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

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Abstract (312 words)

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 high, low and middle 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 and lower income countries have become less distinct, with typical diets falling far short of nutritional recommendations in both settings and especially among adolescents.

Numerous 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 impact on maternal and newborn health outcomes. There have been comparatively few attempts at preconception diet and lifestyle intervention. Improvements in the measurement of pregnancy planning have quantified the degree of pregnancy planning and suggest that this 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 to action 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 disease. Alongside continued efforts to reduce smoking, alcohol 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.

Key messages

Health before conception is strongly linked to the outcome of pregnancy; life course research pin-points the preconception period as critical for health across generations.

The preconception period should be redefined according to: a) the biological perspective - days to weeks before embryo development b) the individual perspective - a conscious intention to conceive, typically weeks to months before pregnancy occurs c) 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 HIC as well as LMIC, will not be prepared nutritionally for pregnancy.

Micronutrient supplementation starting in pregnancy can correct important maternal nutrient deficiencies and dietary interventions in pregnancy can limit weight gain, but they are 'too little, too late' to fundamentally improve child health and pregnancy outcomes respectively.

The preconception period presents a period of special opportunity for intervention; the rationale is based on life course epidemiology, developmental (embryo) programming around the time of conception, maternal motivation and disappointment with interventions starting in pregnancy.

Better measurement shows that pregnancy planning is more common than previously recognised, in both LMIC and HIC.

Identifying 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.

Introduction (text 4512 words)

Health around the time of conception, once a neglected topic, is now a focus of increasing interest, reflected in numerous recent reports from national [1, 2] and international health agencies, [3, 4]. Three linked articles in this issue make the case for preconception health as a key determinant of pregnancy success and next generation health, drawing on evidence across clinical, biological and social/policy fields. In this paper, 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 in low- and middle- income countries (LMIC) and high-income countries (HIC) to have recruited women *before* pregnancy(web appendix) [5] [6, 7] [8] and survey data on the nutrition of a nationally representative sample of women in a HIC [[9]. Using these data, we assess how well women are prepared, in health terms, for pregnancy. Second, since preconception care is largely neglected, we assess the extent to which intervention *during* pregnancy can mitigate the impact of preconception risk behaviours by reviewing systematic reviews of dietary and lifestyle interventions that started in pregnancy (web appendix). Third, efforts to improve preconception health can be aimed at a population level, irrespective of any pregnancy planning, and / or targeted more specifically at women who are planning for pregnancy. We therefore review what is known about the extent of planning for pregnancy, including new data from a low income country on how to measure pregnancy planning[10].   A host of social, medical and environmental conditions can influence pregnancy outcomes, including genetic disorders, pre-existing physical and mental health conditions, teratogenic agents 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 fathers' preconception health is addressed in the second paper in this series and targeting of intervention strategies to improve preconception health is considered in a third paper .

Preconception risk factors in perspective

Life course epidemiology provides a useful perspective for examining preconception factors and their effects on maternal, fetal, and child health by considering the timing and duration of exposures and their potential long term or latent impacts [11]. The relationship of exposures to outcomes can be considered in terms of critical periods, sensitive periods, and cumulative effects. For example, the period around conception (two to three months before and after) 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% [12, 13]. Other benefits of folic acid supplementation during periconception may include decreased risk of pre-eclampsia, miscarriage, low birth weight, small for gestational age, stillbirth, neonatal death and autism in children [14-16]. The consequences of materno-fetal iron deficiency also fit a critical period model in which repletion after an undetermined time-point fails to rectify structural impairments to developing brain structures. In experimental animal models, dietary restriction of iron from the beginning of gestation can induce a 40–50% decrease in brain iron 10 days after birth [17] and preconception zinc deficiency compromises fetal and placental growth and neural tube closure [18]. Adolescence may represent a particularly *sensitive period* as unhealthy lifestyle behaviours - such as 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 impact of poor maternal nutrition and obesity for the child [19].

Maternal Body Composition, Nutrition and Lifestyle factors

i. *Body mass index (BMI)*. Both maternal underweight and overweight are associated with substantial risks for maternal and child health. An analysis of adult BMI in 200 countries from 1975 to 2014 with over 19 million participants found that the age-standardised global prevalence of underweight in women (BMI <18.5 kg/m^2) decreased from 15% to 10%; South Asia had the highest rates with an estimated 24% of women underweight in 2014 [20]. While underweight has decreased, the global prevalence of obesity (BMI ≥30 kg/m^2) has risen from 6% to 15% in women [20]; in many HIC and LMIC, up to 50% are overweight or obese when they become pregnant [21, 22]. Obesity is associated with increased risk of most major adverse maternal and perinatal outcomes, from inability to conceive to complications of pregnancy (pre-eclampsia, gestational diabetes) and delivery (macrosomia), congenital anomalies, stillbirth, and low birth weight, unsuccessful breastfeeding and even maternal death [22-25]. The global increase in obesity among men, from 3% to 11% between 1975 and 2014[20] is not irrelevant; paternal obesity has been linked to impaired fertility by affecting sperm quality and quantity [26] and is associated with increased chronic disease risk in offspring [27]. The cumulative effect of both maternal and paternal obesity on the risk of obesity in future generations has been proposed by numerous studies [28] and causal pathways involving interaction between genetic, epigenetic and environmental factors are emerging (paper 2).

