

## CLINICAL REVIEW

## Prepregnancy care

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Prepregnancy care aims to recognise and amend lifestyle, behavioural, medical, and social risks to a woman's health or pregnancy outcome, and ultimately it aims to reduce maternal and perinatal morbidity and mortality.<sup>1</sup> Where such risks are not modifiable, prepregnancy counselling aims to ensure that a woman is told of the potential risks and can make an informed decision about the pregnancy. Prepregnancy advice can be offered to a woman of reproductive age by any healthcare professional who has contact with her with the aim of optimising pregnancy outcomes. With around half of pregnancies in the United Kingdom<sup>w1</sup> and the United States<sup>w2</sup> unplanned, a proactive approach is needed. This review is relevant to general practitioners, nurses, and family planning doctors in the community and to specialists in secondary care who see women of reproductive age.

### Why should prepregnancy advice become an integral part of healthcare services?

More than half of maternal deaths in the UK are caused by pre-existing medical conditions, particularly cardiac, neurological, and psychiatric illnesses, together with an increasing contribution from obesity.<sup>2</sup> The triennial report on maternal deaths from the Centre for Maternal and Child Enquiries in the UK has highlighted the important role of prepregnancy care, particularly in the management of women with pre-existing medical conditions. The recommendations include routine commissioning of such services as an integral part of the maternity services network. These recommendations reflect the increasing awareness that women may not receive the necessary specialist advice or obtain optimal care, particularly around appropriate use of therapeutic drugs.

### What lifestyle changes should a woman planning pregnancy consider?

Advise women considering pregnancy to start folic acid supplementation and, where appropriate, to stop smoking; limit

alcohol and caffeine intake; avoid use of illicit drugs; and optimise their weight, diet, and physical health. Table 1↓ provides evidence for these interventions and recommendations for prepregnancy advice.

A Cochrane review of randomised controlled trials showed that supplementation with 400 µg of folic acid for three months before conception and during the first trimester of pregnancy decreases the risk of neural tube defects (such as spina bifida) in the fetus by 72% (relative risk 0.28, 95% confidence intervals 0.13 to 0.58).<sup>3</sup> National guidelines recommend increasing the dose of folic acid to as much as 5 mg in patients with a personal or a family history of spina bifida, diabetes,<sup>w3</sup> or sickle cell disease<sup>w4</sup> and in those receiving antiepileptic drugs.<sup>w5</sup>

The implementation of lifestyle changes may be more challenging. In the latest survey from England, 32% of mothers reported smoking in the 12 months before or during pregnancy, but nearly half of these women gave up before or during pregnancy.<sup>w6</sup> Only 17% of mothers continued to smoke throughout pregnancy, and this group may need extra help with smoking cessation. In a similar survey, 29% of adult women had drunk more than three units and 13% of women reported drinking more than six units on at least one day in the week before interview.<sup>w7</sup> In 2010-11, the prevalence of illicit drug use among adults was 8.8%; 6.8% of 16-59 year olds had used cannabis in the past year and 2.1% had used cocaine.<sup>w8</sup>

Offer general health advice where appropriate including optimisation of weight and blood pressure through diet and physical activity, maintenance of good oral hygiene, compliance with cervical screening, need for vitamin D supplementation if appropriate, and screening for intimate partner violence (most prevalent in women of reproductive age) (table 1). A detailed clinical review on travel in pregnancy has been published previously.<sup>4</sup> Advise a woman to consider travelling before, rather than during, pregnancy where possible if she has a medical condition that may deteriorate during pregnancy (such as cardiac disease) or if she intends to visit high risk areas (such as malaria

### Summary points

- Consider offering opportunistic prepregnancy advice to all women of reproductive age, particularly when providing contraception
- Behavioural changes include stopping smoking, reducing alcohol and caffeine intake, avoiding substance misuse, and optimisation of weight
- Folic acid is recommended from before conception until 12 weeks' gestation to prevent neural tube defects
- Check immunity to rubella in women suspected to be non-immune
- Review chronic medical and psychiatric conditions, in addition to therapeutic drugs, to optimise care; liaise with specialists
- Offer genetic counselling to couples with an affected child or family history of a genetic disorder

