

## Preconception health 1



# Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health

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A woman who is healthy at the time of conception is more likely to have a successful pregnancy and a healthy child. We reviewed published evidence and present new data from low-income, middle-income, and high-income countries on the timing and importance of preconception health for subsequent maternal and child health. We describe the extent to which pregnancy is planned, and whether planning is linked to preconception health behaviours. Observational studies show strong links between health before pregnancy and maternal and child health outcomes, with consequences that can extend across generations, but awareness of these links is not widespread. Poor nutrition and obesity are rife among women of reproductive age, and differences between high-income and low-income countries have become less distinct, with typical diets falling far short of nutritional recommendations in both settings and especially among adolescents. Several studies show that micronutrient supplementation starting in pregnancy can correct important maternal nutrient deficiencies, but effects on child health outcomes are disappointing. Other interventions to improve diet during pregnancy have had little effect on maternal and newborn health outcomes. Comparatively few interventions have been made for preconception diet and lifestyle. Improvements in the measurement of pregnancy planning have quantified the degree of pregnancy planning and suggest that it is more common than previously recognised. Planning for pregnancy is associated with a mixed pattern of health behaviours before conception. We propose novel definitions of the preconception period relating to embryo development and actions at individual or population level. A sharper focus on intervention before conception is needed to improve maternal and child health and reduce the growing burden of non-communicable diseases. Alongside continued efforts to reduce smoking, alcohol consumption, and obesity in the population, we call for heightened awareness of preconception health, particularly regarding diet and nutrition. Importantly, health professionals should be alerted to ways of identifying women who are planning a pregnancy.

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This is the first in a **Series** of three papers about preconception health

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### Introduction

Health of women around the time of conception, once a neglected topic, is now a focus of increasing interest, reflected in several reports from national<sup>1,2</sup> and international health agencies.<sup>3,4</sup> This Series on preconception health makes the case for preconception health as a key determinant of pregnancy success and next generation health, drawing on evidence across clinical, biological, social, and policy fields. In this report, we follow three lines of enquiry. First, we review the evidence linking preconception health, particularly nutritional status, to pregnancy and birth outcomes, including analysis of the few cohort studies to have recruited women before pregnancy in low, middle, and high-income countries (appendix),<sup>5–8</sup> and we survey data on the nutrition of a nationally representative sample of women in a high-income country (the UK).<sup>9</sup> Using these data, we assess how well women are prepared, in health terms, for pregnancy. Second, we assess the extent to which intervention during pregnancy can mitigate the effect of preconception risk behaviours by reviewing systematic reviews of dietary and lifestyle interventions that started in pregnancy (appendix). Third, efforts to improve preconception health can be aimed at a population level, irrespective of any pregnancy planning, and can be targeted more specifically at women who are

### Key messages

- Health before conception is strongly linked to the outcome of pregnancy; life-course research pin-points the preconception period as crucial for health across generations.
- The preconception period should be redefined according to (1) the biological perspective—days to weeks before embryo development, (2) the individual perspective—a conscious intention to conceive, typically weeks to months before pregnancy occurs, and (3) the public health perspective—longer periods of months or years to address preconception risk factors, such as diet and obesity.
- Many women of reproductive age in low, middle, and high-income countries will not be prepared nutritionally for pregnancy.
- Micronutrient supplementation started in pregnancy can correct important maternal nutrient deficiencies, but it is not sufficient to fundamentally improve child health; dietary interventions in pregnancy can limit weight gain, but they are also insufficient in improving pregnancy outcomes.
- The preconception period presents a period of special opportunity for intervention; the rationale is based on lifecourse epidemiology, developmental (embryo) programming around the time of conception, maternal motivation, and disappointment with interventions starting in pregnancy.
- Improved measurement shows that pregnancy planning is more common than previously recognised in low, middle, and high-income countries.
- Identification of people contemplating pregnancy provides a window of opportunity to improve health before conception, while population-level initiatives to reduce the determinants of preconception risks, such as obesity and smoking, irrespective of pregnancy planning, are essential to improve outcomes.

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See Online for appendix

planning for pregnancy. We therefore review what is known about the extent of planning for pregnancy, including new data from a low-income country (Malawi) on how to measure pregnancy planning.<sup>10</sup> A host of social, medical, and environmental conditions can influence pregnancy outcomes, including genetic disorders, pre-existing physical and mental health conditions, teratogens, and domestic abuse to name a few. We recognise their importance, but review of these conditions is outside the scope of this paper. The importance of the father's preconception health is addressed in the second Series paper whereas the third Series paper reviews the targeting of intervention strategies to improve preconception health.

### Preconception risk factors in perspective

Life-course epidemiology provides a useful perspective for examination of preconception factors and their effects on maternal, fetal, and child health by consideration of the timing and duration of exposures and their potential long-term or latent effects.<sup>11</sup> The relationship of exposures to outcomes can be considered in terms of critical periods, sensitive periods, and cumulative effects. For example, 2–3 months before and after conception is a critical period for optimising gamete function and early placental development. In this period, folic acid supplementation, for example, can reduce the risk of neural tube defects by as much as 70%.<sup>12,13</sup> Other benefits of folic acid supplementation during periconception might include decreased risk of pre-eclampsia, miscarriage, low birthweight, small for gestational age birth, stillbirth, neonatal death, and autism in children.<sup>14–16</sup> The consequences of maternofetal iron deficiency also fit a critical period model in which repletion after an undetermined timepoint does not rectify structural impairments to developing brain structures. In experimental rodent models, dietary restriction of iron from the beginning of gestation can induce a 40–50% decrease in brain iron 10 days after birth<sup>17</sup> and preconception zinc deficiency compromises fetal and placental growth and neural tube closure.<sup>18</sup> Adolescence might represent a particularly sensitive period as unhealthy life-style behaviours—eg, smoking, poor diet, and eating disorders—often originate in the teenage years. These preconception risk factors can set patterns that have a cumulative effect on health into adulthood and for future generations, as shown by mounting evidence of the long-term effects of poor maternal nutrition and obesity for the child.<sup>19</sup>

### Maternal body composition, nutrition, and life-style factors

Substantial risks for maternal and child health are associated with mothers who are underweight or overweight. An analysis of adult body-mass index (BMI) in 200 countries from 1975 to 2014 with over 19 million participants found that the age-standardised global

proportion of underweight women (BMI <18.5 kg/m<sup>2</sup>) decreased from 15% to 10%; South Asia had the highest proportion of underweight women with an estimated 24% in 2014.<sup>20</sup> Although the proportion of women who are underweight has decreased, the proportion of obese women globally (BMI ≥30 kg/m<sup>2</sup>) has risen from 6% to 15% from 1975 to 2014.<sup>20</sup> In many low, middle, and high-income countries, up to 50% of women are overweight or obese when they become pregnant.<sup>21,22</sup> Obesity is associated with increased risk of most major adverse maternal and perinatal outcomes: the inability to conceive, complications of pregnancy (eg, pre-eclampsia, gestational diabetes) and delivery (eg, macrosomia), congenital anomalies, stillbirth, low birthweight, unsuccessful breastfeeding, and even maternal death.<sup>22–25</sup> The global increase in obesity among men (3–11% between 1975 and 2014)<sup>20</sup> is not irrelevant; paternal obesity has been linked to impaired fertility by affecting sperm quality and quantity<sup>26</sup> and is associated with increased chronic disease risk in offspring.<sup>27</sup> The cumulative effect of maternal and paternal obesity on the risk of obesity in future generations has been proposed by several studies<sup>28</sup> and causal pathways involving interaction between genetic, epigenetic, and environmental factors are emerging (see the second paper of this Series).

Although the benefits of preconception weight loss remain to be established through clinical trials, observational studies indicate the probable effects of preconception weight loss on pregnancy outcomes. In a population-based study<sup>29</sup> in Canada including 226 958 women (64% normal weight, 20% overweight, and 12% obese) with singleton pregnancies, a 10% lower preconception BMI was associated with clinically meaningful risk reduction in pre-eclampsia, gestational diabetes, preterm delivery, macrosomia, and stillbirth. Also, women undergoing bariatric surgery at least 2 years before conception have considerably lower risk of gestational diabetes, hypertensive disorders, and large-for-gestational-age neonates than women of similar BMI who had no bariatric surgery (although this is partially offset by a higher risk of neonates who were small for their gestational age).<sup>30–32</sup> Higher amounts of preconception physical activity were associated with lower risk of gestational diabetes (odds ratio [OR] 0.45, 95% CI 0.28–0.75 in seven cohorts, 34 929 pregnancies)<sup>33</sup> and pre-eclampsia (relative risk [RR] 0.65, 95% CI 0.47–0.89, in five studies, 10 317 pregnancies).<sup>34</sup> Walking at a brisk pace for 4 h or more per week before pregnancy was also associated with lower risk of gestational diabetes.<sup>35</sup> The success of a life-style intervention in reducing weight retention postpartum<sup>36</sup> shows that preparation for health in the next pregnancy can begin straight after the previous pregnancy.