Although the benefits of preconception weight loss remain to be established through clinical trials, observational studies indicate the likely effects of preconception weight loss on pregnancy outcomes. In a population-based study in Canada with 226,958 singleton pregnancies, a preconception weight loss of 10% was associated with clinically meaningful risk reduction in pre-eclampsia, gestational diabetes, preterm delivery, macrosomia, and stillbirth [29]. Women undergoing bariatric surgery at least two years before conception had considerably lower risk or odds of gestational diabetes, hypertensive disorders and large-for-gestational age neonates compared with women of similar BMI who had no bariatric surgery, although this was partially offset by more small-for-gestational-age births [30-32]. Higher levels of preconception physical activity were associated with lower risk of gestational diabetes (OR 0.45, 95% CI 0.28, 0.75 in seven cohorts, 34,929 pregnancies) [33] and pre-eclampsia (RR 0.65, 95% CI 0.47, 0.89, in five studies, 10,317 pregnancies) [34]. Walking at a brisk pace for four hours or more per week before pregnancy was also associated with lower risk of gestational diabetes [35]. The recent success of a lifestyle intervention in reducing weight retention post-partum [[36] shows that preparation for health in the next pregnancy can begin straight after the last pregnancy.

ii. *Preconception diet and nutrition*. Diet and nutrition before pregnancy may modify maternal and perinatal outcomes via effects on BMI (as above) or other nutritional factors, including micronutrient deficiencies. WHO estimates that around two billion people are deficient in micronutrients, with women being at particular risk because of menstruation and the high metabolic demands of pregnancy [37]. Globally, maternal undernutrition and its consequences, including fetal growth restriction, stunting, wasting, vitamin A and/or zinc deficiency, together with sub-optimal breastfeeding, is estimated to account for 3.1 million child deaths annually, or 45% of all child deaths in 2011 [38]. A recent comprehensive review of nutrition among adolescent girls and women of reproductive age in LMIC concluded that, despite the reduction in prevalence of underweight, dietary deficiencies, including iron, vitamin A, iodine, zinc, and calcium remain prevalent [39]. A typical diet in HIC, characterised by 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 [40, 41].

Our analysis in the UK shows that many women of reproductive age will not be nutritionally prepared for pregnancy, even at lower reference nutrient intake (LRNI) levels; this applies especially to young women and mineral intake (**Table 1**). Seventy-seven percent of women aged 18-25 years had dietary intakes below RNI daily recommendations for iodine and 96% of women of reproductive age had intakes below iron and folate recommendations for pregnancy (data not shown). Achieving adequate folate levels in pregnancy (red blood cell folate concentration above 906 nmol/L) for prevention of neural tube defects may be hard to achieve through diet alone[42]. Folic acid supplements or fortified foods are effective alternatives. In a cohort of over 1.5 million women in China, folic acid supplementation three months before pregnancy 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) compared to women who did not take folic acid before pregnancy[16]. In several countries (Canada, Chile, Oman, South Africa, USA), a decrease in neural tube defects has been observed following folic acid fortification ([13]. A mild degree of iodine deficiency in pregnancy has been linked to lower intelligence quotients in offspring [40], although the balance of benefit and risk from iodine supplementation before or during pregnancy remains unclear [43].

Cohort studies have suggested that dietary patterns up to three years before pregnancy, characterised by high intake of fruit, vegetables, legumes, nuts and fish and low intake of red and processed meat, are associated with reduced risk of gestational diabetes [44-47], hypertensive disorders of pregnancy [48-50] and preterm birth [51]. Since few people will plan a pregnancy three years in advance, this highlights the need for population-level interventions. In the UK and Australia, more than 9 out of 10 women aged 18-25 years reported consuming fewer than five fruit and vegetable portions daily (Table 1). As the diet of the young child is determined largely by the mother, this has important implications for future child health.

