

Title: A 'wake-up call' for preconception health: a clinical review

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And the UK Preconception Partnership.

Introduction

Preparing for a healthy pregnancy, preconception care, should be the norm and a more actively managed step in primary care. Decades of improvement in the quality of maternity care have greatly reduced the risks associated with pregnancy and childbirth, but improvements in preconception care have lagged behind. The health of women as they enter pregnancy remains a major challenge to maternity services and two thirds of maternal deaths in the UK are now in women with pre-existing medical conditions (1).

Animal and human research show clear links between preconception influences and offspring health extending across two or more generations (2). In the UK and most other countries, preconception health is frequently compromised by maternal and paternal obesity, dietary deficiencies, smoking, excessive alcohol consumption, mental health issues and recreational drug use, all of which are associated with poorer pregnancy outcomes and frequently rooted in social and economic deprivation.

The rise in obesity among women of reproductive age has been the most pressing 'wake-up call' to improve preconception health. Obesity (BMI ≥ 30 (kg/m²), which affects over one in five (21.6%) pregnant women in the UK (3), is strongly linked to almost all adverse pregnancy and birth outcomes, notably, pre-eclampsia, gestational diabetes and stillbirth, and has lasting consequences for the health of the offspring (4). Unfortunately, attempts to tackle the problem through diet and physical activity interventions *starting* in pregnancy have had negligible effect on immediate and later outcomes (5, 6). Together, these findings call for a new focus on improving health *before* conception.

Review of evidence

This paper draws on comprehensive recent reviews of clinical care from the National Institute for Health and Clinical Excellence (NICE) (7), research evidence from the National Institute for Health Research (NIHR) (8), the scientific rationale (9), the 2018 Lancet series on preconception health (2,5,10), and a suite of resources produced by Public Health England 'making the case for preconception care' (11). In addition, we illustrate the implications of preconception care guidance for a typical general practice.

How can we normalise preconception care?

A common objection to normalising preconception care is that around 40% of pregnancies are not planned. Leaving aside the counter-response that 60% of pregnancies *are* planned (although the intention to conceive is often not declared), this objection merely points to the need for dual action at both individual and population level – a proposal that is emphasised in the Lancet series (5,10).

Action at the population level offers the opportunity to optimise preconception health to those not planning a pregnancy. It is needed not only because of unplanned pregnancies but because many risk factors are set in train well before pregnancy. Changing established patterns of behaviour, such as smoking or diet, and removing barriers to achieving a healthy preconception status can take months or years (5,10). Public health, system-wide interventions avoid some of the limitations of individually targeted interventions which

include burdening women with responsibility for preconception health, widening health inequalities, poor compliance, feelings of blame or shame, and limited impact. These features are well illustrated by prevention of neural tube defects with folic acid: in England in 2017, less than 30% of women took folic acid supplements before a first or subsequent pregnancy, and less than 15% of women aged under 25 where social deprivation is greater (12). The alternative approach, mandatory fortification of food with folic acid, is still under consideration by the UK Government, but has been implemented in 82 countries including the USA, Canada and most of South America. All studies of subsequent impact have shown rapid, population-wide reductions of around 50% in neural tube defects (13). Other less well known benefits of folic acid include a reduction in fetal growth restriction, increase in birthweight (14), and a lower risk of severe language delays in childhood (15).

Action at the individual level is aimed at those who intend to conceive or are considering it. However, planning and preparing for pregnancy is often considered a private matter, with many people waiting at least 12 weeks into established pregnancy before sharing the news. And most women do not visit their general practitioner until after they have had a positive pregnancy test. This reflects a broad lack of awareness of the need to consider health *before* a pregnancy among women and men of reproductive age, as well as many health professionals. Changing this situation requires routinely posing a question such as “...and are you thinking of having a(nother) baby in the next year or so?” to people of reproductive age during healthcare visits. Referring to a period of ‘a year or so’ raises awareness of entrenched health issues affecting pregnancy and child health, such as obesity and mental health problems, that take time and sensitivity to be tackled effectively. Paternal as well as maternal obesity are implicated in infertility and poor pregnancy outcomes (2). In such situations, parental motivation to reduce weight can be very strong. For example, a recent pilot study found that 65% of women with obesity attending a family planning clinic to have their contraceptive device removed to become pregnant were willing to defer removal of the device for 6 months while they followed a challenging weight loss programme. Nearly half completed the programme with an impressive reduction in body mass index (16).

What kind of preconception care is needed, for whom and when?

