MALNUTRITION AND MATERNAL / GLOBAL SOCIAL / HEALTH DEVELOPMENT

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Key words: malnutrition; child; healths; psychosocial; sequent

Abstract

Maternal undernutrition contributes to 800,000 neonatal deaths annually through small for gestational age births; stunting, wasting, and micronutrient deficiencies are estimated to underlie nearly 3.1 million child deaths annually. Progress has been made with many interventions implemented at scale and the evidence for effectiveness of nutrition interventions.

ASSOCIATIONS OF LINEAR GROWTH AND RELATIVE WEIGHT GAIN DURING EARLY LIFE WITH ADULT HEALTH AND HUMAN CAPITAL IN COUNTRIES OF LOW AND MIDDLE INCOME: FINDINGS FROM FIVE BIRTH COHORT STUDIES

Linda S Adair

Lancet 2013, 382: 525-34

Fast weight gain and linear growth in children in low-income and middle-income countries are associated with enhanced survival and improved cognitive development, but might increase risk of obesity and related adult cardiovascular diseases. We investigated how linear growth and relative weight gain during infancy and childhood are related to health and human capital outcomes in young adults.

We used data from five prospective birth cohort studies from Brazil, Guatemala, India, the Philippines, and South Africa. We investigated body-mass index, systolic and diastolic blood pressure, plasma glucose concentration, height, years of attained schooling, and related categorical indicators of adverse outcomes in young adults. With linear and logistic regression models, we assessed how these outcomes relate to birthweight and to statistically independent measures representing linear growth and weight gain independent of linear growth (relative weight gain) in three age periods: 0-2 years, 2 years to mid-childhood, and mid-childhood to adulthood.

We obtained data for 8362 participants who had at least one adult outcome of interest. A higher birthweight was consistently associated with an adult body-mass index of greater than 25 kg/m(2) (odds ratio 1.28, 95% CI 1.21-1.35) and a reduced likelihood of short adult stature (0.49, 0.44-0.54) and of not completing secondary school (0.82, 0.78-0.87). Faster linear growth was strongly associated with a reduced risk of short adult stature (age 2 years: 0.23, 0.20-0.52; mid-childhood: 0.39, 0.36-0.43) and of not completing secondary school (age 2 years: 0.74, 0.67-0.78; mid-childhood: 0.87, 0.83-0.92), but did raise the likelihood of overweight (age 2 years: 1.24, 1.17-1.31; mid-childhood: 1.76, 1.69-1.91) and elevated blood pressure (age 2 years: 1.12, 1.06-1.19; mid-childhood: 1.07, 1.01-1.13). Faster relative weight gain was associated with an increased risk of adult overweight (age 2 years: 1.51, 1.43-1.60; mid-childhood: 1.76, 1.69-1.91) and elevated blood pressure (age 2 years: 1.07, 1.01-1.13; mid-childhood: 1.22, 1.15-1.30). Linear growth and relative weight gain were not associated with dysglycaemia, but a higher birthweight was associated with decreased risk of the disorder (0.89, 0.81-0.98).

Interventions in countries of low and middle income to increase birthweight and linear growth...
during the first 2 years of life are likely to result in substantial gains in height and schooling and give some protection from adult chronic disease risk factors, with few adverse trade-offs.

**NUTRITION-SENSITIVE INTERVENTIONS AND PROGRAMMES: HOW CAN THEY HELP TO ACCELERATE PROGRESS IN IMPROVING MATERNAL AND CHILD NUTRITION?**

Marie T Ruel

Lancet 2013, 382: 536-51

Acceleration of progress in nutrition will require effective, large-scale nutrition-sensitive programmes that address key underlying determinants of nutrition and enhance the coverage and effectiveness of nutrition-specific interventions. We reviewed evidence of nutritional effects of programmes in four sectors—agriculture, social safety nets, early child development, and schooling. The need for investments to boost agricultural production, keep prices low, and increase incomes is undisputable; targeted agricultural programmes can complement these investments by supporting livelihoods, enhancing access to diverse diets in poor populations, and fostering women’s empowerment. However, evidence of the nutritional effect of agricultural programmes is inconclusive—except for vitamin A from biofortification of orange sweet potatoes—largely because of poor quality evaluations. Social safety nets currently provide cash or food transfers to a billion poor people and victims of shocks (eg, natural disasters). Individual studies show some effects on younger children exposed for longer durations, but weaknesses in nutrition goals and actions, and poor service quality probably explain the scarcity of overall nutritional benefits. Combined early child development and nutrition interventions show promising additive or synergistic effects on child development—and in some cases nutrition—and could lead to substantial gains in cost, efficiency, and effectiveness, but these programmes have yet to be tested at scale. Parental schooling is strongly associated with child nutrition, and the effectiveness of emerging school nutrition education programmes needs to be tested. Many of the programmes reviewed were not originally designed to improve nutrition yet have great potential to do so. Ways to enhance programme nutrition-sensitivity include: improve targeting; use conditions to stimulate participation; strengthen nutrition goals and actions; and optimise women’s nutrition, time, physical and mental health, and empowerment. Nutrition-sensitive programmes can help scale up nutrition-specific interventions and create a stimulating environment in which young children can grow and develop to their full potential.

*Figure 1.* Prevalence of stunting in children aged 0–5 years and GDP per person Most observations for prevalence of stunting are from 2000–08.
The fitted curves are locally weighted regressions of prevalence of stunting in children aged 0–5 years and poverty (<$1.25 per person, per day), against GDP per person. The adjustment to international dollar units converts income expressed in nominal dollars to one that is expressed in terms of international dollars, which have the same estimated purchasing power as a dollar in the USA, accounting for local prices. The size of the circles represents the estimated population of stunted children aged 0–5 years, in about 2005, on the basis of multiplication of stunting prevalence by UN estimates of the population of children aged 0–5 years. Data are sourced principally from the Demographic and Health Surveys,18 with observations for some countries sourced from WHO.19 GDP=gross domestic product. BGD=Bangladesh. CIV=Côte d’Ivoire. DOM=Dominican Republic. DRC=Democratic Republic of the Congo. ETH=Ethiopia. IDN=Indonesia. IRQ=Iraq. MDG=Madagascar. MMR=Myanmar (Burma). KEN=Kenya. NGA=Nigeria. PAK=Pakistan. PHN=Philippines. SDN=Sudan. VTN=Vietnam.