iii. *Smoking, alcohol and caffeine.* Evidence for the impact of maternal smoking on health outcomes, (including pregnancy loss, intrauterine growth restriction and low birth weight) comes largely from studies initiated during, rather than before, pregnancy [52, 53]. While there are no published trials showing that reducing smoking before conception improves these outcomes, indirect evidence of impact 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, -2.0; from four cohort studies with 1,366,862 pregnancies) [54]. Maternal alcohol consumption can result in a range of fetal alcohol spectrum disorders resulting in physical, behavioural and learning difficulties. [55] While discussion of any 'safe level' of alcohol is controversial, there is considerable 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 birth weight of a similar size to that caused by alcohol, and a significant trend for greater reduction in birth weight with higher caffeine intake [56]]. 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 individual level is limited by unplanned pregnancy; this in turn highlights the importance of cost-effective public health action (e.g. minimum pricing of alcohol and smoke-free legislation) to reduce risk behaviours in the whole population, with additional benefit for those whose pregnancies are unplanned.

i.v. Lifestyle interventions and micronutrient supplementation during pregnancy. Since women are more likely to engage with health services once they are pregnant than beforehand, we considered whether birth outcomes can be improved by intervening in pregnancy to redress poor dietary patterns that were present before conception. In HIC, 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 2**, detail in web appendix). These reviews, mainly of trials from HIC, provide high quality consistent evidence that diet (with or without exercise) during pregnancy can reduce gestational weight gain, although a recent individual patient data (IPD) meta-analysis of 36 randomised controlled trials with 12,526 women of mixed BMI found an average reduction in gestational weight gain of only 0.7kg (95% CI -0.92 to -0.48) [57]. Some reviews also reported that dietary intervention during pregnancy led to reduction in dietary fat and energy intake, with increased consumption of fibre, protein, fruit and vegetables [58-60]. High quality trials published after these systematic reviews show similar effects on dietary behaviours. The LIMIT trial in Australia showed increased consumption of fruit, vegetables, legumes, fibre, and micronutrients, and a reduction in energy from saturated fat sources among overweight or obese women [61]. The UPBEAT trial in the UK also showed a reduction in consumption of processed foods and snack foods among obese women

[62]. Both trials showed dietary behaviour change at 28 and 36 weeks gestation and UPBEAT reported reduced infant adiposity 6 months postpartum [63]. While improved health behaviours and weight gain restriction should not be ignored as there may be longer term benefits, these interventions have had no significant impact 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 2), although the IPD meta-analysis reported a 9% reduction in caesarean section in women of all BMIs (OR 0.91, 95% CI 0.83 to 0.99) [57]. As attempts to improve outcomes in obese women with insulin sensitising drugs have also failed [64, 65] attention is increasingly focused on improving diet and preventing or reversing 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 LMIC, antenatal dietary interventions have generally focused on the problem of calorific and nutrient deprivation. A single trial in Mumbai found that a daily snack containing leafy green vegetables, fruit and milk before and during pregnancy reduced the prevalence of gestational diabetes (to 7.3% in the intervention group compared with 12.4% in the control group) [[66]]. Numerous studies have examined the impact of antenatal multiple micronutrient supplementation on a range of health outcomes in high-risk populations in LMIC [67, 68] but the findings are disappointing. Systematic reviews of trials of multiple micronutrient supplementation during pregnancy, including over 88,000 women, have consistently shown modest effects on increasing birthweight, but no improvement in childhood survival, growth, body composition, blood pressure, respiratory or cognitive outcomes, compared with control groups receiving iron and folic acid supplementation only[69, 70].

Distinctions between HIC and LMIC have become blurred as many LMIC experience a demographic and obstetric transition [71] coupled with 'western' lifestyles that foster obesity, while HIC populations already dominated by obesity commonly have poor nutrition and specific micronutrient deficiencies that go unrecognized until pregnancy. Iron deficiency anaemia is a case in point: it is the most common deficiency globally affecting around 2 billion people and 30-50% of pregnant women [72], including young women in HIC [73]. Although iron supplementation in pregnancy reduces iron deficiency anaemia and improves haemoglobin levels at term, other benefits seem limited to a reduction in low birthweight [74]. Vitamin D deficiency, increasingly common among pregnant women in HIC, can lead to bone mineral deficiency in the developing child, and has been implicated, but with less certainty, in gestational diabetes, pre-eclampsia, low birthweight and preterm birth [75]. A subsequent trial of vitamin D supplementation during pregnancy showed that most women became vitamin D replete, but infant bone mineral content was not increased overall [76]. Further studies, such as the SPRING trial of vitamin D supplementation during pregnancy [77], are awaited.

