Malnutrition, including micronutrient deficiencies, is the leading risk factor for child mortality in low-income and middle-income countries. About 30% of the world’s population has zinc deficiency (figure). This deficiency occurs because zinc is mainly contained in foods such as red meat that are expensive and in short supply in developing countries. Moreover, zinc has no tissue reserves, unlike vitamin A and iron, and its turnover is rapid, especially during common gastrointestinal infections. Young children in developing countries who have a poor diet and high exposure to gastrointestinal pathogens are at greatest risk of zinc deficiency.

Many clinical trials have shown zinc supplementation to be of benefit to children in the treatment and prevention of diarrhoeal diseases and acute respiratory infections, and in improving growth. Evidence for benefit on morbidity from malaria is less consistent. In view of these results, zinc supplementation was postulated to prevent up to 5% of deaths in children younger than 5 years, in countries that contribute 90% of worldwide child mortality.

Recently, two important reports about the effect of zinc supplementation on child mortality have been published. In today’s Lancet, James Tielsch and colleagues report the results of a large randomised trial in Nepal; previously, Sazawal and colleagues reported on a similar trial in Zanzibar, a region with holoendemic malaria. Neither trial showed that zinc supplementation reduced mortality in children younger than 5 years. Nevertheless, when considering children older than 12 months only, both studies suggested a benefit. In Zanzibar, supplementation resulted in a marginally significant 18% reduction in mortality (relative risk 0.82, 95% CI 0.68–1.00). In Nepal, children aged 12–36 months had a slightly higher survival than did those younger than 12 months (hazard ratio 0.80, 95% CI 0.60–1.06), although this result was not statistically significant.

Interpretation of the results by looking at confidence intervals avoids the yes/no dichotomy of hypothesis testing. In studies with results that do not reach statistical significance, if the upper boundary of the confidence interval includes an important benefit, the possibility that the treatment still might be worthwhile has not been ruled out. The investigators might have missed a true treatment effect, and one should question if the sample size of the study was adequate (type II error). The stronger the non-significant trend in favour of the experimental treatment, the more likely the investigators missed a true treatment effect.

A pooled analysis of the trials exploring zinc’s effect in children older than 12 months shows a significant 18% reduction in total mortality in this subgroup of children (relative risk 0.82, 95% CI 0.70–0.96). The pooled analysis has the advantage of augmenting the sample size and reducing the width of the confidence intervals. Can we consider these pooled results conclusive? Should we then promote supplementation in this age group? First, we should note that in both trials zinc supplementation led to similar results. The point estimates are nearly the same, confidence intervals overlap, and heterogeneity between trials is non-significant (test for heterogeneity, I² = 0). Second, the difference in treatment effect by age is consistent with previous evidence. Third, an age effect is biologically plausible. Infants especially are not thought to be at high risk of zinc deficiency. All these factors suggest that zinc can reduce mortality in children older than 12 months.

However, questions remain. First, what is the size of the protective effect of zinc? From the pooled analysis we know that overall the real reduction of mortality in children older than 12 months lies somewhere between 4% and 30%. A 4% mortality reduction would be clinically relevant. Yet, getting this evidence to practice has many challenges. Second, can we generalise these results? Even if a trend suggesting a beneficial effect of zinc supplementation
is evident in both studies, we do not know if larger trials than these would show differences in the size of effect in areas with malaria compared with regions without malaria. In particular, we are not sure of the real size of the effect of zinc on mortality in areas without malaria (eg, Nepal). Third, should universal supplementation or that of high-risk groups only be promoted? Some groups of children (eg, malnourished, low birthweight, HIV-positive) might benefit more from zinc supplementation than would others (eg, well nourished).

Zinc supplementation seems to have the potential to be an important intervention for the reduction of child mortality in low-income countries. The effect of zinc supplementation when given to children older than 12 months could be even higher than previously expected. Additional evidence is needed if we want to clarify the real size of the effect, especially in regions without malaria, and to decide whether to supplement all children or those at high risk only. However, running such large community-based randomised trials entails objective difficulties. For dichotomous outcomes such as mortality, a very large sample size is needed to detect a small but clinically relevant effect. Additionally, the inclusion of a placebo group would now be ethically questionable, at least in areas with malaria. Alternative study designs that incorporate approaches with consideration of adequacy and plausibility, and that compare integrated nutritional interventions, would perhaps help to solve these issues.14

Marzia Lazerini

Promotion of mental health in poorly resourced countries

The call for action on treatment and prevention of mental disorders1 needs to be matched by a call to integrate mental health into public-health action, otherwise it will send incomplete messages to professionals, ministries, and donors. The connections between mental health and other aspects of health and productivity make mental health promotion in low-income countries a necessity—far from the luxury it is often portrayed as.

Public health is the organised worldwide and local effort to promote and protect the health of populations and reduce health inequities.1 Mental health is intrinsic to health and linked to behaviour, as shown by the several connections between mental disorders and other conditions.1

Mental health is a set of positive attributes in a person or a community. WHO describes it as “a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community.”4 Poor mental health is associated with social disadvantage, human-rights abuses, and poor health and productivity, as well as increased risk of mental disorders.5 Promoting and satisfying mental health needs

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I declare that I have no conflict of interest.