Diet and nutrition before pregnancy might modify maternal and perinatal outcomes via effects on BMI (discussed previously) or other nutritional factors, including micronutrient deficiencies. WHO estimates

	LNRI*	Non-pregnant women of reproductive age (by age at survey)					p value†
		Total (N=509)	Age 18–25 years (n=156, 32%)	Age 26–30 years (n=79, 19%)	Age 31–35 years (n=102, 18%)	Age 36–42 years (n=172, 31%)	
<b>Dietary and lifestyle characteristics</b>							
BMI (SD)	..	26.0 (6.7)	25.1 (5.4)	25.3 (5.2)	26.7 (6.2)	27.7 (6.3)	0.1
Overweight or obese	..	49% (43–54)	41% (32–51)	40% (29–53)	49% (38–60)	62% (54–70)	0.004
Fruit and vegetable consumption (<5 serves per day)	..	77% (73–81)	91% (84–95)	70% (56–80)	70% (60–79)	72% (63–79)	0.003
Current smoker	..	26% (22–30)	33% (25–43)	22% (14–33)	20% (13–29)	24% (17–31)	0.2
High risk alcohol intake‡	..	22% (18–26)	28% (19–38)	16% (9–26)	12% (7–20)	25% (19–33)	0.03
<b>Percentage with diet-only intakes below LRNI</b>							
<b>Vitamins</b>							
Vitamin A	250 µg/day	7% (5–9)	12% (8–19)	5% (5–14)	2% (1–4)	5% (3–10)	0.002
Vitamin B12	1.0 µg/day	2% (1–3)	4% (2–8)	0	1% (0–3)	1% (0–6)	0.1
Folate	100 µg/day	4% (3–7)	8% (4–13)	1% (0–6)	0% (0–2)	5% (2–9)	0.003
Riboflavin	0.8 mg/day	14% (11–18)	22% (15–32)	11% (6–20)	9% (5–15)	11% (7–17)	0.03
<b>Minerals</b>							
Calcium	400 mg/day§	9% (7–12)	13% (9–20)	6% (3–14)	6% (3–12)	9% (5–14)	0.2
Iodine	70 µg/day	15% (11–19)	22% (15–31)	13% (7–23)	7% (4–14)	11% (7–18)	0.02
Iron	8.0 mg/day	30% (25–34)	38% (29–47)	26% (17–37)	23% (16–32)	27% (21–35)	0.09
Potassium	2000 mg/day	29% (25–34)	41% (32–51)	26% (17–38)	19% (12–28)	25% (19–33)	0.003
Selenium	40 µg/day	51% (47–56)	57% (47–66)	37% (26–49)	52% (42–62)	54% (46–61)	0.08
Zinc	4 mg/day	4% (3–7)	6% (3–11)	3% (1–9)	4% (2–9)	4% (2–9)	0.7

Data are % (95% CI). Means (SD) and percentages (95% CIs) are weighted to provide nationally representative results. Data are from the UK National diet and Nutrition Survey Rolling Program (NDNS RP) (2008/2012) years 1–4. § BMI=body-mass index. LNRI=lower reference nutrient intake. \*Micronutrient LRNI are those recommended for the UK in COMA, 1991. †p values for comparison across age groups. ‡Over six units of alcohol in one drinking occasion in the previous 7 days. §LRNI calcium is different for age 18 years (450 mg/day).

**Table 1: Dietary intake and lifestyle characteristics of women of reproductive age in the UK National Diet and Nutrition Survey**

that around 2 billion people are deficient in micro-nutrients, with women being at particular risk because of menstruation and the high metabolic demands of pregnancy.<sup>37</sup> Globally, maternal undernutrition and its consequences, including maternal vitamin A and zinc deficiency, fetal growth restriction, childhood stunting and wasting, together with suboptimal breastfeeding, is estimated to account for 3.1 million child deaths annually, and 45% of all child deaths in 2011.<sup>38</sup> A comprehensive review<sup>39</sup> of nutrition among adolescent girls and women of reproductive age in low-income and middle-income countries (LMICs) concluded that despite the reduction in prevalence of underweight mothers, dietary deficiencies (including iron, vitamin A, iodine, zinc, and calcium) remain prevalent.<sup>39</sup> A typical diet in high-income countries, characterised by a high intake of red meat, refined grains, refined sugars, and high-fat dairy, is also lacking in several important nutrients (including magnesium, iodine, calcium, and vitamin D).<sup>40,41</sup>

Our analysis in the UK shows that many women of reproductive age will not be nutritionally prepared for pregnancy, since they do not meet even the lower reference nutrient intake (RNI) amounts, which applies especially to young women and mineral intake (table 1). 77% of women aged 18–25 years had dietary intakes below

RNI daily recommendations for iodine and 96% of women of reproductive age had intake of iron and folate below daily recommendations for pregnancy (data not shown). Adequate folate concentration in pregnancy (red blood cell folate concentration above 906 nmol/L) for prevention of neural tube defects is hard to achieve through diet alone.<sup>43</sup> Folic acid supplements or fortified foods are effective alternatives. In a cohort of over 1.5 million women in China, folic acid supplementation 3 months before pregnancy (n=1182967) was associated with significantly lower risk of low birthweight (OR 0.74, 95% CI 0.71–0.78), miscarriage (OR 0.53, 0.52–0.54), stillbirth (OR 0.70, 0.64–0.77), and neonatal mortality (OR 0.70, 0.63–0.78) than in women who did not take folic acid before pregnancy (n=352009).<sup>16</sup> In several countries (including Canada, Chile, Oman, Jordan, Costa Rica, South Africa, USA) a decrease in neural tube defects has been observed following mandatory folic acid fortification, typically of wheat flour or cereal grain products, in the country or region.<sup>13</sup> A mild degree of iodine deficiency in pregnancy has been linked to lower intelligence quotients in offspring,<sup>40</sup> although the balance between the benefit and risk from iodine supplementation before or during pregnancy remains unclear.<sup>44</sup>

Cohort studies have suggested that dietary patterns up to 3 years before pregnancy, characterised by high

	All women*		Preconception characteristics of women who gave birth during the study†				p value‡
	Survey 1 (age 18–23 years [n=7047])	Survey 7 (age 37–42 years [n=6981])	Age at first birth				
			Age 18–25 years (n=544, 17.4%)	Age 26–30 years (n=1293, 41.5%)	Age 31–35 years (n=1024, 32.8%)	Age 36–42 years (n=257, 8.2%)	
Mean BMI (SD)	22.8 (4.2)	26.8 (6.4)	23.4 (4.8)	23.9 (4.4)	24.3 (4.5)	25.2 (5.6)	<0.0001
Overweight or obese	1340 (21.0%)	3223 (52.1%)	100 (27.2%)	342 (30.6%)	318 (34.0%)	94 (39.7%)	0.005
Fruit and vegetable consumption (<5 serves per day)	5861 (91.9%)	5659 (91.0%)	..	806 (91.9%)	533 (92.5%)	115 (86.5%)	0.13
Physical activity (<30 min/day)	1908 (37.7%)	2217 (43.3%)	249 (52.1%)	451 (38.8%)	318 (34.4%)	95 (41.1%)	<0.0001
Current smoker	1830 (27.9%)	685 (10.5%)	147 (28.0%)	227 (18.6%)	131 (13.4%)	35 (14.3%)	<0.0001
High risk alcohol intake§	348 (5.1%)	459 (6.9%)	17 (3.2%)	45 (3.6%)	49 (4.9%)	18 (7.1%)	0.008

Data are mean (SD) or n (%). The Australian Longitudinal Study on Women's Health (ALSWH) is a population-based study of women born in 1973–78 who have been surveyed every 3–4 years since 1996 (age 18–23 years). †BMI=body-mass index. ‡All women including women who have not given birth. †Preconception characteristics shown in the table were reported at the survey before the first pregnancy (up to 3 years). §p values for comparison across age groups. §Three or more standard drinks (10 g alcohol) on 5 or more days per week.