Preconception care needs vary enormously - from standard dose (400mcg) folic acid supplementation alone for women in good health, to high dose (5mg) folic acid supplements (available only on prescription in the UK) for those taking epilepsy medicines or with obesity or diabetes, and more specialist care for women and men with a wide range of less common disorders. NICE offers a detailed checklist (7) and somewhat shorter versions are available (17). Well-designed information for women and men considering a pregnancy is also available online <https://www.contraceptionchoices.org/did-you-know/thinking-having-baby>

What does this mean for a typical general practice? According to the RCGP Research and Surveillance Centre, the majority of women of reproductive age have potentially reversible behavioural risk factors (Figure). Sixty-one percent have at least one of the following risk factors: a BMI over 25kg/m²; smoking (current or ex-smoker); alcohol consumption of at least 14 units per week (or other codes consistent with heavy drinking); drug misuse /dependence. Thirty percent have one or more of the following conditions: diabetes;

anxiety; depression; epilepsy or prescription for valproate, and 23% have conditions in both categories. Fewer than 1 in 10 women (9%) have no behavioural or medical risk factors for pregnancy. If other conditions, such as thyroid disease, severe mental disorders, obstetric or genetic risks were considered, the number of women needing dedicated preconception care would be higher. According to these figures, in an average practice with 10,000 patients, including 1,938 women (38%) of reproductive age (15-45 years), 180 women would need folic acid supplementation only, 1,182 would need additional lifestyle support and 620 would require medical or specialist input before becoming pregnant (figure).

Based on this illustration we suggest the following approach to providing preconception care:

- Priorities in preconception care:
 - Folic acid supplementation for all women
 - Advice and support for those with lifestyle risk factors
 - Review of medication, obstetric history and chronic conditions
 - Consider possibility of genetic risk

- Red flags for referral (Box 2)

In many cases, we need to apply conversations about healthy life style, which are commonplace with older patients at risk of cardiovascular disease, to a younger group who may become pregnant. These findings should encourage us to ask all patients of reproductive age routinely whether they are considering a(nother) pregnancy. Those who are planning or are uncertain/ambivalent about pregnancy need information about why health before conception matters and support to achieve what is possible; those who are not planning a pregnancy are likely to need effective contraception. Discussing pregnancy intentions is acceptable to patients (18) and numerous opportunities arise in primary care, particularly during visits for contraception, cervical screening, post-natal and infant health checks, but also during consultations for long term conditions, including diabetes, hypertension, asthma, epilepsy or mental health reviews. For this shift in care to happen, healthcare providers must be equipped to support or refer patients appropriately. NICE provides clinical guidance for primary care professionals (7) but these guidelines are not included in any of the primary care quality frameworks.

In England, neither the Investment and Impact Fund, a government incentive scheme to encourage NHS primary care networks to deliver high quality care to their population (primary care networks are based on GP registered lists, typically of 30,000 to 50,000 individuals), nor the Quality Outcomes Framework - a system for the performance management and payment of GPs in the NHS - have any preconception care indicators. Other barriers to routine preconception care include time, practitioner knowledge and competing priorities in preventative care (19,20), but there are also important enablers (20), including online resources (such as the information for patients and checklists for practitioners above) and the role of the primary care nurse, especially regarding the large category of conditions requiring healthy lifestyle support (figure).

Conclusion

It is time to normalise the notion of discussing pregnancy intentions and preparing for pregnancy. This could start through school health and/or science curricula conveying the simple message that health is something to consider before - rather than after - a pregnancy occurs. Women and men planning a pregnancy need clear information but this will not be enough. System-wide changes that address the wider determinants of health and reproductive rights are crucial, alongside strengthening health literacy. Elsewhere, we have argued for the creation of a social movement to generate the social and environmental changes that make healthy choices easier for adolescents and young people (21). As the evidence for effective preconception interventions is becoming clearer (8,9), attention should now turn to intervention *delivery*, including fortifying food with folic acid and equipping primary care teams to help people receive the preconception care they need at the right time.

Key Messages

- Routinely asking all patients of reproductive age “**...and are you thinking of having a(nother) baby in the next year or so?**” would identify the need for information and support to achieve optimal health before conception, or the need for effective contraception if relevant.
- Preconception care should be offered to women and their partners planning pregnancy. In addition, system-wide public health interventions are needed to optimise health of all women and men of reproductive age.
- Preconception care needs vary widely and care should be tailored to an individual’s physical and mental health conditions, health behaviours and social context.
- Practices and localities can compare their preconception care with the data presented in this paper.