In summary, interventions to improve diet in pregnancy lead to modest reduction in gestational weight gain, but, with few exceptions [63], 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. Likely explanations include starting after early critical periods of fetal programming, and / or inadequate implementation, dose or adherence within this time frame to achieve significant biological influence. In keeping with this hypothesis, one of the few supplementation trials starting before conception found no effect on birth weight unless provided at least 3 months before conception and to women who were not underweight ([78]). To explore adherence to preconception supplementation, we analysed data from the Pune Rural Intervention in Young Adolescents (PRIYA) [8] study. PRIYA is a randomised community-based trial of vitamin B12 supplementation *before* pregnancy in young women and men. Adherence, assessed by pill counts, in this non-pregnant trial population was consistently high at around 80%. While every effort should be made to correct micronutrient deficiencies in a women once pregnant, there is a growing consensus that the greatest gain will be achieved through a lifecourse approach or continuum of improved nutrition in children, adolescents and young women contemplating pregnancy (paper 3).

Defining the preconception period

The preconception period is often defined as the three months before conception, possibly because this is the average time to conception for fertile couples [79, 80] . 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" [81], but they lack practical application.

We therefore propose three new definitions or perspectives that relate to embryo development or point to action at an individual or population level. From a **biological** perspective, there is a critical period spanning the weeks around conception when gametes mature, fertilisation occurs and the developing embryo forms. These are the events most sensitive to environmental factors such as the availability of macro- and micronutrients or exposure to smoking, alcohol, drugs or other teratogens (Paper 2). For prevention of neural tube defects, a minimum of 4-6 weeks folic acid supplementation is required to reach adequate levels before neurulation begins three weeks after conception[13].

In relation to **individual** action, the preconception period starts whenever a woman or couple decides they want to have a baby, as the time to conception is unknown. Since about a third of fertile couples having regular sex without contraception will conceive within one month, [79, 80] optimising nutrition, including folic acid supplementation, should coincide with the decision to become pregnant. The preconception period may reflect the time required by individuals to achieve desired health outcomes in preparation for pregnancy, such as six or more months to attain a healthy BMI. Maternal motivation to improve health at this stage can be strong. In a recent pilot study, 54% of obese women attending a family planning clinic to have their contraceptive implant or uterine device removed in order 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 (Stephenson, unpublished data). From a **public health** perspective**,** the preconception period can relate to a sensitive phase in the life course, such as adolescence, when health behaviours affecting diet, exercise and obesity, along with smoking and drinking, become established before the first pregnancy(paper 3).

These perspectives can be combined into a conceptual framework of the preconception period (**figure 1).** Benefits that can be achieved fairly rapidly, such as adequate folate levels, are indicated at 3 months before conception or whenever an individual first intends to become pregnant. By contrast, substantial weight loss takes months or years to achieve, while 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 1).**

Pregnancy planning for preconception health

Compelling evidence for early developmental programming (paper 2) and disappointment with micronutrient supplements and dietary interventions in pregnancy are 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 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 [82]. Different preconception care approaches are likely to be needed for each group (paper 3).

Our analysis of new data from two preconception cohort studies shows mixed health behaviours reported in relation to pregnancy planning. Women 'trying for pregnancy' were less likely to report smoking or drinking alcohol, and reported lower levels of caffeine consumption, but had a higher BMI, and reported lower levels of physical activity, and similar fruit and vegetable intake compared with women who were using contraception or not planning to become pregnant within the next year (**table 2).** These associations were robust to adjustment for maternal level of educational attainment, age and parity. In the Southampton Womens Study, education had a significant impact on the association between pregnancy status and fruit and vegetable intake before pregnancy. Women educated beyond the age of 16 years with an intended pregnancy were more likely to report eating five portions of fruit and vegetables than those who did not become pregnant and were not planning to (65% vs 57%); whereas no differences between these pregnancy intention groups were seen in women only educated to 16 years of age (46% vs 46%). This suggests that more educated women may improve their diet once a decision has been made for pregnancy, but less educated women do not, demonstrating the effect of disadvantage on women's ability to change their behaviours.

Although numerous studies suggest that awareness of preconception health and care is low [83, 84], 'pregnancy planning' appears relatively common, indicating a missed and unexploited opportunity for intervention. [85, 86] Pregnancy planning has usually been estimated in surveys, either by a single question (e.g. "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[85] categorises pregnancy as intended, mistimed or unwanted, terms now widely adopted and included in the worldwide Demographic and Health Surveys[87]. A combination of all survey information has estimated that 60% of the 213million pregnancies worldwide in 2012 were intended [86].

In the last 20 years, the growing complexity of family formation patterns worldwide, awareness of the need to accommodate women's ambivalence, and the contribution of psychometric methodology to measurement development have indicated the need for a more sophisticated measurement of pregnancy planning. The London Measure of Unplanned Pregnancy (LMUP) has been widely used[88], with nine validated language versions across seven countries, and more in progress [89-95]. 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[10, 83, 89-94, 96, 97] In 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 this, the global standard used in LMIC remains the single Demographic and Health Survey question, asked up to five years after birth: "At the time you became pregnant, did you want to become pregnant then, did you want to wait until later, or did you not want to have any (more) children at all?" with responses categorised, respectively, as "intended", "mistimed" and "unwanted" pregnancy.