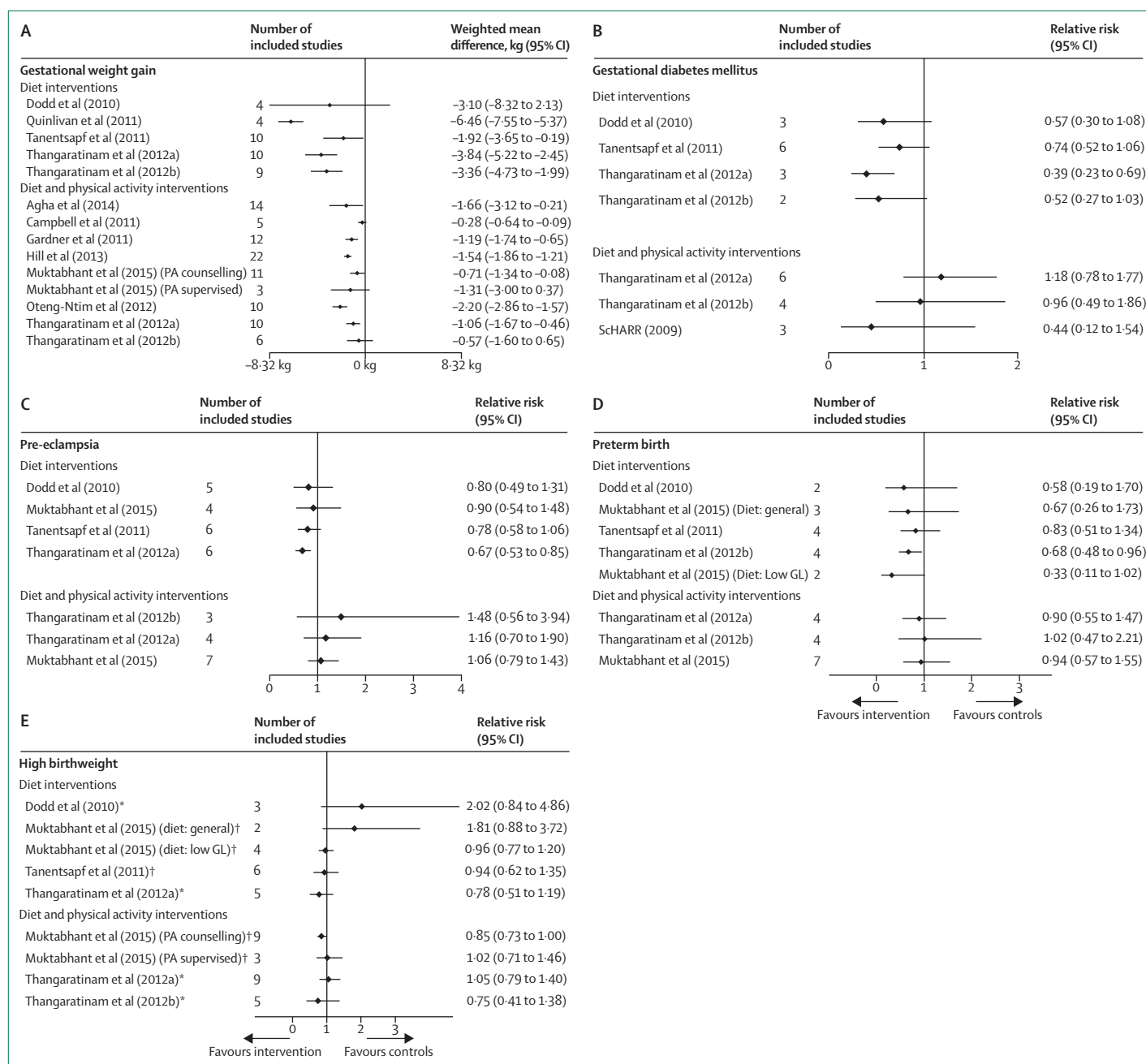
**Table 2: Dietary intake and lifestyle characteristics of women of reproductive age in the Australian Longitudinal Study on Women's Health**

intake of fruit, vegetables, legumes, nuts, and fish, and low intake of red and processed meat, are associated with reduced risk of gestational diabetes,<sup>45–48</sup> hypertensive disorders of pregnancy,<sup>49–51</sup> and preterm birth.<sup>52</sup> Since few people will plan a pregnancy 3 years in advance, this highlights the need for population-level interventions. In the UK and Australia, more than nine of ten young women reported consuming fewer than five fruit and vegetable portions daily (table 1 and table 2). As the diet of a young child is determined largely by the mother, this aspect has important implications for future child health.

Evidence for the effect of maternal smoking on health outcomes (including pregnancy loss, intrauterine growth restriction, and low birthweight) comes largely from studies initiated during, rather than before, pregnancy.<sup>53,54</sup> Although no trials have been published that show reduction in smoking before conception improves these outcomes, indirect evidence of the effect at population level comes from introduction of smoke-free legislation in different countries, which has been associated with substantial reductions in preterm births (–10.4%, 95% CI –18.8 to –2.0, from four cohort studies with 1366862 pregnancies).<sup>55</sup> Maternal alcohol consumption can result in a range of fetal alcohol spectrum disorders that result in physical, behavioural, and learning difficulties.<sup>56</sup> Although discussion of alcohol consumption of any amount being safe during pregnancy is controversial, there is widespread public awareness that avoidance of both smoking and alcohol during pregnancy is important for health. Caffeine consumption during pregnancy has been associated with a reduction in birthweight of a similar proportion to that caused by alcohol, with a significant trend for a greater reduction in birthweight with higher caffeine intake.<sup>57</sup> This relationship was consistent across all three trimesters, suggesting that cutting back on caffeine before

conception could be beneficial. However, as with all preconception risk factors the scope for action at the individual level is limited by unplanned pregnancy, which in turn highlights the importance of cost-effective public health action (eg, minimum pricing of alcohol and smoke-free legislation) to reduce risk behaviours in the whole population, with additional benefit for women whose pregnancies are unplanned.

Since women are more likely to engage with health services once they are pregnant than beforehand, we considered whether birth outcomes can be improved through intervention during pregnancy to redress poor dietary patterns that were present before conception. In high-income countries, the obesity epidemic has dominated efforts to improve pregnancy outcomes. Our overview identified 20 systematic reviews of antenatal interventions with a dietary component, six confined to overweight or obese women (figure 1; appendix). These reviews, mainly of trials from high-income countries, provide high quality consistent evidence that dietary interventions (with or without exercise) during pregnancy can reduce gestational weight gain; however, an individual patient data (IPD) meta-analysis<sup>58</sup> of 36 randomised controlled trials with 12526 women of mixed BMI found an average reduction in gestational weight gain of only 0.7 kg (95% CI –0.92 to –0.48). Some reviews<sup>59–61</sup> also reported that dietary intervention during pregnancy, with increased consumption of fibre, protein, fruit, and vegetables, led to reduction in dietary fat and energy intake. High quality trials published after these systematic reviews show similar effects on dietary behaviours. The LIMIT trial<sup>62</sup> in Australia showed that a diet and physical activity intervention delivered to overweight and obese women increased their consumption of fruit, vegetables, legumes, fibre, and micronutrients, and reduced their energy intake



