Antenatal micronutrient supplements in Nepal

We have pooled the results of our two trials in the southern plains of Nepal,[1,2] which examined the effect of maternal multiple micronutrient supplements on birthweight and other aspects of intrauterine growth, and would like to report the potentially worrisome finding of an apparent association between multiple micronutrient supplementation and increased perinatal and neonatal death.

The first trial[1] randomised 4998 pregnant women in Sarlahi district to receive one of five daily micronutrient supplements, including either a multiple micronutrient or an iron and folic acid (IFA) supplement, from early pregnancy to 3 months post partum. The second trial[2] randomly allocated 1200 women at less than 20 weeks' gestation who presented for antenatal care at Janakpur hospital to receive daily throughout pregnancy either an IFA supplement or a multiple micronutrient supplement of slightly different formulation from that used in Sarlahi. The primary outcome in both trials was birthweight assessed within 72 h of birth.

In Sarlahi, mean birthweight was 64 g greater (95% CI 12–115) in the multiple micronutrient group than in the control group,[1] and in Janakpur it was 77 g greater (24–130) in the multiple micronutrient group than in infants born to IFA-supplemented mothers.[2] The respective relative risks for low birthweight (<2500 g) were 0·84 (0·74–0·99) and 0·75 (0·60–0·94). Maternal demographic and socioeconomic characteristics, and patterns of health-care use, varied across trial populations: women from the entirely rural population of Sarlahi were older; of higher parity and lower socioeconomic standing with respect to education, asset ownership, and husband's occupation; and less likely to have delivered in a health-care facility than women enrolled from the more urban setting in Janakpur. Despite these differences, baseline measurements of anthropometric and haematological status were similar across trials: participants were short, wasted, and prone to anaemia in both populations. Women in Janakpur weighed about 1·6 kg more and were nearly 5 weeks further along in gestation at enrolment than those in Sarlahi. Within each trial, baseline characteristics were similar across randomised groups.

	Iron and folic acid		Multiple micronutrients		Relative risk (95% CI)
	Number	Rate/1000	Number	Rate/1000	
Sarlahi					
Livebirths	773	..	872	..	
Stillbirths	29	36·2	47	51·1	..
Perinatal deaths	50	62·3	80	87·0	1·40 (0·99–1·96)
Neonatal deaths	28	36·2	47	53·9	1·49 (0·94–2·35)
Janakpur					
Livebirths	550	..	556	..	
Stillbirths	18	31·7	15	26·3	..
Perinatal deaths	23	40·5	28	49·0	1·21 (0·71–2·08)
Neonatal deaths	11	20·0	17	30·6	1·53 (0·72–3·23)
Combined					
Livebirths	1323	..	1428	..	
Stillbirths	47	34·3	62	41·6	..
Perinatal deaths	73	53·3	108	72·5	1·36 (1·02–1·81)
Neonatal deaths	39	29·5	64	44·8	1·52 (1·03–2·25)

Table: **Mortality outcomes by treatment group for individual studies and combined**

In both trials, despite being associated with improved birthweight, multiple micronutrient supplementation was associated with a non-significant increase in perinatal mortality (stillbirths and neonatal deaths up to 7 days of age) and neonatal mortality (infant deaths up to 28 days of age) relative to groups that received IFA (table).[2,3] The 95% CIs for the risk ratios in the individual trials included unity, but once effect estimates from both trials were pooled, more stable relative risk estimates for each outcome emerged (table).

Why antenatal micronutrient supplementation could increase the risk of perinatal mortality is unclear. Possibilities include differential effects on birthweight across its distribution, with increased risk of asphyxia at the upper end,[3] effects on uterine sensitivity to oxytocin,[4,5] and increased survival of infants who might otherwise have succumbed to stillbirth.

It is unwise to generalise from our findings, since they arise from a pooled analysis of limited data. Policymakers are understandably interested to implement interventions that improve health in countries where maternal undernutrition is common and is perpetuated by an intergenerational cycle of malnutrition which begins in utero. However, in the south Asian context, increased birthweight due to antenatal multiple micronutrient supplementation may not uniformly confer a survival benefit and may, on the basis of preliminary evidence from our two trials, increase mortality risk in some populations. Further investigation of the safety and efficacy of this intervention is urgently needed before broad policies are adopted in chronically undernourished south Asian populations.

