Ovarian cancer screening

Usha Menon's review of ovarian cancer screening[1] appears to misquote the result of the randomized controlled trial of multimodal screening (with the tumour marker CA125 and ultrasonography) by Jacobs and associates.[2]

In that study the number of deaths from ovarian cancer was 18 among the 10 977 patients in the control group and 9 among the 10 958 patients in the screened group (relative risk of death in the unscreened group 2.0, 95% confidence interval 0.78–5.13); Menon's article seems to state the reverse. Although the difference in number of deaths was not statistically significant, these results represent a possible halving of the death rate by screening, rather than a possible doubling.

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References
1. Menon U. Ovarian cancer screening. *CMAJ* 2004;171(4):323-4.
2. Jacobs IJ, Skates SJ, MacDonald N, Menon U, Rosenthal AN, Davies AP, et al. Screening for ovarian cancer: a pilot randomised controlled trial. *Lancet* 1999;353(9160):1207-10.

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Usha Menon,[1] in an analysis of ovarian cancer screening, points out that the best evidence for screening comes from a study that found significant longer median survival with screening but no significant difference in the number of deaths from ovarian or fallopian tube cancer.[2] This sounds like a classic example of lead-time bias, in which earlier diagnosis of a disease has no impact on the patient's outcome. In other words, the patient may die of the disease at the same time as she would have if the diagnosis had been made 30 months later. Median survival may appear better, but in fact all we've done is to give the patient a longer cancer experience, without better quality or quantity of life.

If this is the best evidence we have for ovarian cancer screening, then I certainly agree that "Screening is not currently recommended for the general population."

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References
1. Menon U. Ovarian cancer screening. *CMAJ* 2004;171(4):323-4.
2. Jacobs IJ, Skates SJ, MacDonald N, Menon U, Rosenthal AN, Davies AP, et al. Screening for ovarian cancer: a pilot randomised controlled trial. *Lancet* 1999;353(9160):1207-10.

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Treating *C. difficile*

In their review of *Clostridium difficile*-associated diarrhea,[1] Susan Poutanen and Andrew Simor note that concurrent administration of probiotic agents (e.g., *Saccharomyces boulardii* and *Lactobacillus GG*) and antibiotics to prevent recurrence of the problem has yielded mixed results.

There is substantial overlap among antibiotic use, *C. difficile* colonization and subsequent *C. difficile*-induced diarrhea. In fact, 26% to 50% of antibiotic-associated diarrhea can be attributed to *C. difficile*.[2] A meta-analysis[3] of *S. boulardii* and *Lactobacillus GG* co-administered with antibiotics (including the antibiotics regarded as the most common inducers of diarrhea [ampicillin, cephalosporins, clindamycin][2,4]) for treatment of antibiotic-associated diarrhea in a diverse population (881 patients of all ages, including inpatients, outpatients and people from developing countries) provided strong evidence to suggest that probiotic agents prevent antibiotic-associated diarrhea (relative risk 0.40, 95% confidence interval [CI] 0.28–0.57). A larger meta-analysis (1380 patients) of 7 probiotic species administered with a host of antibiotics provided further evidence of the effectiveness of probiotics for the prevention of antibiotic-associated diarrhea (odds ratio 0.37, 95% CI 0.26–0.53).[5]

However, these meta-analyses are limited, in that they provided little information about the species and doses that would yield the most beneficial results and did not identify the patient population(s) that would benefit most. In addition, neither author group performed a meta-analysis for adverse events, nor did they comment on why such an analysis was not done. We might assume that only minor adverse events were reported in the randomized controlled trials reviewed; however, meta-analyses of such trials often overlook important details.[6] Although no adverse events were reported in these meta-analyses, infections resulting from probiotic use (e.g., bacteremia, endocarditis, septicemia, pneumonia and deep abdominal abscesses) have been reported in neonates and severely debilitated and immunocompromised individuals.[7] It is unclear, however, whether exogenous or endogenous *Lactobacilli* were the cause of the few cases of *Lactobacillus bacteremia* that have been reported.[8]

The public health burden of this problem is substantial and the preliminary evidence promising; as such, concurrent use of probiotics with antibiotics in the hospital setting is worth further consideration. However, a research agenda is needed to determine which probiotic species and dosages might provide effective prophylaxis and which hospital population(s) would benefit most.

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References
1. Poutanen SM, Simor AE. *Clostridium difficile*-associated diarrhea in adults. *CMAJ* 2004;171(1):51-8.
2. McFarland LV. Epidemiology, risk factors and treatments for antibiotic-associated diarrhea. *Dig Dis* 1998;16:292-307.