In a cohort study of pregnant women in Malawi [10], we compared the LMUP reported during pregnancy with the DHS question up to 16 months afterwards. Forty-five percent of women scored 10 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 using the postnatal DHS question (69%, 95%CI 65% to 73%) than the antenatal LMUP (40%, 95%CI 36% to 44%) in the same group of 623 women followed up at one year (Figure 3). Previous studies have found higher reported intention over time for births[98] but these are the first data to document that this shift occurs within the first year postnatally. This suggests a need for antenatal surveillance of pregnancy intention which would 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 sub-groups.

Most initiatives to reduce unplanned pregnancy, such as Family Planning 2020 [99], rely on uptake of contraception as a proxy measure of impact, whereas the LMUP could provide a direct measure of the desired outcome.

The frequency of pregnancy planning identified by the LMUP in both HIC and LMIC suggests considerable scope for intervention before pregnancy; the challenge is to identify women who are planning a pregnancy. Simply asking women of reproductive age "*Do you plan to have any (more) children at any time in your future?"* is being promoted [100], but is likely to lack predictive validity; more nuanced measures that capture ambivalent intentions are required e.g. the 'Desire to Avoid Pregnancy' (DAP) Scale, currently in development [101]. 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 health impacts 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 HIC and LMIC. A lifecourse model of critical periods, sensitive periods and cumulative effects fits well with current 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 with little impact on pregnancy outcomes, while multiple micronutrient supplementation in pregnancy appears 'too little, too late' to fundamentally improve child health outcomes.

Novel definitions of the preconception period that relate to embryo development (paper 2) or to opportunities for intervention may be useful. Action to improve conditions around the critical time of conception requires a more systematic approach to identify women planning a pregnancy; efforts to do this 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 requires a population-level approach. In general, though, a degree of pregnancy planning is common, in both LMIC and HIC, offering considerable scope for intervention before pregnancy. Currently, pregnancy planning is associated with an inconsistent pattern of reported health behaviours; low awareness of the importance of health before pregnancy and possible actions to take may contribute to this. To make a significant impact on preconception health, we need a dual strategy that improves nutritional status across the lifecourse and particularly during reproductive ages, while targeting all women who are thinking of conceiving. How this might be achieved is considered in the third paper of the series.

Acknowledgements

The idea for this series was conceived by Judith Stephenson and developed during a four day symposium, led by Mary Barker and Judith Stephenson and funded by The Rank Prize Funds, on 'Developmental Programming for Human Disease: Preconception Nutrition and Lifelong Health' in Grasmere, UK, February 2016.

We thank the Australian Government Department of Health for funding ALSWH and Richard Hockey for analysing the data from ALSWH. LP is supported by Tommy's Charity, UK and the NIHR Biomedical Research Centre at King's College London and Guys and St.Thomas' NHS Foundation Trust.

Author contributions

Danielle Schoenaker conducted the review of preconception risk factors and Nicola Heslehurst the overview of systematic reviews of interventions in pregnancy. Further data analysis was provided by Sarah Crozier (SWS), Jayne Hutchinson (UK NDNS), Gita Mishra (ALSWH), Kalyanaraman Kumaran and Chittaranjan Yajnik (PRIYA) and Jennifer Hall (DHS and LMUP). All authors contributed to successive drafts of the manuscript and approved the final version.

Conflict of Interest

Janis Baird and a group of colleagues at the MRC Lifecourse Epidemiology Unit, University of Southampton, have received funding from Danone Nutricia Early Life Nutrition for a specific research study which aims to improve the nutrition and Vitamin D status of pregnant women.

Legends to Tables and Figures.

Table 1.

Dietary intake and lifestyle characteristics of women of reproductive age in the Australian Longitudinal Study of Women's Health and the UK National Diet and Nutrition Survey.

Table 2. Relative risk of diet and lifestyle behaviours according to pregnancy intention in the Australian Longitudinal Study of Women's Health and the Southampton Women's Survey.

Figure 1.

A conceptual diagram of the challenge of improving preconception health.

Figure 2:

Forest plots of reported meta-analyses in systematic reviews of the effect of dietary behaviour change interventions (with or without physical activity elements) in pregnant women on gestational weight gain, pre-term birth, gestational diabetes and preeclampsia.

A summary estimate has not been generated because some intervention studies are included in more than one meta-analysis.