**Figure 2.** Prevalence of women overweight (BMI>25) and GDP per person, for low-income and middle-income countries. Most observations for prevalence of women overweight are from 2000–10.

The fitted curve is a locally weighted regression of prevalence of women overweight against GDP per person. The correlation between prevalence of women underweight and the log of GDP per person is 0.71 and is significant at the 1% level. The size of the circles represents the estimated population of overweight women aged 15–49 years, in about 2005, on the basis of multiplication of prevalence of women overweight by the UN population estimates of the female population aged 15–49 years. Data are sourced principally from the Demographic and Health Surveys18 and WHO.19 GDP=gross domestic product. PPP=purchasing power parity.

**THE POLITICS OF REDUCING MALNUTRITION: BUILDING COMMITMENT AND ACCELERATING PROGRESS**

Stuart Gillespie

Lancet 2013, 382: 552-69

In the past 5 years, political discourse about the challenge of undernutrition has increased substantially at national and international levels and has led to stated commitments from many national governments, international organisations, and donors. The Scaling Up Nutrition movement has both driven, and been driven by, this developing momentum. Harmonisation has increased among stakeholders, with regard to their understanding of the main causes of malnutrition and to the various options for addressing it. The main challenges are to enhance and expand the quality and coverage of nutrition-specific interventions, and to maximise the nutrition sensitivity of more distal interventions, such as agriculture, social protection, and water and sanitation. But a crucial third level of action exists, which relates to the environments and processes that underpin and shape political and policy processes. We focus on this neglected level. We address several fundamental questions: how can enabling environments and processes be cultivated, sustained, and ultimately translated into...
results on the ground? How has high-level political momentum been generated? What needs to happen to turn this momentum into results? How can we ensure that high-quality, well-resourced interventions for nutrition are available to those who need them, and that agriculture, social protection, and water and sanitation systems and programmes are proactively reoriented to support nutrition goals? We use a six-cell framework to discuss the ways in which three domains (knowledge and evidence, politics and governance, and capacity and resources) are pivotal to create and sustain political momentum, and to translate momentum into results in high-burden countries.

MATERNAL AND CHILD UNDERNUTRITION AND OVERWEIGHT IN LOW-INCOME AND MIDDLE-INCOME COUNTRIES

Robert E. Black

Lancet 2013, 382: 427-51

Maternal and child malnutrition in low-income and middle-income countries encompasses both undernutrition and a growing problem with overweight and obesity. Low body-mass index, indicative of maternal undernutrition, has declined somewhat in the past two decades but continues to be prevalent in Asia and Africa. Prevalence of maternal overweight has had a steady increase since 1980 and exceeds that of underweight in all regions. Prevalence of stunting of linear growth of children younger than 5 years has decreased during the past two decades, but is higher in south Asia and sub-Saharan Africa than elsewhere and globally affected at least 165 million children in 2011; wasting affected at least 52 million children. Deficiencies of vitamin A and zinc result in deaths; deficiencies of iodine and iron, together with stunting, can contribute to children not reaching their developmental potential. Maternal undernutrition contributes to fetal growth restriction, which increases the risk of neonatal deaths and, for survivors, of stunting by 2 years of age. Suboptimum breastfeeding results in an increased risk for mortality in the first 2 years of life. We estimate that undernutrition in the aggregate—including fetal growth restriction, stunting, wasting, and deficiencies of vitamin A and zinc along with suboptimum breastfeeding—is a cause of 3.1 million child deaths annually or 45% of all child deaths in 2011. Maternal overweight and obesity result in increased maternal morbidity and infant mortality. Childhood overweight is becoming an increasingly important contributor to adult obesity, diabetes, and non-communicable diseases. The high present and future disease burden caused by malnutrition in women of reproductive age, pregnancy, and children in the first 2 years of life should lead to interventions focused on these groups.
**Figure 3.** Trends in thinness (BMI <18.5 kg/m²), overweight (BMI ≥25 kg/m²), and obesity (BMI ≥30 kg/m²), using population weighted average prevalences for women aged 20–49 years UN regions and globally, 1980–2008. Error bars are 95% CIs.

BMI = body-mass index.

**Table 1.** Prevalence of vitamin A deficiency (1995–2005), iodine deficiency (2013), inadequate zinc intake (2005), and iron deficiency anaemia (2011)

<table>
<thead>
<tr>
<th></th>
<th>Vitamin A deficiency</th>
<th>Iodine deficiency (UIC &lt;100 μg/L)</th>
<th>Zinc deficiency (weighted average of country means)</th>
<th>Iron deficiency anaemia (haemoglobin &lt;110 g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children &lt;5 years</td>
<td>Pregnant women</td>
<td>Children &lt;5 years</td>
<td>Pregnant women</td>
</tr>
<tr>
<td>Night blindness</td>
<td>Serum retinol &lt;0.70 μmol/L</td>
<td>Serum retinol &lt;0.70 μmol/L</td>
<td>28.5% (28.2–28.9)</td>
<td>17.3% (15.9–18.8)</td>
</tr>
<tr>
<td>Global</td>
<td>0.9% (0.1–1.8)</td>
<td>33.3% (29.4–37.1)</td>
<td>15.3% (6.5–9.1)</td>
<td>18.1% (15.6–20.8)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>19.2% (17.1–21.5)</td>
</tr>
</tbody>
</table>
Table 2. Global deaths in children younger than 5 years attributed to nutritional disorders