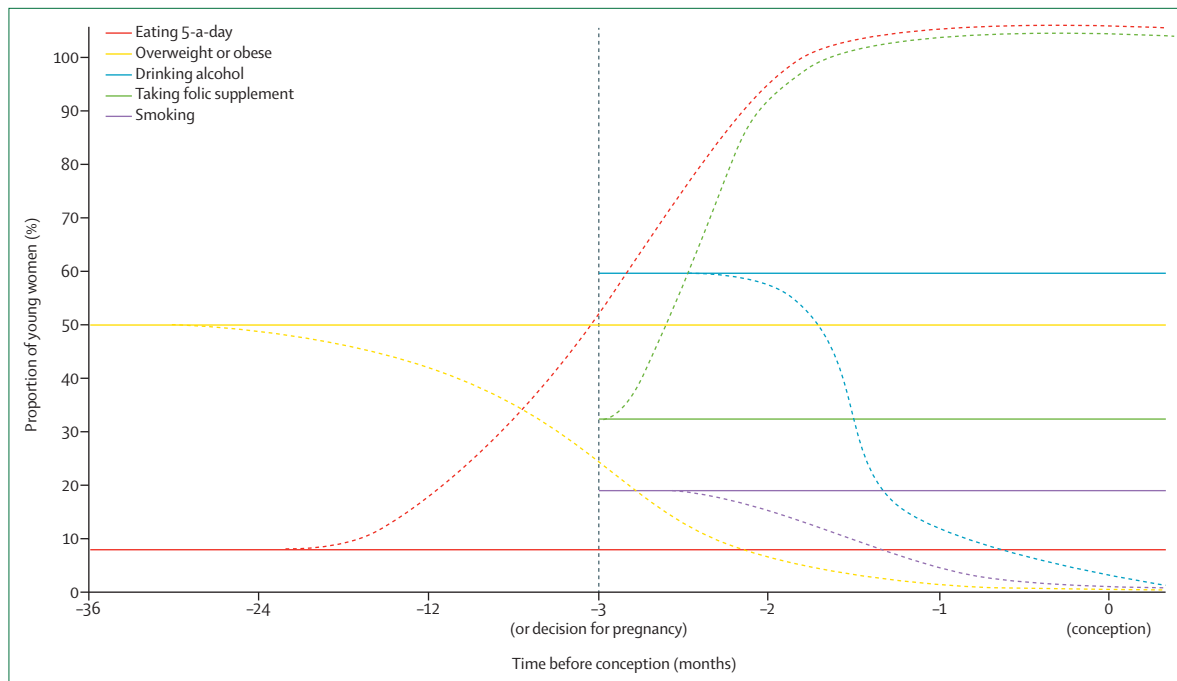
**Figure 1: Meta-analyses of the effect of dietary behaviour change interventions (with or without physical activity elements) in pregnant women**

Effect estimates of dietary behaviour change interventions (with or without physical activity components) in pregnant women. Each estimate is from a systematic review with meta-analysis. A summary estimate has not been generated because some intervention studies are included in more than one meta-analysis. GL=glycaemic load. PA=Physical activity.

sourced from saturated fat. The UPBEAT trial<sup>63</sup> in the UK also showed a reduction in the consumption of processed foods and snack foods among obese women after diet and physical activity intervention. Both trials showed dietary behaviour change at 28 weeks and 36 weeks gestation, and the UPBEAT trial reported reduced infant adiposity 6 months postpartum.<sup>64</sup> Although improved health behaviours and weight gain restriction should not be ignored due to the potential

longer-term benefits, these interventions have had no significant effect on common adverse pregnancy outcomes, including gestational diabetes, pre-eclampsia, large for gestational age, or preterm births, in women of mixed BMI or in obese women (figure 1); however, the IPD meta-analysis<sup>58</sup> reported a 9% reduction in caesarean section in women of all BMIs (OR 0.91, 95% CI 0.83–0.99). Because attempts to improve outcomes in obese women with the use of





**Figure 2: Challenges of improving preconception health**

Typical levels of each preconception behaviour in young women in high-income countries (solid lines) and optimal behaviours before conception (dashed lines).

insulin-sensitising drugs have also been unsuccessful,<sup>65,66</sup> attention is increasingly focused on the improvement of diet and prevention or reverse of obesity in the preconception period. Given the substantial time needed to reach a healthy weight, early intervention at a population level is vital to reduce obesity-related outcomes in pregnancy.

In LMICs, antenatal dietary interventions have generally focused on the problem of calorific and nutrient deprivation. A single trial<sup>67</sup> in Mumbai found that women who ate a daily snack containing leafy green vegetables, fruit, and milk before and during pregnancy had reduced prevalence of gestational diabetes (7.3% in the intervention group compared with 12.4% in the control group). Several studies<sup>68,69</sup> have examined the effect of antenatal multiple micronutrient supplementation on a range of health outcomes in high-risk populations in LMICs, but the findings are disappointing. Systematic reviews<sup>70,71</sup> of trials of multiple micronutrient supplementation during pregnancy, including over 88 000 women, have consistently shown modest effects on increasing birthweight when compared with control groups receiving iron and folic supplementation only; however, these reviews have shown no improvement in childhood survival, growth, body composition, blood pressure, or respiratory or cognitive outcomes when comparing the intervention and control groups.

Distinctions between high-income countries and LMICs have become blurred because many LMICs have had a demographic and obstetric transition<sup>72</sup> coupled with

high-income lifestyles that foster obesity, whereas populations in high-income countries already dominated by obesity commonly have poor nutrition and specific micronutrient deficiencies that go unrecognised until pregnancy. Iron deficiency anaemia, for example, is the most common deficiency globally affecting around 2 billion people and 30–50% of pregnant women,<sup>73</sup> including young women in high-income countries.<sup>74</sup> Although iron supplementation in pregnancy reduces iron deficiency anaemia and improves haemoglobin concentrations at term, other benefits seem limited to a reduction in low birthweight.<sup>75</sup> Vitamin D deficiency, increasingly common among pregnant women in high-income countries, can lead to bone mineral deficiency in the developing child and has been implicated in gestational diabetes, pre-eclampsia, low birthweight, and preterm birth but with less certainty.<sup>76</sup> A subsequent trial<sup>77</sup> of cholecalciferol supplementation during pregnancy showed that most women became vitamin D replete, but infant bone mineral content was not increased overall.<sup>77</sup> Further studies, such as the SPRING trial<sup>78</sup> of cholecalciferol supplementation during pregnancy, are awaited.

In summary, interventions to improve diet in pregnancy lead to modest reductions in gestational weight gain, but (with few exceptions)<sup>64</sup> they have not improved important maternal or newborn health outcomes. Micronutrient supplementation starting in pregnancy can correct important maternal nutrient deficiencies with modest effects on increasing birthweight, but no subsequent improvement in child health outcomes. Explanations might include starting interventions after early critical

	ALSWH cohort			SWS cohort			
	Using contraception or no male sexual partner (n=6256, 77%)*	Trying for pregnancy (n=536, 7%)*	Not using contraception (n=1285, 15.9%)*	Not planning pregnancy and not pregnant (n=9932, 80%)	Unintended pregnancy (n=301, 2%)	Intended pregnancy (n=584, 5%)	Planning a pregnancy but not pregnant (n=1623, 13%)
Smoking (yes vs no)	1.00 (ref)	0.84 (0.76–0.93)	1.09 (1.01–1.18)	1.00 (ref)	1.15 (1.00–1.33)	0.72 (0.61–0.83)	0.89 (0.82–0.96)
Alcohol consumption (yes vs no)	1.00 (ref)	0.70 (0.56–0.87)	0.91 (0.77–1.09)	1.00 (ref)	1.01 (0.98–1.05)	1.03 (1.01–1.06)	0.99 (0.97–1.00)
Fruit and vegetable consumption (<5 vs ≥5 serves per day)	1.00 (ref)	1.01 (0.99–1.03)	0.97 (0.96–0.99)	1.00 (ref)	1.05 (0.94–1.17)	0.94 (0.85–1.03)	0.97 (0.92–1.03)
Physical activity (<30 vs ≥30 min/day)	1.00 (ref)	1.06 (1.01–1.11)	1.14 (1.09–1.18)	..	..	..	..
Body-mass index (≥25 vs <25 kg/m <sup>2</sup> )	1.00 (ref)	1.05 (1.00–1.10)	1.16 (1.12–1.21)	1.00 (ref)	0.98 (0.85–1.13)	1.10 (1.00–1.21)	1.13 (1.07–1.20)
Caffeine consumption (>300 mg caffeine per day)	..	..	..	1.00 (ref)	1.15 (1.01–1.31)	0.89 (0.79–0.99)	0.94 (0.88–1.01)

Data are relative risk (95% CI) using Poisson regression with robust variance, adjusted for maternal age, level of educational attainment and parity. The Australian Longitudinal Study on Women's Health (ALSWH) is a population-based study of women born in 1973–78 who have been surveyed every 3–4 years since 1996 (age 18–23 years).<sup>3</sup> The Southampton Women's Survey (SWS) recruited 12 583 non-pregnant women (20–34 years) between 1998 and 2002.<sup>6,7</sup> When not pregnant, women in the SWS were asked whether they anticipated trying for a baby within the following year. Data about pregnancy within a year were then used to define four groups of women: not planning pregnancy and not pregnant, unintended pregnancy, intended pregnancy, and planning a pregnancy but not pregnant. \*N was taken from Survey 3, which was the first survey where women were asked about pregnancy intention.