### Sources and selection criteria

We searched PubMed (in January 2012) for articles on prepregnancy care, advice, and counselling, together with those on modification of lifestyle behaviour before pregnancy. The MeSH terms for the search included: "preconception", "periconception", "pre-pregnancy", "pre-conceptual", in addition to keyword variations. We obtained information from prospective randomised clinical trials, cohort studies, systematic reviews, and meta-analyses. We searched national guidelines for those including advice on prepregnancy care.

endemic countries and those with high rates of traveller's diarrhoea or other infections).

## Which infections can harm the fetus?

Exposure to rubella in early pregnancy can result in congenital rubella syndrome (including sensorineural deafness, ocular abnormalities, cardiovascular defects, mental retardation, microcephaly, and spastic diplegia; table 2). Many women in developed countries will have been vaccinated as children; women from other countries may not be immunised. In the absence of a vaccination history, check for rubella antibodies and arrange subsequent vaccination if the woman is not immune.<sup>5</sup> Advise women to avoid conception for a month after vaccination.<sup>9</sup>

If acquired during pregnancy, varicella, cytomegalovirus, and toxoplasmosis can lead to congenital malformations in the fetus (table 2). However, the UK has no national screening programmes for prepregnancy or prenatal testing for these infections.<sup>10</sup> This is because the National Screening Committee in the UK has concluded that either no good quality evidence is available on the efficacy of screening or research has found that screening for a particular condition causes more harm than good.<sup>6</sup>

Consider specific viral testing (for example, for HIV, hepatitis B, or hepatitis C), if appropriate, to minimise viral load before or during pregnancy and reduce vertical transmission. The British Association for Sexual Health and HIV recommends that HIV testing be offered routinely to all adults registering in general practice in the UK in areas where the prevalence of diagnosed HIV infection is greater than two in 1000.<sup>7</sup>

Prepregnancy screening for sexually transmitted infections—such as chlamydia, gonorrhoea, and syphilis—is not routinely indicated in the UK, but there is a national programme of opportunistic screening for chlamydia (which can cause pelvic infection and difficulty in conceiving) for women under 25 years old.

## Which drugs should be avoided and which are safe to continue?

A cohort study in 81 975 pregnant women from the UK general practice research database showed that 65% of participants received one or more prescriptions in the three months before and 10 weeks after conception.<sup>8</sup> In this study, 7% of prescriptions were for US Food and Drug Administration category "X" drugs (with potential teratogenic risk that outweighs maternal benefit). The safety of these therapeutic

drugs needs to be considered in women of reproductive age, to ensure that potentially teratogenic drugs are avoided if possible and that women are given correct advice on when it is safer to continue with drugs during pregnancy (table 3). Advice on teratogenicity is available from the *British National Formulary* and the National Teratology Information Service.<sup>9 10</sup>

Depending on the severity of the medical condition, the safety profile of the drug, and the period of exposure that is related to teratogenicity, some drugs may need to be stopped (for example, methotrexate, isotretinoin, and mycophenolate mofetil) or timed (for example, radioactive iodine) before conception to allow for a wash out period. Other drugs can be continued until a menstrual period is first missed, with advice for an early pregnancy test and cessation of the drug on confirmation of pregnancy (for example, angiotensin converting enzyme inhibitors used for renoprotection and warfarin used for women with a high risk of a thromboembolic event). Women who are advised to stop a drug on successful conception must be given clear advice on obtaining safe alternatives to avoid prolonged times with no appropriate treatment (for example, women who switch from warfarin to low molecular weight heparin).

