-antibiotic world is hardly a "mole hill," and our recommendations for widespread prophylactic antibiotic use should reflect that concern.

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#### REFERENCES

1. Kunim CM. Resistance to antimicrobial drugs: a worldwide calamity. *Ann Intern Med* 1993;118(7):557-561.
2. Cohen ML. Epidemiology of drug resistance: implications for a post-antimicrobial era. *Science* 1992;257(5073):1050-1055.
3. Schito GC, Debbia EA, Marchese A. The evolving threat of antimicrobial resistance in Europe: new data from the Alexander project. *J Antimicrob Chemother* 2000;46 Suppl T1:3-9.
4. Kallet RH, Quinn TE. The gastrointestinal tract and ventilator-associated pneumonia. *Respir Care* 2005;50(7):910-923.
5. Levy SB. Antibiotic resistance: consequences of inaction. *Clin Infect Dis* 2001;33 Suppl 3:S124-S129.