Red flags for referral

- Women with obesity, particularly BMI ≥ 35 , is best addressed pre-pregnancy
- Women taking medication known to be harmful or not recommended in pregnancy; some such as valproate should be avoided, and others such as angiotensin modulating drugs should be substituted for safer options.
- Women intending to become pregnant who have chronic or complex disease or disability. These include poorly controlled epilepsy, hypertension, diabetes, thyroid disease (including subclinical hypothyroidism), renal or heart disease, or inflammatory conditions such as rheumatoid arthritis and inflammatory bowel disease.
- Women with depression should have their need for medication reviewed; those with severe mental health diagnoses, including alcohol and drug addiction, cocaine can be particularly harmful, should be referred
- Women with history of venous thromboembolism and haemoglobinopathies
- Women with three or more consecutive miscarriages
- Women with previous complications of pregnancy, e.g. pre-eclampsia, gestational diabetes or obstetric cholestasis
- Women with a personal or family history of an inherited disorder e.g. Polycystic kidney disease
- Women in social circumstances where an additional child or the pregnancy may be at risk

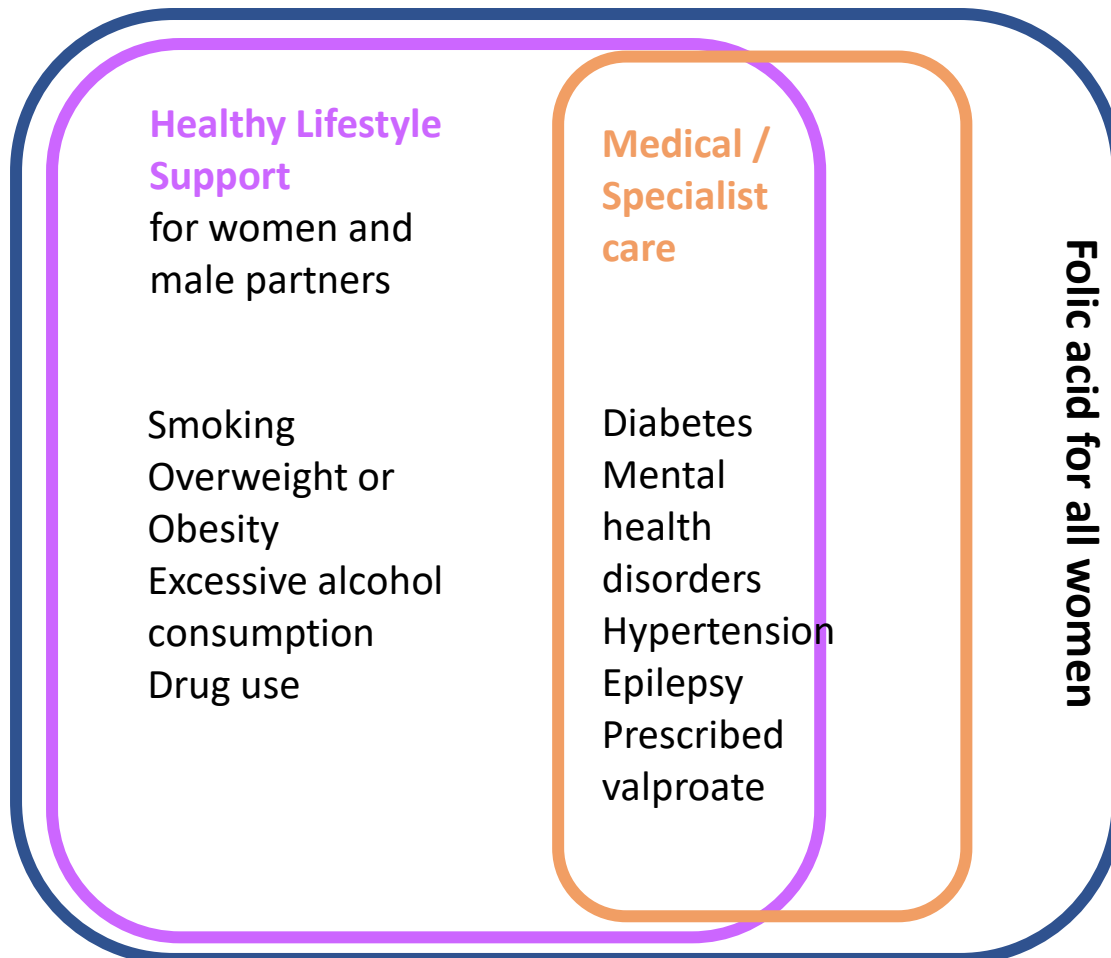
Key Questions for Future Research

Research should focus on addressing the impact of disparities on preconception health and how to address them.

Key research questions might include:

- What are the main facilitators and barriers to planning for pregnancy?
- How do we best engage potential young mothers and their partners?
- What interventions reduce risky behaviour and optimise wellbeing in those looking to become pregnant?
- How to optimise long term condition management pre-pregnancy?
- How can primary care teams be supported to provide timely preconception assessment and care?

Figure. Illustration of the relative size and overlap of selected common preconception care needs in women of reproductive age in general practice in England.



Legend: 61% of women aged 15-45 years (n=361,125) have at least one of the following risk factors: a BMI over 25kg/m²; smoking (current or ex-smoker); alcohol consumption of at least 14 units per week (or other codes consistent with heavy drinking); drug misuse /dependence. 30% (n=177,635) have one or more of the following conditions: diabetes; hypertension; anxiety; depression; epilepsy or prescription for valproate. 23% have both lifestyle and medical / specialist care needs, while 9% had neither.