Give women specific advice that it is safe and important to continue certain drugs. Examples include the continued use of steroid inhalers in asthma; immunosuppression for transplant recipients, women with inflammatory bowel disease, or those with connective tissue disorders; proton pump inhibitors for women taking steroids; and antiepileptic drugs. In these instances, discontinuing the drug may cause a flare of the underlying disease that puts the pregnancy at considerably greater risk than any theoretical risk from the drug itself.

## What advice should be given to a woman with a chronic medical condition?

Substandard care in women with pre-existing medical conditions has been a recurrent theme of the report on maternal deaths from the Centre for Maternal and Child Enquiries in the UK, and the report advises prepregnancy counselling for women with epilepsy, diabetes, asthma, congenital or known acquired cardiac disease, autoimmune disorders, renal or liver disease, obesity (body mass index of 30 or more), severe pre-existing or past mental illness, and HIV infection.<sup>2</sup> The impact of pregnancy on the disease and potential impact of the condition on the pregnancy should be considered, together with appropriate changes to drugs or levels of surveillance. Vulnerable groups such as migrant women or those with poor socioeconomic status

may be particularly at risk. The box provides recommendations for prepregnancy advice for specific medical conditions.

Asthma is the most common chronic medical condition in pregnancy; reassure women that well controlled asthma does not adversely affect the outcome of pregnancy and that they should not discontinue their regular drugs.<sup>11</sup>

Cardiac disease is the leading cause of maternal deaths in the UK,<sup>2</sup> and liaison with specialist care is essential for women with pre-existing heart disease. Women at increased risk of undetected cardiac disease (such as migrant women) require a clinical cardiovascular examination including blood pressure and urinalysis.

Women with epilepsy need specialist prepregnancy advice (box). Additional risk factors such as low socioeconomic status can predispose to poor seizure control; these women may need additional support and monitoring to ensure that their epilepsy is well controlled.

Women with type 1 and type 2 diabetes are at risk of complications.<sup>12</sup> Women with type 2 diabetes may not be under specialist review, but a population based cohort reported that they have the same risk of adverse pregnancy outcomes and require the same level of prepregnancy counselling as those with type 1 diabetes (box). In a systematic review, preconception care (including improving glycaemic control to keep glycated haemoglobin (HbA<sub>1c</sub>) at 53 mmol/mol or lower; educating patients; screening for complications; using contraception until tighter control is achieved; supplementing with folic acid) was shown to reduce congenital malformations, preterm delivery, and perinatal mortality, with a parallel reduction in first trimester HbA<sub>1c</sub>.<sup>13</sup> Treatment with metformin is now often continued throughout pregnancy.<sup>14</sup>

Normal concentrations of maternal thyroid hormone are essential for fetal brain development; a recent review summarised the evidence that untreated maternal hypothyroidism is associated with lower IQ in children.<sup>15</sup> Check thyroid function tests in women with known hypothyroidism who are planning a pregnancy to ensure that thyroid stimulating hormone is within the normal range. A randomised controlled trial of population based thyroid screening (at 15 weeks' gestation) and treatment of women found to have hypothyroidism found no benefit on childhood cognitive function,<sup>16</sup> so universal screening is not recommended.

Specialists managing women with other chronic conditions (renal disease, gastroenterological disease, and liver disease; neurological and autoimmune disorders; HIV infection) need to offer prepregnancy advice proactively, including discussion of risks, management of drugs, optimisation of the condition, and surveillance that will be needed during pregnancy.

## Why is prepregnancy advice important to women with mental health disorders?

In the past, the risks of deterioration of psychiatric disorders in pregnancy and the impact on maternal deaths (particularly suicide) were poorly appreciated. More recently, the need for identification and appropriate management of such women has been recognised, largely due to capture of data for the report on maternal deaths from the Centre for Maternal and Child Enquiries in the UK.<sup>2</sup> Prepregnancy counselling includes review of drugs and symptoms and referral to psychiatric services as needed. The most recent report on maternal deaths recommends that general practitioners be aware of the risks and refer women for specialist psychiatric input. The need to recognise the increased risk of suicide (either related to a history of psychiatric

disorder or substance misuse) is also emphasised.<sup>2</sup> Assess smoking, alcohol intake, and substance misuse and provide specific advice and support to help women reduce these behaviours. Input from a multidisciplinary team (mental health nurse, general practitioner, and psychiatrist) before pregnancy may help prepare women for the additional vulnerabilities of pregnancy and the postpartum period.