**Table 3: Relative risk of diet and lifestyle behaviours according to pregnancy intention in the ALSWH and the SWS.**

periods of fetal development or inadequate implementation, dose, or adherence within this timeframe to achieve substantial biological influence. In keeping with this hypothesis, one of the few supplementation trials<sup>79</sup> starting before conception found no effect on birthweight unless it was provided at least 3 months before conception and to women who were not underweight. To explore adherence to preconception supplementation, we analysed data from the Pune Rural Intervention in Young Adolescents (PRIYA)<sup>8</sup> study. PRIYA is a randomised community-based trial of cyanocobalamin (vitamin B) supplementation given to men and to young women before pregnancy. Adherence, assessed by pill counts, in this non-pregnant trial population was consistently high at around 80%. Although every effort should be made to correct micronutrient deficiencies in women once pregnant, there is a growing consensus that the greatest gain will be achieved through a life-course approach or continuum of improved nutrition in children, adolescents, and young women contemplating pregnancy (see the third paper of this Series).

### Defining the preconception period

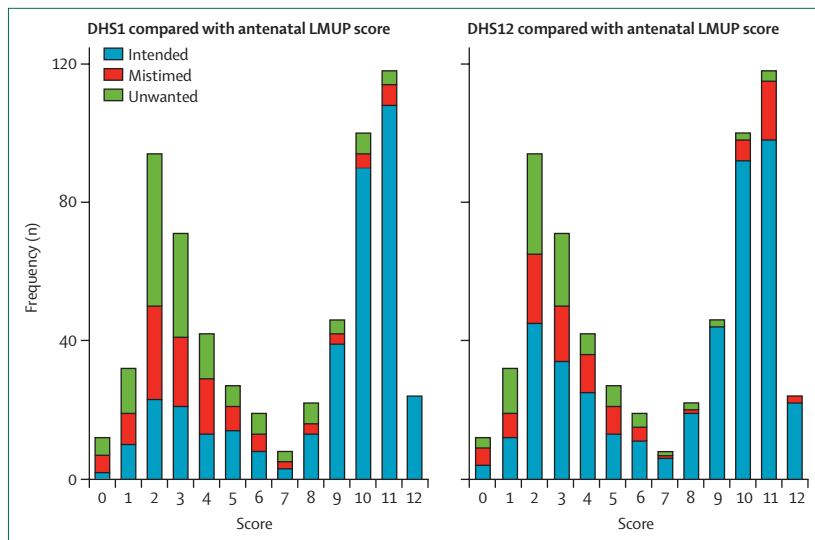
The preconception period is often defined as the 3 months before conception, probably because this is the average time to conception for fertile couples.<sup>80,81</sup> However, a time period before conception can only be identified after a woman has become pregnant. Some definitions avoid this problem, for instance “a minimum of one year prior to the initiation of any unprotected sexual intercourse that could possibly result in a pregnancy”,<sup>82</sup> but cannot be applied practically.

We therefore propose three new definitions or perspectives that relate to embryo development or point to interventions at an individual or population level. From a biological perspective, a critical period spans the weeks around conception when gametes mature,

fertilisation occurs, and the developing embryo forms. These events are the most sensitive to environmental factors, such as the availability of macronutrients and micronutrients, or exposure to smoking, alcohol, drugs, or other teratogens. For prevention of neural tube defects, a minimum of 4–6 weeks folic acid supplementation is required to reach adequate concentrations before neurulation begins 3 weeks after conception.<sup>13</sup>

In relation to an individual, the preconception period starts whenever a woman or couple decides they want to have a baby because the time to conception is unknown. Since about a third of fertile couples having regular sex without contraception will conceive within one month,<sup>80,81</sup> optimising nutrition, including folic acid supplementation, should coincide with the decision to become pregnant. The preconception period might reflect the time required by individuals to achieve desired health outcomes in preparation for pregnancy, such as 6 or more months to attain a healthy BMI. Maternal motivation to improve health at this stage can be strong. In a pilot study,<sup>83</sup> 65% of obese women attending a family planning clinic to have their contraceptive implant or uterine device removed to become pregnant were willing to improve their preconception health by deferring removal of contraception for 6 months while they followed an intensive weight loss plan. From a public health perspective, the preconception period can relate to a sensitive phase in the lifecourse, such as adolescence, when health behaviours affecting diet, exercise, and obesity, along with smoking and drinking, become established before the first pregnancy.

These perspectives can be combined into a conceptual framework of the preconception period (figure 2). Benefits that can be achieved fairly rapidly, such as adequate folate concentrations, are indicated at 3 months before conception or whenever an individual first intends to become pregnant. Conversely, substantial weight loss takes months or years to achieve, whereas



**Figure 3: Comparison of women's antenatal LMUP score**  
Responses to the DHS question completed at least one month (DHS1) and at least 12 months (DHS12) after birth. DHS=Demographic and Health Survey. LMUP=London Measure of Unplanned Pregnancy.

the length of time to establish new dietary patterns is highly variable. Together, these findings point to the scale of the challenge in improving preconception health, with vast room for improvement particularly in nutritional status and the need for intervention strategies at the population level to support action at the individual level (figure 2).

### Pregnancy planning for preconception health

Compelling evidence for early developmental programming, along with the disappointment from micronutrient supplements and dietary interventions in pregnancy, is shifting attention to the challenge of intervening before conception. Awareness of the importance of health before pregnancy, some level of pregnancy planning, and uptake of interventions before conception are distinct but related requirements for improving preconception health. Qualitative research<sup>84</sup> has identified three groups: women with high levels of pregnancy planning who take up interventions, women who plan but describe themselves as having poor awareness of preconception actions, and women for whom the preconception period has little meaning. Different preconception care approaches are likely to be needed for each group.

Our analysis of new data from two preconception cohort studies<sup>5-7</sup> shows mixed health behaviours reported in relation to pregnancy planning. Women trying for pregnancy when compared with those who were using contraception or not planning to become pregnant within the next year, were less likely to report smoking or drinking alcohol, reported lower amounts of caffeine consumption, had a higher BMI, reported lower amounts of physical activity, but had similar fruit and vegetable intake (table 3). These associations were robust to adjustment for maternal educational attainment, age, and parity. In the

Southampton Women's Study,<sup>6,7</sup> education had a significant effect on the association between pregnancy status and fruit and vegetable intake before pregnancy. Women educated beyond 16 years of age who were intentionally pregnant were more likely to report eating five portions of fruit and vegetables a day (65%) than those who did not become pregnant and were not planning to (57%); whereas no differences were seen between the same pregnancy intention groups in women who were educated up to 16 years of age only (46% in the intended pregnancy group vs 46% in the group with no pregnancy). This result suggests that more educated women might improve their diet once a decision has been made for pregnancy but less educated women do not, highlighting the effect of disadvantage on the ability of women to change their behaviours.

Although some studies<sup>85,86</sup> suggest that awareness of preconception health and care is low, pregnancy planning appears relatively common, indicating a missed and unexploited opportunity for intervention.<sup>87,88</sup> Pregnancy planning has usually been estimated in surveys, either by a single question (eg, Did you plan your pregnancy?) or by more detailed questioning to probe (variously) intentions, reactions to pregnancy, timing of pregnancy, and family size desires. The most influential survey the US National Survey of Family Growth<sup>87</sup> categorises pregnancy as intended, mistimed, or unwanted—terms now widely adopted and included in the worldwide Demographic and Health Surveys (DHS).<sup>89</sup> A combination of all survey information has estimated that 60% of the 213 million pregnancies worldwide in 2012 were intended.<sup>88</sup>

In the past 20 years, the growing complexity of family formation patterns worldwide, awareness of the need to accommodate women's ambivalence, and the contribution of psychometric methods to measurement development have indicated the need for a more sophisticated measurement of pregnancy planning. The London Measure of Unplanned Pregnancy (LMUP)<sup>90</sup> has been widely used, with nine validated language versions across seven countries and more in progress.<sup>91-97</sup> Six questions produce a score (0–12), with higher scores indicating a more planned pregnancy. Use of the LMUP has shown that pregnancy planning at various levels of intensity is globally common particularly among pregnancies leading to birth.<sup>10,85,91-96,98,99</sup> By providing a finer gradation of pregnancy planning the LMUP is more reliable than previous tools, opening the door to improved prediction of health outcomes associated with pregnancy intention. Despite the availability of this superior tool, the global standard remains the DHS, in which women are asked, "When you got pregnant, did you want to get pregnant at the time?" Women who respond yes are categorised as intended pregnancies, those who respond no are asked "Did you want to have a baby later on or did you not want any (more) children?" An answer of later defines the pregnancy as mistimed and no more as unwanted.