<table>
<thead>
<tr>
<th></th>
<th>Attributable deaths with UN prevalences*</th>
<th>Proportion of total deaths of children younger than 5 years</th>
<th>Attributable deaths with NIMS prevalences†</th>
<th>Proportion of total deaths of children younger than 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal growth restriction (&lt;1 month)</td>
<td>817 000</td>
<td>11.8%</td>
<td>817 000</td>
<td>11.8%</td>
</tr>
<tr>
<td>Stunting (1–59 months)</td>
<td>1 017 000</td>
<td>14.7%</td>
<td>1 179 000</td>
<td>17.0%</td>
</tr>
<tr>
<td>Underweight (1–59 months)</td>
<td>999 000</td>
<td>14.4%</td>
<td>1 180 000</td>
<td>17.0%</td>
</tr>
<tr>
<td>Wasting (1–59 months)</td>
<td>875 000</td>
<td>12.6%</td>
<td>800 000</td>
<td>11.5%</td>
</tr>
<tr>
<td>Severe wasting (1–59 months)</td>
<td>516 000</td>
<td>7.4%</td>
<td>540 000</td>
<td>7.8%</td>
</tr>
<tr>
<td>Zinc deficiency (12–59 months)</td>
<td>116 000</td>
<td>1.7%</td>
<td>116 000</td>
<td>1.7%</td>
</tr>
<tr>
<td>Vitamin A deficiency (6–59 months)</td>
<td>157 000</td>
<td>2.3%</td>
<td>157 000</td>
<td>2.3%</td>
</tr>
<tr>
<td>Suboptimum breastfeeding (0–23 months)</td>
<td>804 000</td>
<td>11.6%</td>
<td>804 000</td>
<td>11.6%</td>
</tr>
<tr>
<td>Joint effects of fetal growth restriction and suboptimum breastfeeding in neonates</td>
<td>1 348 000</td>
<td>19.4%</td>
<td>1 348 000</td>
<td>19.4%</td>
</tr>
<tr>
<td>Joint effects of fetal growth restriction, suboptimum breastfeeding, stunting, wasting, and vitamin A and zinc deficiencies (&lt;5 years)</td>
<td>3 097 000</td>
<td>44.7%</td>
<td>3 149 000</td>
<td>45.4%</td>
</tr>
</tbody>
</table>

Data are to the nearest thousand.*Prevalence estimates from the UN.†Prevalence estimates from Nutrition Impact Model Study (NIMS).
Figure 4. Trends in prevalence and numbers of children with stunted growth (HAZ < -2), by selected UN regions and globally, 1990–2010, and projected to 2025 on the basis of UN prevalence estimates. HAZ=height-for-age Z score.

Data from UNICEF, WHO, World Bank.

Figure 5. Trends in prevalence and numbers of overweight (WHZ > 2) children, by selected UN regions and globally, 1990–2010, and projected to 2025, on the basis of UN prevalence estimates. WHZ=weight-for-height Z score.
Figure 6. Prevalence of stunting (HAZ < -2 Z scores below median) and overweight (BAZ > 2 Z scores above median) for highest and lowest wealth quintiles in selected countries. Red circles are lowest wealth quintiles, blue circles are highest wealth quintiles.

HAZ=height-for-age Z score. DHS=Demographic and Health Survey. MICS=Multiple Indicator Cluster Survey. BAZ=body-mass index for age Z score.
Globaly, 165 million children are student, undernutrition underlies 3.1 million.

Promising interventions exist to improve maternal nutrition and reduce fetal growth restriction and small-for-gestational-age (SGA) births in appropriate settings in developing countries, if scaled up before and during pregnancy. These interventions include balanced energy protein, calcium and multiple micronutrient supplementation and preventive strategies for malaria in pregnancy.

Reduction of SGA in at-risk populations, although further evidence from effectiveness assessments might be needed to guide a universal policy change.

Data for the effect of various.

Conditional cash transfers and related.

Innovative delivery strategies.

Nearly 15% of deaths of children younger than 5 years can be reduced.

The maximum effect on lives saved is noted with management of acute malnutrition.

The estimated total of deaths in children younger than 5 years can be reduced by 15% if populations can access ten evidence-based nutrition interventions at 90% coverage. Additionally, access to and uptake of iodised salt can alleviate iodine deficiency and improve health outcomes.

A

Folic acid supplementation

Neural tube defects can be a 72% reduction in risk of development of neural tube defects and a 68% reduction in risk. Review of folic acid supplementation during pregnancy showed that folic acid supplementation improved mean birthweight, with a 79% reduction in the incidence of megaloblastic anaemia. Fortification of cereals and other foods might be a feasible way to reach the population in need.

Iron or iron and folic acid supplementation

Maternal multiple micronutrient supplementation.

Maternal calcium supplementation.

Maternal iodine supplementation or fortification.

Balanced energy and protein supplementation.

B

Neonates delayed cord clamping

Neonatal vitamin K administration

Neonatal vitamin A supplementation

Kangaroo mother care

C

Nutrition interventions in infants and children.

Promotion of breastfeeding and supportive strategies.

EVIDENCE-BASED INTERVENTIONS FOR IMPROVEMENT OF MATERNAL AND CHILD NUTRITION: WHAT CAN BE DONE AND AT WHAT COST?

Zulfiqar A. Bhutta

Lancet 2013, 382: 452-77

Maternal undernutrition contributes to 800 000 neonatal deaths annually through small for gestational age births; stunting, wasting, and micronutrient deficiencies are estimated to underlie nearly 3.1 million child deaths annually. Progress has been made with many interventions implemented at scale and the evidence for effectiveness of nutrition interventions and delivery strategies has grown since The Lancet Series on Maternal and Child Undernutrition in 2008. We did a comprehensive update of interventions to address undernutrition and micronutrient deficiencies in women and children and used standard methods to assess emerging new evidence for delivery platforms. We modelled the effect on lives saved and cost of these interventions in the 34 countries that have 90% of the world’s children with stunted growth.

We also examined the effect of various delivery platforms and delivery options using community health workers to engage poor populations and promote behaviour change, access and uptake of interventions. Our analysis suggests the current total of deaths in children younger than 5 years can be reduced by 15% if populations can access ten evidence-based nutrition interventions at 90% coverage. Additionally, access to and uptake of iodised salt can alleviate iodine deficiency and improve health outcomes. Accelerated gains are possible and about a fifth of the existing burden of stunting can be averted using these approaches, if access is improved in this way. The estimated total additional annual cost involved for scaling up access to these ten direct nutrition interventions in the 34 focus countries is Int$9.6 billion per year. Continued investments in nutrition-specific interventions to avert maternal and child undernutrition and micronutrient deficiencies through community engagement and delivery strategies that can reach poor segments of the population at greatest risk can make a great difference.