## When should women with a pre-existing medical condition conceive?

In women with certain medical conditions, conception during a period of disease quiescence or stability is associated with improved pregnancy outcome. This includes women with lupus nephritis,<sup>17</sup> recipients of a liver or renal transplant,<sup>18 19</sup> and women with inflammatory bowel disease.<sup>20</sup>

## Should prepregnancy genetic screening be carried out?

Genetic screening includes testing asymptomatic carriers who might be at increased risk of a disease because of their ethnicity or familial ancestry and screening women with a known genetic disease who may pass on the mutation to the fetus. The consequences of offering genetic screening must first be discussed with the woman (for example, an offer of termination of pregnancy for an affected fetus diagnosed through invasive testing such as amniocentesis or chorionic villus sampling, or preimplantation genetic diagnosis for a small number of conditions).

The cystic fibrosis gene is most commonly carried by people of white European descent, with about one in 25 carrying one of the mutations. A prenatal screening policy for cystic fibrosis in the UK is currently under consideration. In the US, the American Congress of Obstetricians and Gynecologists' committee on genetics recommends screening for the 23 most common mutations for cystic fibrosis (of 1700 identified) in all women of reproductive age.<sup>21</sup>

Screening for sickle cell disease and thalassaemia in the antenatal period was implemented in 2005 by the National Screening Committee in the UK.<sup>22</sup> In areas of high prevalence of sickle cell disease ( $\geq 1.5/10\ 000$  pregnancies), all pregnant women are offered screening, whereas in areas of low prevalence ( $< 1.5/10\ 000$  pregnancies), screening is undertaken after using the family origin questionnaire. Evaluation of red cell indices is used to screen for thalassaemia. Prepregnancy screening for sickle cell disease or thalassaemia is not routine in the UK, but some couples may request screening to increase the chance of conceiving a non-affected child (for example, through preimplantation genetic diagnosis or artificial insemination by a donor).

The UK National Screening Committee recommends additional screening for certain population groups, such as Ashkenazi Jews, who are at increased risk of Tay-Sachs disease, a life threatening metabolic disorder.<sup>10</sup> In all cases where screening is offered, appropriate genetic counselling is needed to explain and provide information for a couple about their reproductive options.

Some women may also have a known genetic mutation, either as an asymptomatic carrier (for example, haemophilia) or as an affected person (for example, achondroplasia). Offer these women access to specialist genetic counselling services before pregnancy, to enable mutation testing where appropriate and a discussion of choices for pregnancy.

**Recommendations for pre-pregnancy counselling in specific medical conditions****Asthma**

Counsel regarding the importance of good asthma control during pregnancy and that  $\beta_2$  agonists, inhaled steroids, and oral steroids are safe in pregnancy

Avoid trigger factors (allergens such as pollen, environmental pollutants, dust, indoor mould, smoking)

**Cardiac disease**

Refer a woman with pre-existing disease to specialist centres to optimise her medical condition before pregnancy

**Hypertension**

Optimise blood pressure to reduce risk of superimposed pre-eclampsia

Consider changing drugs (stop angiotensin converting enzyme inhibitors or angiotensin receptor blockers at conception and switch to safer alternatives)

**Epilepsy**

Advise regarding teratogenic risks (particularly neural tube defects) of antiepileptic drugs

Give a higher dose of periconceptional folic acid supplements (5 mg rather than 400  $\mu$ g daily)

Advise on benefits to the fetus of good seizure control through scrupulous adherence to drugs

Consider increasing the dose of certain antiepileptic drugs (particularly lamotrigine) to ensure optimal seizure control

