Kramer attacks the Canada Prenatal Nutrition Program (CPNP) because it is based on the US Women, Infants, and Children (WIC) program. Yet on the basis of evidence that WIC reduced low-birth-weight births by 25% and very-low-birth-weight births by 44%, the US General Accounting Office concluded that WIC was a cost-effective program, resulting in savings of US$2.89 to US$3.50 for each federal dollar spent during the first 18 years of life.[8]

We should clarify that "providing milk, eggs and orange juice" is only one component of the CPNP, which addresses a number of issues that affect women's overall health, including drug and alcohol use, smoking, family violence and social isolation, in addition to maternal nutrition and breastfeeding. We realize that Health Canada has a challenging task in evaluating the CPNP, and we look forward to the results. Although we agree with Kramer that more funding should be allocated to research, this should not occur at the expense of other worthwhile interventions.

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[The author responds:]

By continuing to espouse low birth weight as a useful outcome, Sheela Basrur and Mary-Jo Makarchuk persist in clouding the important distinction between preterm births and small-for-gestational-age births that perinatal epidemiologists and child health policymakers have been trying to clarify over the last 15 to 20 years. Preterm birth, particularly birth before 32 completed weeks of gestation, is indeed "one of the most important biologic predictors of infant death and deficiencies in physical and mental development during childhood among those babies who survive." However, small-for-gestational-age birth is not. And the evidence is quite clear that maternal nutrition in pregnancy has a far greater impact on small-for-gestational-age birth than on preterm birth.

Basrur and Makarchuk have been selective in citing references that support their prior belief and have failed to orient the reader to the methodologic strengths and weaknesses of the studies cited. None of the "positive" studies mentioned was a randomized trial. Basrur and Makarchuk argue that nutrition is just one component of the CPNP, but randomized trials of routine advice to reduce smoking[1] or of providing psychosocial support[2] or intensive prenatal care[3–5] to high-risk women have yielded consistently negative results. Even the recently published trial of balanced energy–protein supplementation in marginally nourished pregnant women in a rural area of The Gambia, which reported large beneficial effects on fetal growth (i.e., birth weight for gestational age), found no effect whatsoever on the duration of gestation.[6] Surely the results of systematic reviews and large individual trials should take precedence over selectively cited observational studies.

Proponents of the WIC program in the US cite evidence of effectiveness from comparisons of WIC participants and nonparticipants. But women who participate in WIC (or any other public health program, for that matter) are different from those who do not. Women who deliver very early, for example, will not have had the same time to enrol in WIC as those who deliver at term. Thus preterm birth can lead to nonparticipation, and an observational study may well put the cart before the horse by attributing to WIC the lower rate of preterm birth among participants. Participants also tend to be more committed to their pregnancies, are more conscious of their health in general, have the psychological and financial wherewithal to enrol and attend WIC clinic visits and are likely to eat better on their own. It is quite impossible to control for such potent confounding effects. Because no amount of replication using a similar scientifically flawed design can replace comparison based on randomized allocation, the "evaluation" of CPNP so eagerly awaited by Basrur and Makarchuk will be as useless as the WIC evaluations.

I am also concerned about the belief that randomized trials are splendid tools for evaluating health care interventions in individuals but are unfeasible or unethical for evaluating community interventions. To be sure, randomization of individuals living in the same community is difficult because of the inevitable dilutional effect ("contamination") caused by shared experiences and behaviours. Is is for this reason that cluster randomization (in which the clinic, the hospital or the entire community becomes the unit of randomization) has be-

come such a powerful tool. Examples of perinatal trials using cluster randomization include studies of counts of fetal movement in the prevention of antepartum stillbirth,[7] of early breast-feeding to prevent postpartum hemorrhage[8] and of counselling for smoking cessation in prenatal care,[1] as well as a WHO-sponsored evaluation of a new model of prenatal care.[9] My colleagues and I are currently conducting a cluster-randomized evaluation (funded in part by Health Canada) of an intervention to promote breast-feeding based on the WHO/UNICEF Baby-Friendly Hospital Initiative. Cluster-randomized trials require highly trained research teams, large sample sizes and substantial funding. If individual-based interventions deserve rigorous methods of evaluation, the far larger number of individuals whose health and welfare may be affected argues for better, not worse, methods of evaluating community-based interventions.

I have no objection to funding truly "worthwhile interventions," whose effectiveness has been rigorously demonstrated. In the maternal–child health arena alone, postnatal support of breast-feeding, provision of automobile restraints and bicycle helmets, and improvement in vaccination coverage are public health promotion efforts whose scientific basis is far stronger than that of CPNP.

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What causes chronic fatigue?

Even though the 3 articles on chronic fatigue syndrome[1–3] in the Sept. 8 issue commendably demolish the obsolete claim that chronic fatigue syndrome is a psychiatric illness, they also offer outdated biological explanations for the syndrome, namely, either a chronic viral infection or a weakened immune system. Although the first of these explanations seemed convincing until a few years ago, it is hardly tenable now, because no specific virus has been identified in these patients.[4]

Both the viral reactivation and the immunological abnormalities observed in patients with chronic fatigue syndrome may well be accounted for by the cortisol deficiency that characterizes these patients.[5] This explanation is supported by the striking similarities between chronic fatigue syndrome and Addison's disease, which share 26 features,[6] including all of the neuropsychological symptoms.[5]

My conviction that chronic fatigue syndrome is an adrenal insufficiency similar to Addison's disease lies primarily in the fact that 4 years ago I recovered from chronic fatigue syndrome in the course of a few days thanks to the consumption of licorice,[7] with which addisonian patients were successfully treated before hydrocortisone and fludrocortisone became available.[7] These steroids, which currently represent the lifelong therapy for Addison's disease,[7] should be investigated in the treatment of patients with "true" chronic fatigue syndrome, as diagnosed according to the original criteria.[8] Conversely, patients in whom chronic fatigue syndrome is diagnosed on the basis of subsequent revised criteria[9] (which do not include the only physical signs — enlarged lymph nodes, fever and sore throat — that clearly distinguish chronic fatigue syndrome from depression) should avoid both steroid replacement therapy and licorice. In fact, depressed patients misdiagnosed as having chronic fatigue syndrome have abnormally high cortisol levels,[10] instead of the abnormally low cortisol levels found in patients with "true" chronic fatigue syndrome.[10] Therefore, administration of licorice or hydrocortisone would further increase their already-high cortisol levels.[7]

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