If this improved access is linked to nutrition-sensitive approaches—ie, women’s empowerment, agriculture, food systems, education, employment, social protection, and safety nets—they can greatly accelerate progress in countries with the highest burden of maternal and child undernutrition and mortality.

Case fatality rates were typically 20–30% in children with SAM treated in hospitals or rehabilitation units, and rates were higher (50–60%) for oedematous malnutrition. A previous review of existing studies had estimated that following the WHO protocol, as opposed to standard care, would lead to a 55% reduction in deaths.

Community-based management of SAM ready-to-use therapeutic foods (RUTF) with standard care, RUTF had faster rates of weight gain.

Notably, a new randomised controlled trial compared standard RUTF with RUTF and additional 7 day, either amoxicillin or cefdinir, in children with uncomplicated SAM. This trial showed that the children receiving an antibiotic had a lower mortality rate, faster recovery rate, SAM. RUTF for community-based treatment, which has substantially. Available evidence shows use of RUTF compared. SAM as research to fill.


Table 4. Review of nutrition interventions for women of reproductive age and during pregnancy

<table>
<thead>
<tr>
<th>Evidence reviewed</th>
<th>Setting</th>
<th>Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Folic acid supplementation</strong></td>
<td></td>
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</tr>
<tr>
<td>Women of reproductive age</td>
<td>Systematic review of five trials of peri-conceptual folic acid supplementation</td>
<td>Developing and developed countries</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Systematic review of 31 trials</td>
<td>Mostly developed countries</td>
</tr>
<tr>
<td><strong>Iron and Iron-folate supplementation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women of reproductive age</td>
<td>Systematic review of 21 RCTs and quasi-experimental studies</td>
<td>Developing and developed countries. Intervention mostly given in school settings. Mostly effectiveness studies</td>
</tr>
</tbody>
</table>
### Pregnant women

**Systematic review of 43 RCTs and quasi-experimental studies (34 iron alone, eight iron-folate)**

Developed and developing countries. Intervention delivered in community or at facility antenatal clinic. Mostly effectiveness studies

Daily iron-alone supplementation

Significant effects: low birthweight (RR 0.81, 95% CI 0.68–0.97), birthweight (MD 30.81 g, 95% CI 5.94–55.68), serum haemoglobin concentration at term (MD 8.88 g/L, 95% CI 6.96–10.80), anaemia at term (RR 0.30, 95% CI 0.19–0.46), iron deficiency (RR 0.43, 95% CI 0.27–0.66), iron deficiency anaemia (RR 0.33, 95% CI 0.16–0.69), side-effects (RR 2.36, 95% CI 0.96–5.82)

Non-significant effects: premature delivery, neonatal death, congenital anomalies

Iron-folate supplementation

Significant effects: birthweight (MD 57.7 g, 95% CI 7.66–107.79), anaemia at term (RR 0.34, 95% CI 0.21–0.54), serum haemoglobin concentration at term (MD 16.13 g/L, 95% CI 12.74–19.52)

Non-significant effects: low birthweight, premature birth, neonatal death, congenital anomalies

**MMN supplementation**

**Pregnant women**

Systematic review of 21 RCTs

Developed and developing countries. Studies compared MMN with two or fewer micronutrients

Significant effects: low birthweight (RR 0.88, 95% CI 0.85–0.91), SGA (RR 0.89, 95% CI 0.83–0.96), preterm birth (RR 0.97, 95% CI 0.94–0.99)

Non-significant effects: miscarriage, maternal mortality, perinatal mortality, stillbirths, and neonatal mortality

Insufficient data for neurodevelopmental outcomes

**Calcium supplementation**

**Pregnant women**

Systematic review of 15 RCTs

Developed and developing countries. Mostly effectiveness trials

Preterm birth (RR 0.76, 95% CI 0.60–0.97)

Non-significant effects: perinatal mortality, low birthweight, neonatal mortality

**Iodine through iodisation of salt**

**Pregnant women**

Systematic review of five RCTs

Mostly developing countries. Mostly effectiveness trials

Significant effects: cretinism at 4 years of age (RR 0.27, 95% CI 0.12–0.60), developmental scores 10–20% higher in young children, birthweight 3.82–6.30% higher

**Maternal supplementation with balanced energy protein**

**Pregnant women**

Systematic review of 16 RCTs and quasi-experimental studies

Developing and developing countries

Significant effects: SGA (RR 0.66, 95% CI 0.49–0.89), stillbirths (RR 0.62, 95% CI 0.40–0.98), birthweight (MD 73g, 95% CI 30–117)

Non-significant effects: Bayley mental scores at 1 year

NTD=neural tube defects. RR=relative risk. MD=mean difference. RCT=randomised controlled trial. MMN=multiple micronutrient. SGA=small-for-gestational age.
## Table 5. Review of nutrition interventions in neonates

