**Eating for two? The unresolved question of optimal diet in pregnancy**

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Unequivocal evidence of the importance of fetal nutrition as a driver of intrauterine growth has come from a range of experimental studies in which nutrient supply to the fetus is manipulated [1]. The dependence of the fetus on a sufficient supply of nutrients to support its successful growth and development, highlights the importance of adequate maternal nutrition to ensure fetal nutrient needs can be met. However, the complex supply chain between maternal diet and fetal nutrient supply means that fetal nutrition and maternal nutrition are not the same [1] - and for human pregnancies, the definition of what is optimal, in terms of maternal diet before and during pregnancy, remains unknown. Across the world diets vary hugely, both in quantity and quality, and even in developed settings there is significant variation in the quality of young women’s diets, with consequent differences in patterns of micro- and macronutrient intake [2]. But do such variations in maternal diet matter to the fetus?

Growing recognition of the influence of intrauterine experience, both for short-term pregnancy outcomes and long-term health of the offspring [3,4], demands that we need to understand more about the role of maternal nutrition, and its effects on fetal growth and development. Given this interest in maternal nutrition, it may be surprising that we do not know more about what is optimal. However, there are a number of challenges in understanding the existing evidence. Firstly, much of the evidence is observational, and collation of data across studies may be difficult – for example to address differences in confounding influences in different settings or in the dietary assessment methods used. Secondly, although diet is a complex exposure, comprised of an array of nutrients and other food components, many dietary interventions have focused on individual nutrients or small groups of nutrients. This fails to take account of nutrient-nutrient or other interactions, and may limit our understanding of effects of supplementation [4]. Thirdly, common effects are sometimes sought across groups of women who differ significantly in their habitual diets, nutrient status and body composition before conception – each of which would be expected to impact on the likely success of supplementation. Fourthly, an essential difference between trial protocols, that is the timing and duration of supplementation in pregnancy, is not always recognised sufficiently well [4].

In this month’s American Journal of Clinical Nutrition, Gresham and colleagues report a systematic review and meta-analysis that examine the effects of dietary interventions in pregnancy on offspring outcomes [5]. The paper provides an up-to-date synthesis of findings of intervention studies which, together with the reported sub-group analyses, address some of these challenges. The included studies used dietary counselling, provision of foods and/or fortified food products, or a combination of both to achieve changes in dietary intake in pregnancy. The focus on foods and whole diet studies moves away from individual nutrient supplements, and enables the effects of broader dietary changes to be evaluated. Separate consideration was given to counselling interventions, which most commonly aimed to align dietary patterns more closely with recommendations, and the provision of foods/fortified foods. The authors describe how effects on birth outcomes differed in women who were underweight or at nutritional risk, and according to country’s income. The main messages are that dietary interventions increased birth weight and reduced the incidence of low birth weight. Although the effect sizes were modest, there were clear benefits of provision of foods and fortified food products, and amongst more vulnerable women. Effects on other perinatal outcomes were not found, but insufficient reporting of results hindered meta-analysis and the included studies were not necessarily powered to address these.

So how does this review inform us regarding what is optimal in terms of maternal diet? The methods used for the selection of studies and the data extraction were thorough, and the authors took account of the quality of included studies [5,6]. The systematic review is the largest to date, and the findings provide some clues. However, the varied nature of the interventions and study populations provide a number of challenges. For example, the overall effects of on birth weight were largely attributable to the effects of provision of foods and fortified foods which, in the meta-analysis, were dominated by interventions carried out in more vulnerable populations. The opposite was true for the dietary counselling studies, few of which had included nutritionally ‘at risk’ women. The balance and nature of included studies also has implications for conclusions with respect to interventions focused on macronutrient intake [5], and evidence on the role of micronutrients may still be insufficient [7].

Despite these limitations, the review shows that altering dietary intake in pregnancy can change immediate pregnancy outcomes, and it highlights the need for ongoing and future research efforts to understand what maternal diets are optimal to support successful pregnancies. As part of these efforts, different types of evidence may also need to be considered. For example, interventions to improve maternal nutrition are likely to be complex and, as such, may not lend themselves to a simple randomised design. Additionally, as maternal nutrition has been shown to alter epigenetic processes in the fetus [8], and nutritionally-influenced epigenetic processes may be associated with later body composition in the offspring independently of size at birth [9], there is an urgent need to consider the effects of maternal nutrition on longer-term outcomes [10]. Lastly, the importance of the nutritional environment in early embryonic life, and its impact on establishing the fetal growth trajectory, directs attention to the importance of the preconception period, and the possibility of earlier interventions [3]. Getting maternal nutrition right may mean that efforts to ensure all women have access to adequate diets before conception, as well as during pregnancy, should be our ambition.

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**REFERENCES**

1. Bloomfield FH, Spiroski AM, Harding JE. Fetal growth factors and fetal nutrition. Semin Fetal Neonatal Med. 2013; 18: 118-23.

2. Crozier SR, Robinson SM, Borland SE, Inskip HM, SWS Study Group. Dietary patterns in the Southampton Women’s Survey. Eur J Clin Nutr 2006; 60: 1391-1399.

3. Barker D, Barker M, Fleming T, Lampl M. Developmental biology: Support mothers to secure future public health. Nature 2013; 504: 209-11.

4. Jackson AA, Robinson SM. Dietary guidelines for pregnancy: a review of current evidence. Public Health Nutr 2001; 4: 625-630.

5. Gresham E, Byles JE, Bisquera A, Hure AJ. The effects of dietary interventions on neonatal and infant outcomes: a systematic review and meta-analysis. Am J Clin Nutr 2014; [in press]

6. Gresham E, Bisquera A, Byles JE, Hure AJ. Effects of dietary interventions on pregnancy outcomes: a systematic review and meta-analysis. Matern Child Nutr 2014; [Epub Jul 22]

7. Christian P, Stewart CP. Maternal micronutrient deficiency, fetal development, and the risk of chronic disease. J Nutr 2010; 140: 437-45.

8. Dominguez-Salas P, Moore SE, Baker MS, Bergen AW, Cox SE, Dyer RA, Fulford AJ, Guan Y, Laritsky E, Silver MJ, et al. Maternal nutrition at conception modulates DNA methylation of human metastable epialleles. Nat Commun 2014; 5: 3746.

9. Godfrey KM, Sheppard A, Gluckman PD, Lillycrop KA, Burdge GC, McLean C, Rodford J, Slater-Jefferies JL, Garratt E, Crozier SR, et al. Epigenetic gene promoter methylation at birth is associated with child’s later adiposity. Diabetes 2011; 60: 1528-34.

10. Hawkesworth S. Exploiting dietary supplementation trials to assess the impact of the prenatal environment on CVD risk. Proc Nutr Soc 2009; 68: 78-88.