In a cohort study of pregnant women in Malawi,<sup>10</sup> we compared the LMUP scores reported during pregnancy with the DHS categorisation reported up to 16 months after. 45% of women scored ten or more on the LMUP antenatally, showing that pregnancy planning is a relevant concept in a rural, low-income setting. The estimated prevalence of intended pregnancies was higher with the use of the postnatal DHS question (69%, 95% CI 65–73) than the antenatal LMUP (40%, 95% CI 36–44) in the same group of 623 women at 1-year follow-up (figure 3). Previous studies have found that the same birth is reported as more intended as time passes,<sup>100</sup> but these are the first data to document that this shift occurs within the first year postnatally. This result suggests a need for antenatal surveillance of pregnancy intention that could improve accuracy in assessing the scale of unplanned pregnancies and provide an opportunity to act antenatally to mitigate the adverse effects for the mother and child. A measure, such as the LMUP, would also be sensitive enough to monitor changes in the rate of unplanned pregnancy over time and across population subgroups. Most initiatives to reduce unplanned pregnancy, such as Family Planning 2020,<sup>101</sup> rely on uptake of contraception as a proxy measure of effect, whereas the LMUP could provide a direct measure of the desired outcome.

The frequency of pregnancy planning identified by the LMUP in low, middle, and high-income countries suggests considerable scope for intervention before pregnancy; the challenge is to identify women who are planning a pregnancy. Asking a woman of reproductive age, “How many (more) children would you like to have and when?”, is being promoted,<sup>102</sup> but the question is likely to have limited predictive validity. More nuanced measures that capture ambivalent intentions are required—eg, the Desire to Avoid Pregnancy (DAP) scale that is in development.<sup>103</sup> Robust measures, such as the LMUP and DAP, are opening up a largely unexplored area of research into how people plan and prepare for pregnancy, the associated effects on health, and how health professionals can identify individuals planning a pregnancy.

## Summary

A consistent picture is emerging of the importance of maternal health before conception and the key risk factors for adverse birth outcomes, one that blurs previous distinctions between low, middle, and high-income countries. A life-course model of critical periods, sensitive periods, and cumulative effects fits well with data linking preconception exposures to birth outcomes and risk of disease in later life. The adverse consequences of poor nutrition combined with obesity, rife in women of reproductive age, extend across generations. Dietary interventions starting in pregnancy can reduce weight gain and adiposity in obese women but have little effect on pregnancy outcomes, whereas the few benefits of multiple micronutrient supplementation in pregnancy

appear to occur too late to fundamentally improve child health outcomes.

Novel definitions of the preconception period that relate to embryo development or to opportunities for intervention might be useful. Action to improve conditions around the crucial time of conception requires a more systematic approach to identify women planning a pregnancy, and efforts are underway. A healthy weight can take longer to achieve than dietary changes and should ideally become established during the sensitive period of adolescence when most women will not be planning pregnancy; this intervention requires a population-level approach. Generally, however, a degree of pregnancy planning is common in LMICs and high-income countries, offering considerable scope for intervention before pregnancy. Pregnancy planning is associated with an inconsistent pattern of reported health behaviours potentially due to low awareness of the importance of health before pregnancy and possible actions to take. To have a substantial impact on preconception health, a dual strategy is needed that improves nutritional status across the life-course and particularly during reproductive ages, while targeting all women who are thinking of conceiving. How this strategy might be achieved is considered in the third paper of this Series, which focuses on preconception care.

### Contributors

DJAMS reviewed reports on preconception risk factors. NH reviewed reports on interventions in pregnancy. Further data analysis was provided by SRC, JHa, GDM, KK, CY, and JHu. All authors contributed to successive drafts and approved the final version.

### Declaration of interests

JB and MB report receiving research funding from Danone Nutricia Early Life Nutrition. JB is evaluating the effect of changes within Iceland Foods Ltd stores on the diets of women. No research funding is received from Iceland Foods Ltd. All other authors declare no competing interests.

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### References

- 1 Davies SC. Annual report of the chief medical officer, 2014. The health of the 51%: women. London: Department of Health, 2015: 167.
- 2 Johnson KA, Floyd RL, Humphrey JR, et al. Action plan for the national initiative on Preconception Health and Health Care (PCHHC)—a report of the PCHHC steering committee. Atlanta, GA: Centers for Disease Control and Prevention, 2012–14: 1–49.
- 3 Hanson MA, Bardsley A, Dr-Regil LM, et al. The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: “Think Nutrition First”. *Int J Gynaecol Obstet* 2015; **131** (suppl 4): S213–53.