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Evidence reviewed</th>
<th>Setting</th>
<th>Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delayed cord clamping</strong></td>
<td></td>
<td></td>
<td><strong>Term neonates</strong>&lt;br&gt;Systematic review of 11 RCTs 24 and 36 weeks’ gestation at birth&lt;br&gt;Significant effects: increased newborn haemoglobin concentration (MD 2.17 g/dL, 95% CI 0.28–4.06)&lt;br&gt;Non-significant effects: postpartum haemorrhage, severe postpartum haemorrhage&lt;br&gt;Delayed cord clamping was associated with an increased requirement for phototherapy for jaundice</td>
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<td><strong>Preterm neonates</strong>&lt;br&gt;Systematic review of 15 RCTs Developing and developed countries&lt;br&gt;Significant effects: reduced need for blood transfusion (RR 0.61, 95% CI 0.46–0.81), decrease in intraventricular haemorrhage (RR 0.59, 95% CI 0.41–0.85), reduced risk of necrotising enterocolitis (RR 0.62, 95% CI 0.43–0.90)&lt;br&gt;Peak bilirubin concentration was higher for delayed cord clamping group (MD 15.01 mmol/L, 95% CI 5.62–24.40)</td>
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<td></td>
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<td><strong>Neonatal vitamin K administration</strong>&lt;br&gt;Systematic review of two RCTs for intramuscular vitamin K and 11 RCTs for oral vitamin K&lt;br&gt;Significant effects: One dose of intramuscular vitamin K reduced clinical bleeding at 1–7 days and improved biochemical indices of coagulation status. Oral vitamin K also improved coagulation status</td>
</tr>
<tr>
<td><strong>Neonates</strong></td>
<td></td>
<td></td>
<td><strong>Vitamin A supplementation</strong></td>
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<td></td>
<td><strong>Very low birthweight infants</strong>&lt;br&gt;Systematic review of nine RCTs Developing countries&lt;br&gt;Significant effects: reduced number of deaths and oxygen requirement at 1 month of age.&lt;br&gt;Non-significant effects: one large trial showed no significant effect on neurodevelopment assessment at 18–22 months of age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Term neonates</strong>&lt;br&gt;Systematic review of five RCTs and quasi-experimental studies Developing countries&lt;br&gt;Significant effects: reduction in infant mortality at 6 months (RR 0.86, 95% CI 0.77–0.97)&lt;br&gt;Non-significant effects: infant mortality at 12 months (RR 1.03, 95% CI 0.87–1.23)&lt;br&gt;Little data available for cause specific mortality, morbidity, vitamin A deficiency, anaemia, and adverse events</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Kangaroo mother care for promotion of breastfeeding and care of preterm and SGA infants</strong></td>
</tr>
<tr>
<td><strong>Healthy neonates</strong></td>
<td></td>
<td></td>
<td><strong>Healthy neonates</strong>&lt;br&gt;Systematic review of 34 RCTs Developing and developed countries&lt;br&gt;Significant effects: increase in breastfeeding at 1–4 months after birth (RR 1.27, 95% CI 1.06–1.53), increased breastfeeding duration (MD 42.55 days, 95% CI 1.69–86.79)</td>
</tr>
<tr>
<td><strong>Preterm neonates</strong></td>
<td></td>
<td></td>
<td><strong>Preterm neonates</strong>&lt;br&gt;Systematic review of 16 RCTs Developing and developed countries&lt;br&gt;Significant effects: reduction in the risk of mortality (RR 0.60, 95% CI 0.39–0.93), reduction in nosocomial infection and sepsis (RR 0.42, 95% CI 0.24–0.73), reduction in hypothermia (RR 0.23, 95% CI 0.10–0.55), reduced length of hospital stay (MD 2.4 days, 95% CI 0.7–4.1)</td>
</tr>
</tbody>
</table>

**RCT**=randomised controlled trial. **MD**=mean difference. **RR**=relative risk. **SGA**=small-for-gestational age.
Table 6. Review of nutrition interventions for women of reproductive age and during pregnancy

<table>
<thead>
<tr>
<th>Setting</th>
<th>Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast feeding promotion in infants</strong></td>
<td>Significant effects: educational or counselling interventions increased EBF by 43% (95% CI 9–87) at day 1, by 30% (19–42) till 1 month, and by 90% (54–134) from 1–6 months. Significant reductions in rates of no breastfeeding also noted; 32% (13–46) at day 1, 30% (20–38) 0–1 month, and 18% (11–23) for 1–6 months. Non-significant effects: predominant and partial breastfeeding</td>
</tr>
<tr>
<td>Systematic review of 110 RCTs and quasi-experimental studies</td>
<td>Developing and developed countries</td>
</tr>
</tbody>
</table>
| **Complementary feeding promotion in children 6–24 months of age** | Nutrition education in food secure populations  
Significant effects: increased height gain (SMD 0.35; 95% CI 0.08–0.62), HAZ (SMD 0.22; 95% CI 0.01–0.43), weight gain (SMD 0.40, 95% CI 0.02–0.78)  
Non-significant effects: stunting, WAZ  
Nutrition education in food insecure populations  
Significant effects: HAZ (SMD 0.25, 95% CI 0.09–0.42), stunting (RR 0.68, 95% CI 0.60–0.76), WAZ (SMD 0.26, 95% CI 0.12–0.41)  
Complementary food provision with or without education in food insecure populations  
Significant effects: HAZ (SMD 0.39, 95% CI 0.05–0.73), WAZ (SMD 0.26, 95% CI 0.04–0.48)  
Non-significant effects: stunting (RR 0.33, 95% CI 0.11–1.00) |
| 16 RCTs and quasi-experimental studies       | Mostly from food secure populations. Various foods used                                                                                                                                                  |
| **Preventive vitamin A supplementation in children 6 months to 5 years of age** | Significant effects: reduced all-cause mortality (RR 0.76, 95% CI 0.69–0.83), reduced diarrhoea-related mortality (RR 0.72, 95% CI 0.57–0.91), reduced incidence of diarrhoea (RR 0.85, 95% CI 0.82–0.87), reduced incidence of measles (RR 0.50, 95% CI 0.37–0.67)  
Non-significant effects: measles-related and ARI-related mortality |
| Systematic review of 43 RCTs                 | Developing and developed countries                                                                                                                                                                       |
| **Iron supplementation in children**         | Intermittent iron supplementation  
Significant effects: decreased anaemia (RR 0.51, 95% CI 0.37–0.72), decreased iron deficiency (RR 0.24, 95% CI 0.06–0.91), increased haemoglobin concentration (MD 5.20 g/L, 95% CI 2.51–7.88), increased ferritin concentration (MD 14.17 mcg/L, 95% CI 3.53–24.81)  
Non-significant effects: HAZ, WAZ  
Evidence for mental development, motor skill development, school performance, and physical capacity was assessed by very few studies and showed no clear effect |
| Systematic review of 33 RCTs and quasi-experimental studies | LMICs. Participant’s ages ranged from neonates to 19 years                                                                                                                                               |
| **MMN supplementation including iron in children** | Significant effects: length (MD 0.13, 95% CI 0.06–0.21), increased intelligence quotient scores (≥8 years age; SMD 0.41, 95% CI 0.20–0.62)  
Non-significant effects: Bayley mental development index in younger children (≤27 months old), motor development |
| Systematic review of 17 RCTs                 | Developing and developed countries. In children aged 6 months to 15 years                                                                                                                               |
| Mostly developing countries. In children aged 6 months to 16 years | MMN supplementation  
Significant effects: increased length (MD 0.13, 95% CI 0.06–0.21), increased weight (MD 0.14, 95% CI 0.03–0.25)  
MMN might be associated with marginal increase in fluid intelligence and academic performance in healthy school children |
Clinical Social Work Vol.4 No.2, 2013