We declare that we have no conflict of interest.

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A stain on medical ethics

In his Comment (Aug 6, p 429),[1] Michael Wilks claims that the American Psychological Association (APA) and our Task Force on Psychological Ethics and National Security permits psychologists to "dispense with any ethical responsibilities when their training and expertise is used outside a strictly therapeutic context". This statement is false. A central finding of the recent Task Force report[2] and the position of the APA is that psychologists are always bound by the ethical responsibilities set forth in the APA ethics code—irrespective of the work setting and irrespective of whether they are referred to as psychologists, behavioural consultants, scientists, or another term. Our code of ethics always applies—there are no exceptions.

Wilks states that, according to certain reports, medical personnel have "failed to report evidence of torture, failed to intervene to stop it being repeated, and made available to interrogators information from confidential medical files". The APA Task Force report states explicitly that psychologists have an ethical obligation to report evidence of torture and other cruel, inhuman, or degrading treatment to appropriate authorities, and that it is unethical for psychologists to use information from a medical file to the detriment of an individual's safety and wellbeing.

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1 Wilks M. A stain on medical ethics. *Lancet* 2005; **366:** 429–31.

2 American Psychological Association. Report of the Presidential Task Force on Psychological Ethics and National Security. http://www.apa.org/releases/PENSTaskForceReportFinal.pdf (accessed Aug 10, 2005).

MRC CLASICC trial

The short term results of the MRC CLASICC trial, which compared laparoscopically assisted surgery with open resection for colorectal cancer (May 14, p 1718)[1] are similar to those of the US COST trial[2] for colon cancer alone, with similar 30-day mortality, lymph-node harvest, and oncological clearance in both open and laparoscopic groups.

The pathological data show similar longitudinal resection margins and lymph-node yield in both groups. Although circumferential resection-margin positivity was higher in the laparoscopic group, the difference was not significant. We are surprised that the authors chose a finding that did not reach significance as a principle conclusion of the study. Their conclusions are difficult to justify with regard to laparoscopically assisted anterior resection which, we would suggest, confers many advantages. Even when pelvic dissection proves to be difficult and requires conversion to open surgery, patients still have much to gain from laparoscopic mobilisation of the splenic flexure and avoidance of a long midline incision. Our experience of more than 500 resections suggests that the conversion rate to open surgery can be as low as 11% for all laparoscopically assisted colorectal resections and 16% for anterior resection.

The CLASICC trial authors discuss the training difficulties with regard to laparoscopy that result from the scarcity of surgeons who regularly do these operations for colorectal disease in the UK.[3] Joint consultant operating may help circumvent these difficulties, and a prospective audit of 88 joint laparoscopically assisted colorectal resections[4] shows very similar results to those of the CLASICC and COST trials (mortality 4·8%, conversion rate 20%).

With the extension of the learning curve shown in the CLASICC trial, and indeed in our own experience, laparoscopic surgery for rectal cancer with careful selection using MRI may result in similar outcomes to those seen in laparoscopically assisted colon cancer surgery. There do not seem to be sufficient data from the CLASICC trial to suggest otherwise.

We declare that we have no conflict of interest.

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The results of the MRC CLASICC trial[1] on laparoscopic surgery for colorectal cancers were long awaited and their publication is welcome. However, as with the COST[2] and Spanish[3] trials, some flaws in the trial design do not allow us to state that laparoscopic surgery is formally validated for all colon cancers.

What about right-sided cancers? Neither the CLASICC trial nor the other trials included a subgroup analysis: only overall results were reported. It is well known among laparoscopic surgeons that "laparoscopic" right colectomy can in fact mean three different kinds of procedure: a true or totally laparoscopic right colectomy (with both dissection and anastomosis done intracorporeally), laparoscopically assisted colec-