- 4 WHO. Preconception care: Maximizing the gains for maternal and child health. Policy brief. Geneva: World Health Organization, 2013: 1–8.
- 5 Lee C, Dobson AJ, Brown WJ, et al. Cohort profile: the Australian Longitudinal Study on Women's Health. *Int J Epidemiol* 2005; **34**: 987–91.
- 6 Crozier SR, Robinson SM, Borland, et al. Do women change their health behaviours in pregnancy? Findings from the Southampton Women's Survey. *Paediatr Perinat Epidemiol* 2009; **23**: 446–53.
- 7 Inskip HM, Godfrey KM, Robinson SM, et al. Cohort profile: the Southampton Women's Survey. *Int J Epidemiol* 2006; **35**: 42–48.
- 8 Kumaran K, Yajnik P, Lubree H, et al. The Pune Rural Intervention in Young Adolescents (PRIYA) study: design and methods of a randomised controlled trial. *BMC Nutrition* 2017; **3**: 41.
- 9 Bates B, Lennox A, Prentice A, et al. National diet and nutrition survey: results from years 1, 2, 3, and 4 (combined) of the rolling programme (2008/2009–2011/2012). Executive summary. London: Public Health England, 2014.
- 10 Hall JA, Barrett, Phiri T, et al. Prevalence and determinants of unintended pregnancy in Mchinji District, Malawi; using a conceptual hierarchy to inform analysis. *PLoS One* 2016; **11**: e0165621.
- 11 Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol* 2002; **31**: 285–93.
- 12 De-Régil LM, Peña-Rosas JP, Fernández-Gaxiola AC, Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst Rev* 2015; **12**: CD007950.
- 13 Mastroiacovo P, Leoncini E. More folic acid, the five questions: why, who, when, how much, and how. *Biofactors* 2011; **37**: 272–79.
- 14 Hodgetts VA, Morris RK, Francis A, Gardosi J, Ismail KM. Effectiveness of folic acid supplementation in pregnancy on reducing the risk of small-for-gestational age neonates: a population study, systematic review and meta-analysis. *BJOG* 2015; **122**: 478–90.
- 15 Gao Y, Sheng C, Xie RH, et al. New perspective on impact of folic acid supplementation during pregnancy on neurodevelopment/autism in the offspring children—a systematic review. *PLoS One* 2016; **11**: e0165626.
- 16 He Y, Pan A, Hu FB, Ma X. Folic acid supplementation, birth defects, and adverse pregnancy outcomes in Chinese women: a population-based mega-cohort study. *Lancet* 2016; **388**: S91.
- 17 Rao R, Tkac I, Townsend EL, Gruetter R, Georgieff MK. Perinatal iron deficiency alters the neurochemical profile of the developing rat hippocampus. *J Nutr* 2003; **133**: 3215–21.
- 18 Tian X, Anthony K, Neuberger T, Diaz FJ. Preconception zinc deficiency disrupts postimplantation fetal and placental development in mice. *Biol Reprod* 2014; **90**: 83.
- 19 Hanson M, Barker M, Dodd JM, et al. Interventions to prevent maternal obesity before conception, during pregnancy, and post partum. *Lancet Diabetes Endocrinol* 2017; **5**: 65–76.
- 20 NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet* 2016; **387**: 1513–30.
- 21 Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; **384**: 766–81.
- 22 Poston L, Caleyachetty R, Cnattingius S, et al. Preconceptional and maternal obesity: epidemiology and health consequences. *Lancet Diabetes Endocrinol* 2016; **4**: 1025–36.
- 23 Gesink Law DC, Maclehorse RF, Longnecker MP. Obesity and time to pregnancy. *Hum Reprod* 2007; **22**: 414–20.
- 24 Marchi J, Berg M, Dencker A, Olander EK, Begley C. Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. *Obes Rev* 2015; **16**: 621–38.
- 25 Turcksin R, Bel S, Galjaard S, Devlieger R. Maternal obesity and breastfeeding intention, initiation, intensity and duration: a systematic review. *Matern Child Nutr* 2014; **10**: 166–83.
- 26 Kort HI, Massey JB, Elsner CW, et al. Impact of body mass index values on sperm quantity and quality. *J Androl* 2006; **27**: 450–52.
- 27 Kaati G, Bygren LO, Edvinsson S. Cardiovascular and diabetes mortality determined by nutrition during parents' and grandparents' slow growth period. *Eur J Hum Genet* 2002; **10**: 682–88.
- 28 Godfrey KM, Reynolds RM, Prescott SL, et al. Influence of maternal obesity on the long-term health of offspring. *Lancet Diabetes Endocrinol* 2017; **5**: 53–64.
- 29 Schummers L, Hutcheon JA, Bodnar LM, Lieberman E, Himes KP. Risk of adverse pregnancy outcomes by prepregnancy body mass index: a population-based study to inform prepregnancy weight loss counseling. *Obstet Gynecol* 2015; **125**: 133–43.
- 30 Yi XY, Li QF, Zhang J, Wang ZH. A meta-analysis of maternal and fetal outcomes of pregnancy after bariatric surgery. *Int J Gynaecol Obstet* 2015; **130**: 3–9.
- 31 Galazis N, Docheva N, Simillis C, Nicolaides KH. Maternal and neonatal outcomes in women undergoing bariatric surgery: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2014; **181**: 45–53.
- 32 Johansson K, Cnattingius S, Näslund I, et al. Outcomes of pregnancy after bariatric surgery. *N Engl J Med* 2015; **372**: 814–24.
- 33 Tobias DK, Zhang C, van Dam RM, Bowers K, Hu FB. Physical activity before and during pregnancy and risk of gestational diabetes mellitus: a meta-analysis. *Diabetes Care* 2011; **34**: 223–29.
- 34 Aune D, Saugstad OD, Henriksen T, Tonstad S. Physical activity and the risk of preeclampsia: a systematic review and meta-analysis. *Epidemiology* 2014; **25**: 331–43.
- 35 Zhang C, Solomon CG, Manson JE, Hu FB. A prospective study of pregravid physical activity and sedentary behaviors in relation to the risk for gestational diabetes mellitus. *Arch Intern Med* 2006; **166**: 543–48.
- 36 Phelan S, Hagobian T, Brannen A, et al. Effect of an internet-based program on weight loss for low-income postpartum women: a randomized clinical trial. *JAMA* 2017; **317**: 2381–91.
- 37 WHO, Food and Agricultural Organization of the United Nations. Guidelines on food fortification with micronutrients. Geneva: World Health Organization, 2006.
- 38 Black RE, Victoria CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* 2013; **382**: 427–51.
- 39 US AID, Strengthening Partnerships, Results, and Innovations in Nutrition Globally (SPRING). Nutrition of adolescent girls and women of reproductive age in low- and middle-income countries: current context and scientific basis for moving forward. Mar 16–17, 2015. Arlington, VA: SPRING, 2015.
- 40 Bath SC, Steer CD, Golding J, Emmett P, Rayman MP. Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Lancet* 2013; **382**: 331–37.
- 41 Cordain L, Eaton SB, Sebastian A, et al. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr* 2005; **81**: 341–54.
- 42 Public Health England. Government dietary recommendations. Government recommendations for energy and nutrients for males and females aged 1–18 years and 19+ years. London: Public Health England, 2016.
- 43 Cuskelly GJ, McNulty H, Scott JM. Effect of increasing dietary folate on red-cell folate: implications for prevention of neural tube defects. *Lancet* 1996; **347**: 657–59.
- 44 Harding KB, Peña-Rosas JP, Webster AC, et al. Iodine supplementation for women during the preconception, pregnancy and postpartum period. *Cochrane Database Syst Rev* 2017; **3**: CD011761.
- 45 Bao W, Bowers K, Tobias DK, et al. Prepregnancy low-carbohydrate dietary pattern and risk of gestational diabetes mellitus: a prospective cohort study. *Am J Clin Nutr* 2014; **99**: 1378–84.
- 46 Tobias DK, Zhang C, Chavarro J, et al. Prepregnancy adherence to dietary patterns and lower risk of gestational diabetes mellitus. *Am J Clin Nutr* 2012; **96**: 289–95.
- 47 Zhang C, Schulze MB, Solomon CG, Hu FB. A prospective study of dietary patterns, meat intake and the risk of gestational diabetes mellitus. *Diabetologia* 2006; **49**: 2604–13.
- 48 Schoenaker DA, Soedamah-Muthu SS, Callaway LK, Mishra GD. Pre-pregnancy dietary patterns and risk of gestational diabetes mellitus: results from an Australian population-based prospective cohort study. *Diabetologia* 2015; **58**: 2726–35.