Systematic review of 17 RCTs
Developing countries. Mostly effectiveness studies. In children aged 6 months to 11 years

Micronutrient powders
Significant effects: Reduced anaemia (RR 0.66, 95% CI 0.57–0.77), reduced iron deficiency anaemia (RR 0.43, 95% CI 0.35–0.52), reduced retinol deficiency (RR 0.79, 95% CI 0.64–0.98). Improved haemoglobin concentrations (SMD 0.98, 95% CI 0.55–1.40). MNP was associated with a significant increase in diarrhoea (RR 1.04, 95% CI 1.01–1.06)
Non-significant effects: serum ferritin, zinc deficiency, stunting, wasting, underweight, HAZ, WAZ, WHZ, fever, URI

Zinc supplementation in children

Systematic review of 18 RCTs
Mostly developing countries. In children younger than 5 years

Preventive zinc supplementation
Significant effects: mean height improved by 0.37 cm (SD 0.25) in children supplemented for 24 weeks, diarrhoea reduced by 13% (95% CI 6–19), pneumonia reduced by 19% (95% CI 10–27)
Non-significant effects: mortality (cause specific and all-cause)

Systematic review of 13 trials
Developing and developed countries. In children younger than 5 years

Non-significant effects: Mental developmental index, psychomotor development index

Table 7. Review of evidence for disease prevention and management

<table>
<thead>
<tr>
<th>Setting</th>
<th>Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WASH interventions</strong></td>
<td></td>
</tr>
<tr>
<td>Overview of three systematic reviews</td>
<td>Developing countries</td>
</tr>
<tr>
<td>DHS data from 65 countries</td>
<td>Developing countries</td>
</tr>
<tr>
<td><strong>Maternal deworming</strong></td>
<td></td>
</tr>
<tr>
<td>Systematic review of five RCTs</td>
<td>Developing countries</td>
</tr>
<tr>
<td><strong>Deworming in children (for soil-transmitted intestinal worms)</strong></td>
<td></td>
</tr>
<tr>
<td>Systematic review of 34 RCTs</td>
<td>Developing countries</td>
</tr>
<tr>
<td><strong>Feeding practices in diarrhoea</strong></td>
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</tbody>
</table>
| Review of 29 RCTs | Developing countries | Significant effects: in acute diarrhoea, lactose-free diets, when compared with lactose-containing diets, significantly reduced incidence of diarrhoea (SMD $-0.36$, 95% CI $-0.62$ to $-0.10$) and treatment failure (RR $0.53$, 95% CI $0.40$–$0.70$)  
Non-significant effects: weight gain |
|---|---|---|

| Zinc therapy for diarrhoea | Systematic review of 13 studies | Mostly Asia | Significant effects: reduced all-cause mortality reduced by 46% (95% CI $12$–$68$), diarrhoea-related admissions to hospital by 23% (95% CI $15$–$31$)  
Non-significant effects: diarrhoea-specific mortality, diarrhoea-prevalence  
Zinc reduced duration of acute diarrhoea by 0.50 days and persistent diarrhoea by 0.68 days |
|---|---|---|---|

| IPTp/ITN for malaria in pregnancy | Systematic review of 16 RCTs | Mostly Africa | Significant effects: Anti-malarials to prevent malaria in all pregnant women reduced antenatal parasitemia (RR $0.53$, 95% CI $0.33$–$0.86$), increased birthweight (MD $126.7$ g, 95% CI $88.64$–$164.75$), reduced low birthweight by 43% (RR $0.57$, 95% CI $0.46$–$0.72$) and severe antenatal anaemia 38% (RR $0.62$, 95% CI $0.50$–$.$)  
Non-significant effects: perinatal deaths |
|---|---|---|---|

| Systematic review of six RCTs | Developing countries | Significant effects: ITNs in pregnancy reduced low birthweight (RR $0.77$, 95% CI $0.61$–$0.98$) and reduced fetal loss (first to fourth pregnancy; RR $0.67$, 95% CI $0.47$–$0.97$)  
Non-significant effects: anaemia and clinical malaria |
|---|---|---|---|

| Malaria prophylaxis in children | Systematic review of seven RCTs | Developing countries of West Africa | Significant effects: Reduced clinical malaria episodes (RR $0.26$, 95% CI $0.17$–$0.38$), reduced severe malaria episodes (RR $0.27$, 95% CI $0.10$–$0.76$). IPTc also reduced risk of moderately severe anaemia (RR $0.71$, 95% CI $0.52$–$0.98$)  
Non-significant effects: all-cause mortality |
|---|---|---|---|

| Systematic review of 22 RCTs | Developing countries in Africa | Significant effects: ITNs improved packed cell volume of children by 1.7 absolute packed cell volume percent. When the control group used untreated nets, the difference was 0.4 absolute packed cell volume percent.  
ITNs and IRS reduced malaria-attributable mortality in children (1–59 months) by 55% (95% CI $49$–$61$) in Plasmodium falciparum settings |
|---|---|---|---|

**WASH**=water, sanitation, and hygiene. RCT=randomised controlled trial. DHS=Demographic and Health Survey. GDP=gross domestic product. RR=relative risk. MD=mean difference. SMD=standard mean difference. WAZ=weight-for-age Z score. HAZ=height-for-age Z score. DEVTA=de-worming and enhanced vitamin A. IPTp=intermittent preventive treatment of malaria in pregnancy. IPTc=IPT in children. ITN=insecticide-treated bednets. IRS=indoor residual spraying.
**Figure 7.** Countries with the highest burden of malnutrition These 34 countries account for 90% of the global burden of malnutrition.

**Figure 8.** Effect of scale up of interventions on cause-specific deaths Error bars are ranges.
**Figure 9.** Effect of scale up of interventions on deaths in children younger than 5 years. Error bars are ranges. Promotion and use of iodised salt not modelled for mortality effect.

SAM=severe acute malnutrition. MAM=moderate AM.