Source: Oxford-Royal College of General Practitioners (RCGP) Research and Surveillance Centre database (22)

References

1. Knight M, Bunch K, Tuffnell D, Shakespeare J, Kotnis R, Kenyon S, Kurinczuk JJ (Eds.) on behalf of MBRRACW-UK. Saving Lives, Improving Mothers' Care – Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2015-17. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2019.
2. Fleming T, Watkins A, Velazquez MA, et al. Lancet series on preconception health. Origins of lifetime health around the time of conception: causes and consequences. *The Lancet*. 2018; 391(10132):1842-1852.
3. Health of women before, during and after pregnancy: health behaviours, risk factors and health inequalities 2019. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/844210/Health_of_women_before_and_during_pregnancy_2019.pdf
4. Godfrey KM, Reynolds RM, Prescott SL, et al. Influence of maternal obesity on the long-term health of offspring. *Lancet Diabetes Endocrinol*. 2017;5(1):53-64.
5. Stephenson J, Heslehurst N, Hall J, et al. Lancet series on preconception health. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *The Lancet*. 2018; 391(10132):1830-1841.
6. The International Weight Management in Pregnancy (i-WIP) 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 doi.org/10.1136/bmj.j3119
7. NICE Clinical Knowledge Summaries. Pre-conception – advice and management. <https://cks.nice.org.uk/pre-conception-advice-and-management>
8. National Institute for Health Research (NIHR). Themed Review: Better Beginnings. 2017. Available from: <https://evidence.nihr.ac.uk/wp-content/uploads/2020/03/Better-beginnings-web-interactive.pdf>.
9. Atrash H, and Jacks B. Preconception care to improve pregnancy outcomes: the science. *J Hum Growth Dev*. 2020; 30(3):334-341.
10. Barker M, Dombrowski SU, Colbourn T, et al. Lancet series on preconception health. Intervention strategies to improve nutrition and health behaviours before conception. *The Lancet*. 2018; 391(10132):1853-1864.
11. Public Health England. Making the case for preconception care. 2018. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/729018/Making_the_case_for_preconception_care.pdf.

12. Stephenson J, Vogel C, Hall J et al. Preconception health in England: a proposal for annual reporting with core metrics. *The Lancet* 2019; 393:2262-2271.
13. Wald NJ, Morris, JK and Blakemore C. Public health failure in the prevention of neural tube defects: time to abandon the tolerable upper intake level of folate. *Public Health Rev.* 2018; 39: 2 doi: [10.1186/s40985-018-0079-6](https://doi.org/10.1186/s40985-018-0079-6)
14. Fekete K, et al. Effect of folate intake on health outcomes in pregnancy: a systematic review and meta-analysis on birth weight, placental weight and length of gestation. *Nutr J.* 2012; (11):75.
15. Roth C, Magnus P, Schjolberg S, et al. Folic acid supplements in pregnancy and severe language delay in children. *JAMA.* 2011;306(14):1566–1573.
16. Brackenridge L, Finer N, Batterham R L, Pedram K, Ding T, Stephenson J, Barry J & Hardiman P (2018). Pre-pregnancy weight loss in women with obesity requesting removal of their intra-uterine contraceptive device in order to conceive: a pilot study of full meal replacement. *Clinical obesity* doi.org/10.1111/cob.12252
17. Dorney E and Black K. Preconception care. *AJGP* 2018; 47: 424-429.
18. Hammarberg K, Hassard J, de Silva R, and Johnson L. Acceptability of screening for pregnancy intention in general practice: a population survey of people of reproductive age. *BMC Family Practice* 2020; 21:40 <https://doi.org/10.1186/s12875-020-01110-3>
19. Ojukwu O, Patel D, Stephenson J, Howden E and Shawe (2016). General practitioners' knowledge, attitudes and views of providing preconception care: a qualitative investigation, *Upsala Journal of Medical Sciences*, 121:4, 256-263, DOI: [10.1080/03009734.2016.1215853](https://doi.org/10.1080/03009734.2016.1215853)
20. Mazza, D., Chapman, A. & Michie, S. Barriers to the implementation of preconception care guidelines as perceived by general practitioners: a qualitative study. *BMC Health Serv Res* **13**, 36 (2013). <https://doi.org/10.1186/1472-6963-13-36>
21. Vogel C, Kriznik N, Stepheon J and Barker M. *J Dev Orig Health Dis.* 2020; 18:1–6. Preconception nutrition: building advocacy and social movements to stimulate action.
22. Correa A, Hinton W, McGovern A, et al. Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) sentinel network: a cohort profile. *BMJ Open* 2016;6:e011092. doi:10.1136/bmjopen-2016- 011092

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