- 49 Schoenaker DA, Soedamah-Muthu SS, Mishra GD. Quantifying the mediating effect of body mass index on the relation between a Mediterranean diet and development of maternal pregnancy complications: the Australian Longitudinal Study on Women's Health. *Am J Clin Nutr* 2016; **104**: 638–45.
- 50 Schoenaker DA, Soedamah-Muthu SS, Callaway LK, Mishra GD. Prepregnancy dietary patterns and risk of developing hypertensive disorders of pregnancy: results from the Australian Longitudinal Study on Women's Health. *Am J Clin Nutr* 2015; **102**: 94–101.
- 51 Gresham E, Collins CE, Mishra GD, Byles JE, Hure AJ. Diet quality before or during pregnancy and the relationship with pregnancy and birth outcomes: the Australian Longitudinal Study on Women's Health. *Public Health Nutr* 2016; **19**: 2975–83.
- 52 Grieger JA, Grzeskowiak LE, Clifton VL. Preconception dietary patterns in human pregnancies are associated with preterm delivery. *J Nutr* 2014; **144**: 1075–80.
- 53 National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. The health consequences of smoking—50 years of progress: a report of the surgeon general. Atlanta, GA: Centers for Disease Control and Prevention (US), 2014.
- 54 Reeves S, Bernstein I. Effects of maternal tobacco-smoke exposure on fetal growth and neonatal size. *Expert Rev Obstet Gynecol* 2008; **3**: 719–30.
- 55 Been JV, Nurmatov UB, Cox B, Nawrot TS, van Schayck CP. Effect of smoke-free legislation on perinatal and child health: a systematic review and meta-analysis. *Lancet* 2014; **383**: 1549–60.
- 56 British Medical Association (BMA). Alcohol and pregnancy: preventing and managing fetal alcohol spectrum disorders. June, 2007 (updated February, 2016). London: BMA, 2016.
- 57 CARE Study Group. Maternal caffeine intake during pregnancy and risk of fetal growth restriction: a large prospective observational study. *BMJ* 2008; **337**: a2332.
- 58 International Weight Management in Pregnancy Collaborative Group. Effect of diet and physical activity based interventions in pregnancy on gestational weight gain and pregnancy outcomes: meta-analysis of individual participant data from randomised trials. *BMJ* 2017; **358**: j3119.
- 59 Gardner B, Wardle J, Poston L, Croker H. Changing diet and physical activity to reduce gestational weight gain: a meta-analysis. *Obesity Rev* 2011; **12**: e602–20.
- 60 Campbell F, Messina J, Johnson M, Guillaume L, Madan J, Goyder E. Systematic review of dietary and/or physical activity interventions for weight management in pregnancy. Sheffield: The University of Sheffield School of Health and Related Research Public Health Collaborating Centre, 2010.
- 61 Muktabant B, Lawrie TA, Lumbiganon P, Laopaiboon M. Diet or exercise, or both, for preventing excessive weight gain in pregnancy. *Cochrane Database Syst Rev* 2015; **6**: CD007145.
- 62 Dodd JM, Cramp C, Sui Z, et al. The effects of antenatal dietary and lifestyle advice for women who are overweight or obese on maternal diet and physical activity: the LIMIT randomised trial. *BMC Med* 2014; **12**: 161–80.
- 63 Flynn AC, Seed PT, Patel N, et al. Dietary patterns in obese pregnant women; influence of a behavioral intervention of diet and physical activity in the UPBEAT randomized controlled trial. *Int J Behav Nutr Phys Act* 2016; **13**: 124.
- 64 Patel N, Godfrey KM, Pasupathy D, et al. Infant adiposity following a randomised controlled trial of a behavioural intervention in obese pregnancy. *Int J Obes* 2017; **41**: 1018–26.
- 65 Chiswick C, Reynolds RM, Denison F, et al. Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWaR): a randomised, double-blind, placebo-controlled trial. *Lancet Diabetes Endocrinol* 2015; **3**: 778–86.
- 66 Syngelaki A, Corapcioglu D. Metformin versus placebo in obese pregnant women without diabetes mellitus. *N Engl J Med* 2016; **374**: 434–43.
- 67 Sahariah SA, Potdar RD, Gandhi M, et al. A daily snack containing leafy green vegetables, fruit, and milk before and during pregnancy prevents gestational diabetes in a randomized, controlled trial in Mumbai, India. *J Nutr* 2016; **146**: 1453S–60S.
- 68 Dean SV, Lassi ZS, Imam AM, Bhutta ZA. Preconception care: nutritional risks and interventions. *Reprod Health* 2014; **11** (suppl 3): S3.
- 69 Ramakrishnan U, Grant F, Goldenberg T, Zongrone A, Martorell R. Effect of women's nutrition before and during early pregnancy on maternal and infant outcomes: a systematic review. *Paediatr Perinat Epidemiol* 2012; **26** (suppl 1): 285–301.
- 70 Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2015; **4**: CD004905.
- 71 Devakumar D, Fall CH, Sachdev HS, et al. Maternal antenatal multiple micronutrient supplementation for long-term health benefits in children: a systematic review and meta-analysis. *BMC Med* 2016; **14**: 90.
- 72 Graham W, Woodd S, Byass P, et al. Diversity and divergence: the dynamic burden of poor maternal health. *Lancet* 2016; **388**: 2164–75.
- 73 Stoltzfus R. Defining iron-deficiency anemia in public health terms: a time for reflection. *J Nutr* 2001; **131**: 565S–67S.
- 74 Baker PN, Wheeler SJ, Sanders TA, et al. A prospective study of micronutrient status in adolescent pregnancy. *Am J Clin Nutr* 2009; **89**: 1114–24.
- 75 Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, Dowswell T. Daily oral iron supplementation during pregnancy. *Cochrane Database Syst Rev* 2015; **7**: CD004736.
- 76 De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2016; **1**: CD008873.
- 77 Cooper C, Harvey NC, Bishop NJ, et al. Maternal gestational vitamin D supplementation and offspring bone health (MAVIDOS): a multicentre, double-blind, randomised placebo-controlled trial. *Lancet Diabetes Endocrinol* 2016; **4**: 393–402.
- 78 Baird J, Barker M, Harvey NC, et al. Southampton Pregnancy Intervention for the Next Generation (SPRING): protocol for a randomised controlled trial. *Trials* 2016; **17**: 493.
- 79 Potdar RD, Sahariah SA, Gandhi M, et al. Improving women's diet quality preconceptionally and during gestation: effects on birth weight and prevalence of low birth weight—a randomized controlled efficacy trial in India (Mumbai Maternal Nutrition Project). *Am J Clin Nutr* 2014; **100**: 1257–68.
- 80 Potter RG, Parker MP. Predicting the time required to conceive. *Population Studies* 1964; **18**: 99–116.
- 81 Gnoth C, Godehardt D, Godehardt E, Frank-Herrmann P, Freundl G. Time to pregnancy: results of the German prospective study and impact on the management of infertility. *Hum Reprod* 2003; **18**: 1959–66.
- 82 Dean S, Rudan I, Althabe F, et al. Setting research priorities for preconception care in low- and middle-income countries: aiming to reduce maternal and child mortality and morbidity. *PLoS Med* 2013; **10**: e1001508.
- 83 Brackenridge L, Finer N, Batterham RL, et al. Pre-pregnancy weight loss in obese women requesting removal of their intra uterine contraceptive device in order to conceive: a pilot study of full meal replacement. *Clin Obes* (in press).
- 84 Barrett G, Shawe J, Howden B, et al. Why do women invest in pre-pregnancy health and care? A qualitative investigation with women attending maternity services. *BMC Pregnancy Childbirth* 2015; **15**: 236.
- 85 Stephenson J, Patel D, Barrett G, et al. How do women prepare for pregnancy? Preconception experiences of women attending antenatal services and views of health professionals. *PLoS One* 2014; **9**: e103085.
- 86 Mitchell EW, Levis DM, Prue CE. Preconception health: awareness, planning, and communication among a sample of US men and women. *Matern Child Health J* 2012; **16**: 31–39.
- 87 Mosher WD, Jones J, Abma JC. Intended and unintended births in the United States: 1982–2010. *Natl Health Stat Report* 2012; **55**: 1–28.
- 88 Sedgh G, Singh S, Hussain R. Intended and unintended pregnancies worldwide in 2012 and recent trends. *Stud Fam Plann* 2014; **45**: 301–14.
- 89 The Demographic and Health Surveys Programme. Model women's questionnaire. Section 2 reproduction. Questions 405 and 406. <https://dhsprogram.com/pubs/pdf/DHSQ7/DHS7-Womans-QRE-EN-07Jun2017-DHSQ7.pdf> (accessed March 14, 2018).
- 90 Barrett G, Smith SC, Wellings K. Conceptualisation, development, and evaluation of a measure of unplanned pregnancy. *J Epidemiol Community Health* 2004; **58**: 426–33.

- 91 Rocca CH, Krishnan S, Barrett G, Wilson M. Measuring pregnancy planning: an assessment of the London Measure of Unplanned Pregnancy among urban, south Indian women. *Demogr Res* 2010; **23**: 293–334.
- 92 Morof D, Steinauer J, Haider S, Liu S, Darney P, Barrett G. Evaluation of the London Measure of Unplanned Pregnancy in a United States population of women. *PLoS One* 2012; **7**: e35381.
- 93 Hall J, Barrett G, Mbwana N, Copas A, Malata A, Stephenson J. Understanding pregnancy planning in a low-income country setting: validation of the London measure of unplanned pregnancy in Malawi. *BMC Pregnancy Childbirth* 2013; **13**: 200.
- 94 Roshanaei S, Shaghghi A, Jafarabadi MA, Kousha A. Measuring unintended pregnancies in postpartum Iranian women: validation of the London Measure of Unplanned Pregnancy. *East Mediterr Health J* 2015; **21**: 572–78.
- 95 Borges AL, Barrett G, Dos Santos OA, Nascimento Nde C, Cavalhieri FB, Fujimori E. Evaluation of the psychometric properties of the London Measure of Unplanned Pregnancy in Brazilian Portuguese. *BMC Pregnancy Childbirth* 2016; **16**: 244.
- 96 Habib MA, Raynes-Greenow C, Nausheen S, et al. Prevalence and determinants of unintended pregnancies amongst women attending antenatal clinics in Pakistan. *BMC Pregnancy Childbirth* 2017; **17**: 156.
- 97 Almaghaslah E, Rochat R, Farhat G. Validation of a pregnancy planning measure for Arabic-speaking women. *PLoS One* 2017; **12**: e0185433.
- 98 Wellings K, Jones KG, Mercer CH, et al. The prevalence of unplanned pregnancy and associated factors in Britain: findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). *Lancet* 2013; **382**: 1807–16.
- 99 Goossens J, van Den Branden Y, van der Sluys L, et al. The prevalence of unplanned pregnancy ending in birth, associated factors, and health outcomes. *Hum Reprod* 2016; **31**: 2821–33.
- 100 Bankole A, Westoff CF. The consistency and validity of reproductive attitudes: evidence from Morocco. *J Biosoc Sci* 1998; **30**: 439–55.
- 101 FP2020 Partnership in Action 2012-2013, Family Planning 2020 Core Indicators. 2013. <http://www.familyplanning2020.org/microsite/measurement-hub/whatwemeasure> (accessed March 14, 2018).
- 102 Centers for Disease Control and Prevention. Preconception health and reproductive life plan. <https://www.hhs.gov/opa/title-x-family-planning/preventive-services/preconception-health-and-reproductive-life-plan/index.html> (accessed March 14, 2018).
- 103 Rocca C, Gould H, Barar R, Ralph L, Rowlan B, Foster D. Operationalizing pregnancy preferences: development of a new instrument to measure strength of desire to avoid pregnancy. *Contraception* 2016; **94**: 423.