**Table 8.** Total additional annual cost of achieving 90% coverage with nutrition interventions, excluding management of moderate acute malnutrition, in 34 countries with more than 90% of the burden

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt iodisation</td>
<td>$68</td>
</tr>
<tr>
<td>Multiple micronutrient supplementation in pregnancy (includes iron-folate)</td>
<td>$472</td>
</tr>
<tr>
<td>Calcium supplementation in pregnancy</td>
<td>$1914</td>
</tr>
<tr>
<td>Energy-protein supplementation in pregnancy</td>
<td>$972</td>
</tr>
<tr>
<td>Vitamin A supplementation in childhood</td>
<td>$106</td>
</tr>
<tr>
<td>Zinc supplementation in childhood</td>
<td>$1182</td>
</tr>
<tr>
<td>Breastfeeding promotion</td>
<td>$653</td>
</tr>
<tr>
<td>Complementary feeding education</td>
<td>$269</td>
</tr>
<tr>
<td>Complementary food supplementation</td>
<td>$1359</td>
</tr>
<tr>
<td>SAM management</td>
<td>$2563</td>
</tr>
</tbody>
</table>

**PRACTICAL DOSING OF PRAZIQUANTEL FOR SCHISTOSOMIASIS IN PRESCHOOL-AGED CHILDREN**

Piero L. Olliaro

Tropical Medicine and International Health, Vol. 18, No. 9, pp: 1085-1089, Sept 2013

Schistosomiasis is known to occur in preschool-aged children, but achieving accurate dosing of praziquantel in its current form is challenging. While waiting for a paediatric formulation, there is a need to develop a means for using the available products to treat this age group. Current 600-mg tablets are differently scored to give units of 150 mg (a quarter of a tablet) or 300 mg (half a tablet).

We examined several dosing schemes to dose accurately (40-60 mg/kg) children aged 3-72 months (weight range 4-25 kg, based on available weight-for-age growth references from sub-Saharan Africa and Brazil, n = 106,230).

Adequate dosing can be achieved with formulations that can be split into four 150 mg quarters for children weighing 5 kg or more, and with tablets than can be split into two 300 mg halves for children weighing 10 kg or more. Giving ½ tablet for 5-7 kg; ¾ tablet for 8-10 kg; 1 tablet for 11-15 kg; 1 ½ tablet for 16-21 kg; and two tablets for 22-25 kg will have 100% of subjects correctly dosed within the target 40-60 mg/kg range.

Formulations that can be divided into four parts (to give 150 mg increments) are preferred for children weighing less than 11 kg; the same dosing can be applied with 600 mg praziquantel formulations that can be divided into four quarters or two halves from 11 kg body weight.

**UNNECESSARY INJECTING OF MEDICINES IS STILL A MAJOR PUBLIC HEALTH CHALLENGE**
Globally

Gore C.

Tropical Medicine and International Health, Vol. 18, No. 9, pp: 1157-1159, Sept 2013

It is dismaying to learn that such a large number of countries do not appear to have these data available in light of what has been documented regarding injection overuse in developing countries. Much of the evidence is from the 1980s and 1990s, but more recent studies in China and Egypt found unnecessary health facility injection rates of 57% and 95%, respectively (Yan et al. 2006; Bodenschatz et al. 2009). A 2006 Pakistani study estimated that 94% of therapeutic injections nationally are unnecessary (Altaf et al. 2006). A 1999 review article summarising earlier evidence noted levels of unnecessary injections ranging from 70% to 99% in various patient populations in India, Indonesia, the Russian Federation and Tanzania.

It is dismaying to learn that such a large number of countries do not appear to have these data available in light of what has been documented regarding injection overuse in developing countries. Much of the evidence is from the 1980s and 1990s, but more recent studies in China and Egypt found unnecessary health facility injection rates of 57% and 95%, respectively (Yan et al. 2006; Bodenschatz et al. 2009). A 2006 Pakistani study estimated that 94% of therapeutic injections nationally are unnecessary (Altaf et al. 2006). A 1999 review article summarising earlier evidence noted levels of unnecessary injections ranging from 70% to 99% in various patient populations in India, Indonesia, the Russian Federation and Tanzania.

The accident at the nuclear site in Fukushima has fostered a fear of the consequences of radioactive contamination among many, especially regarding travel to Japan and the import of Japanese goods. We give a general overview of the assessment of the effects of ionizing radiation and a summary of the consequences of the Japanese accident. We report the results of the measurement of radionuclide intake among travelers returning from Japan, carried out at the whole-body counter of the Institute for Work Design of North Rhine-Westphalia (LIA.NRW) in Düsseldorf.

In summary, there are no indications against travel to Japan from a radiological point of view. The external exposure as well as the internal exposure from ingestion of radionuclides will, on average, not be higher than the world average. The total radiation exposure for people living in Japan will remain within the range of natural exposure in Japan. The total radiation exposure in Japan will be lower than the natural radiation exposure for a large part of the European population. Only the restricted areas and evacuation zones around the Fukushima nuclear site should be avoided, but they are not freely accessible anyway. Higher than average exposure is possible when staying in Fukushima prefecture. The consumption of purchased Japanese food is possible without restrictions as the food is subject to monitoring in line with international standards, and the current data strongly indicates that the ingestion pathway is of minor importance.

Eye Problems on Expeditions

Daniel S. Morris

Travel Medicine and Infectious Disease 2013, 11, 152-158

Visual loss in the wilderness setting is at best disabling and at worst potentially fatal. However many physicians have a poor knowledge of ophthalmology and the basic skills that could be applied in situations away from definitive care.

This paper is intended for physicians, interested non-medical people and expedition operators as a practical guide to the treatment and prevention of eye problems on expeditions.

Some of the eye conditions described in this paper are unique to the high altitude setting, such as high altitude retinopathy and some could happen in any environment, such as trauma, dry eyes and contact lens problems. As with any aspect of an expedition, preparation is vital to prevent and avoid eye problems. It is therefore important that pre-existing ocular conditions are known about and appropriate drugs and equipment are available in expedition first aid kits.

In the event of a visual problem, it is always
better to be cautious and evacuate a patient rather than a risk a sight-threatening complication. However this paper should provide a non-ophthalmologist with the skills to treat the eye conditions described.