Figure 3:

Comparison of women's antenatal LMUP score (0-12) with their response to the DHS question completed at least one (DHS1) and at least 12 (DHS12) months after birth

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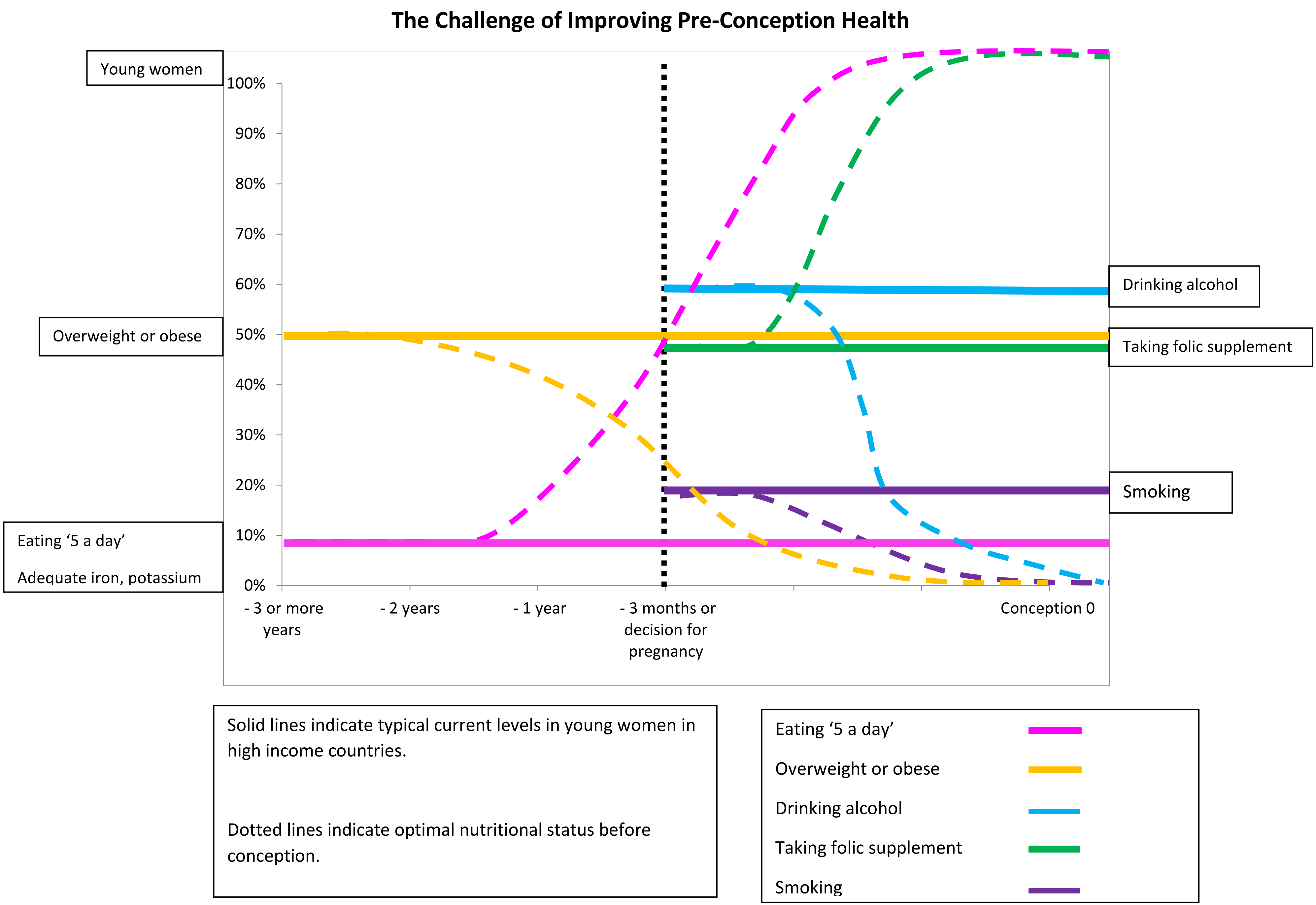
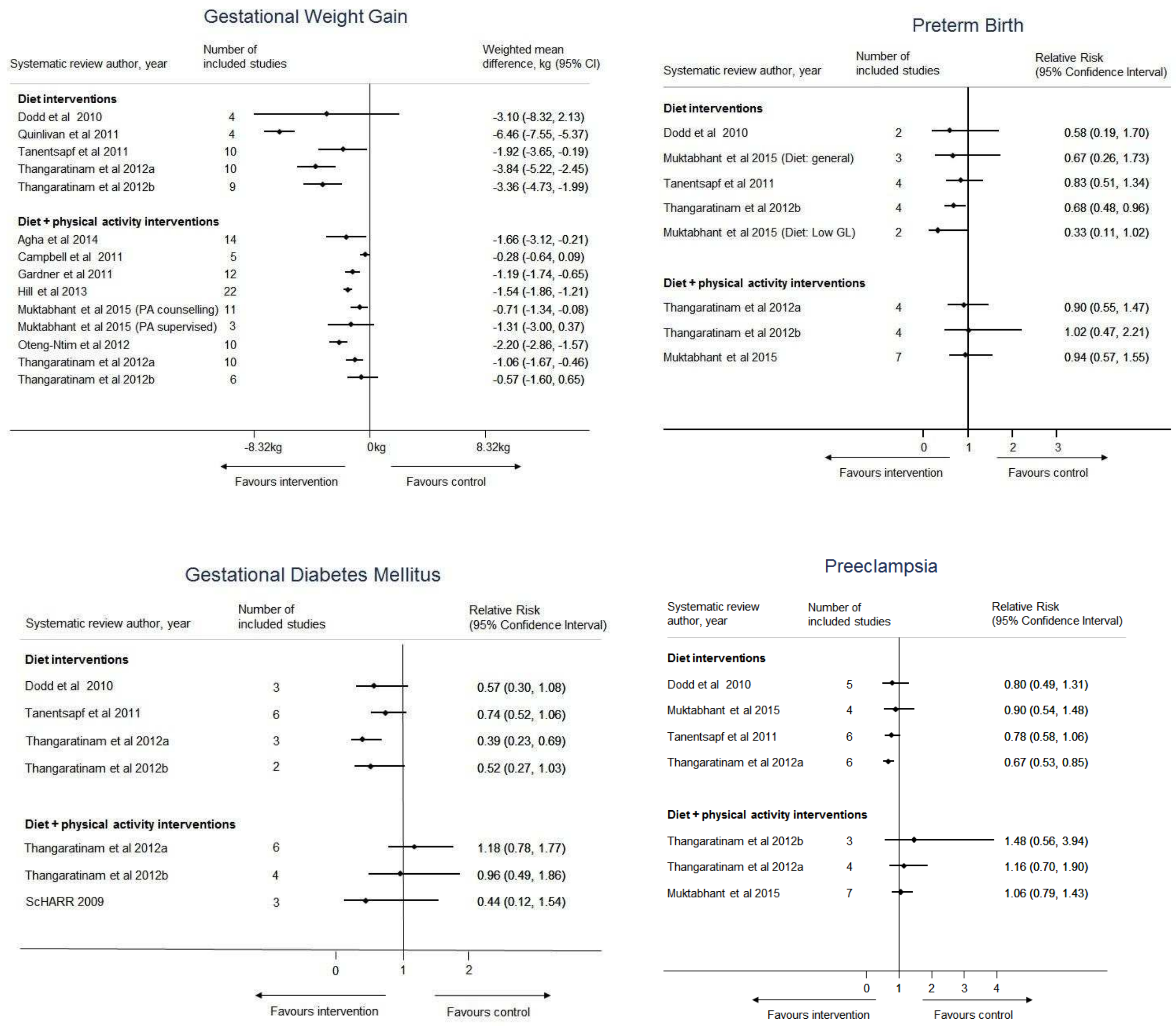
Paper 1 - Figure 1