TRAVEL-ASSOCIATED FAECAL COLONIZATION WITH ESBL-PRODUCING ENTEROBACTERIAEAE: INCIDENCE AND RISK FACTORS

Äse Östholm-Balkhed


To study the acquisition of extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-PE) among the faecal flora during travel, with a focus on risk factors, antibiotic susceptibility and ESBL-encoding genes.

An observational prospective multicentre cohort study of individuals attending vaccination clinics in south-east Sweden was performed, in which the submission of faecal samples and questionnaires before and after travelling outside Scandinavia was requested. Faecal samples were screened for ESBL-PE by culturing on ChromID ESBL and an in-house method. ESBL-PE was confirmed by phenotypic and genotypic methods. Susceptibility testing was performed with the Etest. Individuals who acquired ESBL-PE during travel (travel-associated carriers) were compared with non-carriers regarding risk factors, and unadjusted and adjusted ORs after manual stepwise elimination were calculated using logistic regression.

Of 262 enrolled individuals, 2.4% were colonized before travel. Among 226 evaluable participants, ESBL-PE was detected in the post-travel samples from 68 (30%) travellers. The most important risk factor in the final model was the geographic area visited: Indian subcontinent (OR 24.8, P<0.001), Asia (OR 8.63, P<0.001) and Africa north of the equator (OR 4.94, P=0.002). Age and gastrointestinal symptoms also affected the risk significantly. Multiresistance was seen in 77 (66%) of the ESBL-PE isolates, predominantly a combination of reduced susceptibility to third-generation cephalosporins, trimethoprim/sulfamethoxazole and aminoglycosides. The most common species and ESBL-encoding gene were Escherichia coli (90%) and CTX-M (73%), respectively.

Acquisition of multiresistant ESBL-PE among the faecal flora during international travel is common. The geographical area visited has the highest impact on ESBL-PE acquisition.

RISK OF GUILLAIN-BARRÉ SYNDROME AFTER SEASONAL INFLUENZA VACCINATION AND INFLUENZA HEALTH-CARE ENCOUNTERS: A SELF-CONTROLLED STUDY

Jeffrey C. Kwong

Lancet Infect Dis 2013, 13: 769-76

The possible risk of Guillain-Barré syndrome from influenza vaccines remains a potential obstacle to achieving high vaccination coverage. However, influenza infection might also be associated with Guillain-Barré syndrome. We aimed to assess the risk of Guillain-Barré syndrome after seasonal influenza vaccination and after influenza-coded health-care encounters.

We used the self-controlled risk interval design and linked universal health-care system databases from Ontario, Canada, with data obtained between 1993 and 2011. We used physician billing claims for influenza vaccination and influenza-coded health-care encounters to ascertain exposures. Using fixed-effects conditional Poisson regression, we estimated the relative incidence of hospitalisation for primary-coded Guillain-Barré syndrome during the risk interval compared with the control interval.

We identified 2831 incident admissions for Guillain-Barré syndrome; 330 received an influenza vaccine and 109 had an influenza-coded health-care encounter within 42 weeks before hospitalisation. The risk of Guillain-Barré syndrome within 6 weeks of vaccination was 52% higher than in the control interval of 9-42 weeks (relative incidence 1.52; 95% CI 1.17-1.99), with the greatest risk during weeks 2-4 after vaccination. The risk of Guillain-Barré syndrome within 6 weeks of an influenza-coded health-care encounter was greater than for vaccination (15.81; 10.28-24.32). The attributable risks were 1.03 Guillain-Barré syndrome admissions per million vaccinations, compared with 17.2 Guillain-Barré syndrome admissions per million influenza-coded health-care encounters. The relative and attributable risks of Guillain-Barré syndrome after seasonal influenza vaccination are lower than those after influenza illness. Patients considering immunisation should be fully informed of the risks of Guillain-Barré syndrome from both influenza vaccines and influenza illness.
CLINICAL EPIDEMIOLOGY OF THE GLOBAL EXPANSION OF KLEBSIELLA PNEUMONIAE CARBAPENEMASES
Silvia Munoz-Price L.

Lancet Infect Dis 2013, 13: 785-96

Klebsiella pneumoniae carbapenemases (KPCs) were originally identified in the USA in 1996. Since then, these versatile β-lactamases have spread internationally among Gram-negative bacteria, especially K pneumoniae, although their precise epidemiology is diverse across countries and regions. The mortality described among patients infected with organisms positive for KPC is high, perhaps as a result of the limited antibiotic options remaining (often colistin, tigecycline, or aminoglycosides). Triple drug combinations using colistin, tigecycline, and imipenem have recently been associated with improved survival among patients with bacteraemia. In this Review, we summarise the epidemiology of KPCs across continents, and discuss issues around detection, present antibiotic options and those in development, treatment outcome and mortality, and infection control. In view of the limitations of present treatments and the paucity of new drugs in the pipeline, infection control must be our primary defence for now.

THE EMERGENCE OF INFLUENZA A H7N9 IN HUMAN BEINGS 16 YEARS AFTER INFLUENZA A H5N1: A TALE OF TWO CITIES
Kelvin K. W. To

Lancet Infect Dis 2013, 13: 809-21

Infection with either influenza A H5N1 virus in 1997 or avian influenza A H7N9 virus in 2013 caused severe pneumonia that did not respond to typical or atypical antimicrobial treatment, and resulted in high mortality. Both viruses are reassortants with internal genes derived from avian influenza A H9N2 viruses that circulate in Asian poultry. Both viruses have genetic markers of mammalian adaptation in their haemagglutinin and polymerase PB2 subunits, which enhanced binding to human-type receptors and improved replication in mammals, respectively. Hong Kong (affected by H5N1 in 1997) and Shanghai (affected by H7N9 in 2013) are two rapidly flourishing cosmopolitan megacities that were increasing in human population and poultry consumption before the outbreaks. Both cities are located along the avian migratory route at the Pearl River delta and Yangtze River delta. Whether the widespread use of the H5N1 vaccine in east Asia—with suboptimum biosecurity measures in live poultry markets and farms—predisposed to the emergence of H7N9 or other virus subtypes needs further investigation. Why H7N9 seems to be more readily transmitted from poultry to people than H5N1 is still unclear.

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