Paper 1 - Figure 2



Paper 1 - Figure 3

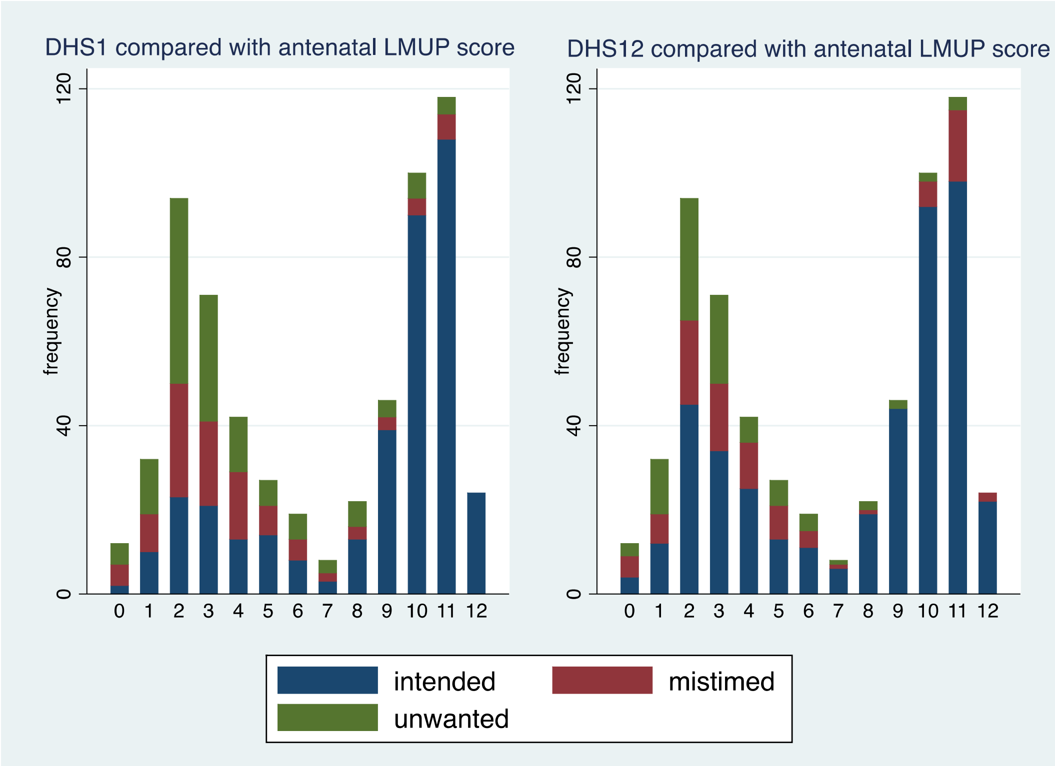


Figure 3: Comparison of women's antenatal LMUP score with their response to the DHS question completed at least one (DHS1) and at least 12 (DHS12) months after birth

Paper 1 - Table 1

Table 1 Dietary intake and lifestyle characteristics of women of reproductive age in the ALSWH and UK NDNS

ALSWH[1]	All women (N)[2]		Preconception characteristics[3]				
			Age at first birth (N,%)				
	Survey1 Age 18-23 (7863)	Survey 7 Age 37-42 (6981)	Age 18-25 (544, 17.4%)	Age 26-30 (1293, 41.5%)	Age 31-35 (1024, 32.8%)	Age 36-42 (257, 8.2%)	P-value[4]
BMI, mean (SD)	22.8 (4.1)	26.8 (6.4)	23.4 (4.7)	23.9 (4.4)	24.3 (4.5)	25.2 (5.6)	<0.0001
Overweight/obese, %	21.3	52.2	27.1	30.8	34.6	39.7	0.02
F&V (<5 serves/day), %	91.9	91.0	..	91.9	92.5	86.5	0.13
Physical activity (<30 mins/day), %	38.8	45.0	52.0	38.9	34.4	41.9	<0.0001
Current smoker, %	28.4	10.5	28.0	18.6	13.4	14.3	<0.0001
~~Current illicit drug user, %~~	~~26.6~~	~~7.3~~	~~22.1~~	~~17.1~~	~~19.0~~	~~15.4~~	~~0.002~~
High risk alcohol intake* %	5.3	6.9	3.2	3.6	4.9	7.1	0.008

UK NDNS RP (2008/2012)[5]		Non-pregnant women of reproductive age					
			Age at survey (N,%)				
		Total (N) (509)	Age 18-25 (156, 32%)	Age 26-30 (79, 19%)	Age 31-35 (102, 18%)	Age 36-42 (172, 31%)	P-value[4]
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/obese, %		49 (43, 54)	41 (32, 51)	40 (29, 53)	49 (38, 60)	62 (54, 70)	0.004
F&V(<5 serves/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[6], % (95% CIs)		22 (18, 26)	28 (19, 38)	16 (9, 26)	12 (7, 20)	25 (19, 33)	0.03
Vitamins	LNRI[7]	Percentage (95%CIs) with diet only intakes below Lower Reference Nutrient Intakes (LRNIs)					
Vitamin A	250 µg/d	7 (5, 9)	12 (8, 19)	5 (5, 14)	2 (1, 4)	5 (3, 10)	0.002
Vitamin B12	1.0µg/d	2 (1,3)	4 (2, 8)	0	1 (0, 3)	1 (0, 6)	0.1
Folate	100µg/d	4 (3, 7)	8 (4, 13)	1 (0, 6)	0 (0, 2)	5 (2, 9)	0.003
Riboflavin	0.8mg/d	14 (11, 18)	22 (15, 32)	11 (6, 20)	9 (5, 15)	11 (7, 17)	0.03
Minerals							
Calcium	400mg/d[8]	9 (7, 12)	13 (9, 20)	6 (3, 14)	6 (3, 12)	9 (5, 14)	0.2
Iodine	70µg/d	15 (11, 19)	22 (15, 31)	13 (7, 23)	7 (4, 14)	11 (7, 18)	0.02
Iron	8.0mg/d	30 (25, 34)	38 (29, 47)	26 (17, 37)	23 (16, 32)	27 (21, 35)	0.09
Potassium	2000mg/d	29 (25, 34)	41 (32, 51)	26 (17, 38)	19 (12, 28)	25 (19, 33)	0.003
Selenium	40µg/d	51 (47, 56)	57 (47, 66)	37 (26, 49)	52 (42, 62)	54 (46, 61)	0.08
Zinc	4mg/d	4 (3, 7)	6 (3, 11)	3 (1, 9)	4 (2, 9)	4 (2, 9)	0.7