Refer for regular specialist review

**Diabetes**

Advise on consequences of poor glycaemic control (congenital anomalies, miscarriage, pre-eclampsia, stillbirth)

Discuss benefits of tight glycaemic control through a balanced diet, appropriate treatment, and regular monitoring before and during pregnancy

Discuss the identification and management of hypoglycaemic episodes

Offer pre-pregnancy screening for nephropathy (urinalysis for proteinuria, measurement of serum creatinine) and retinopathy (by ophthalmological assessment)

**What is the best way to get pregnant?**

In couples who do not use contraception and have regular sexual intercourse, conception rates are 84% within one year and 92% by the end of the second year.<sup>23</sup> Sexual intercourse every two to three days optimises the chances of getting pregnant; couples do not need to time intercourse with ovulation because this often causes undue stress and does not increase the chances of success. Conception rates may be lower in women who do not have a regular menstrual cycle.<sup>24</sup> One in six couples will not have achieved a pregnancy after a year of unprotected intercourse; consider referral for investigation of fertility and possible assisted reproductive techniques at this stage.

**What is the evidence that pre-pregnancy health promotion works?**

Several studies have evaluated pre-pregnancy health promotion; a systematic review assessed four trials that looked at interventions of brief advice, health education, and lifestyle education against usual care or no specific care.<sup>25</sup> Although health interventions seemed to have some effects on maternal behaviour (such as a lower rate of binge drinking), there was little evidence of improved pregnancy outcome (evaluated in only one trial). The authors concluded that more research was needed in this area and that, in view of the high unplanned pregnancy rate, consideration needed to be given to reaching all women of reproductive age. The Centre for Maternal and Child Enquiries' report, however, has emphasised the importance of pre-pregnancy counselling for women with a medical condition.<sup>2</sup> We now need to increase our understanding of those components of pre-pregnancy advice that are most likely to improve outcomes, and of the best means of implementing effective interventions.

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**Ongoing research and questions for future research**

PRAMS (Pregnancy Risk Assessment Monitoring System) is a surveillance project of the Centers for Disease Control and Prevention and state health departments, which is collecting state specific population based data on maternal attitudes and experiences before, during, and shortly after pregnancy ([www.cdc.gov/prams/](http://www.cdc.gov/prams/))

What is the best way to offer pre-pregnancy care so that it reaches the greatest number of women and those with most need? Should it be part of routine contraceptive care?

What might motivate a higher proportion of women of reproductive age to plan a pregnancy and follow recommendations to optimise outcome? Should any such effort be part of sex and relationship education at school?

What is the best way of monitoring the use of therapeutic drugs in pregnancy through a national registry system?

What is the effect of offering routine genetic screening for mutations most common in a particular population?

Do pre-pregnancy and peripregnancy vitamin D supplements benefit pregnancy outcomes in some ethnic groups?

What is the best way to ensure that ethnic minority groups have adequate periconceptional intake of folic acid?

**Additional educational resources***Resources for healthcare professionals*

UK National Screening Committee ([URL here](#))—Database for screening policy

Health Protection Agency ([URL here](#))—Information on infectious diseases in relation to pregnancy

Confidential Enquiry into Maternal and Child Health ([URL here](#))—Mission statement of the Centre for Maternal and Child Enquiries

Royal College of Obstetricians and Gynaecologists ([URL here](#))—Guidelines on a variety of topics related to pre-pregnancy care (such as weight management) and pregnancy (such as vitamin supplementation and infections in pregnancy)

American Congress of Obstetricians and Gynecologists ([URL here](#))—ACOG committee opinion no 313, 2005. The importance of preconception care in the continuum of women's health care

*Resources for patients*

NHS Choices. Getting pregnant ([URL here](#))—NHS pregnancy and baby guide

Centers for Disease Control and Prevention ([URL here](#))—Getting ready for a healthy pregnancy: advice on preconception care, sexual health, and women's health in general

Tommy's ([URL here](#))—Getting pregnant: tips for planning a pregnancy from this UK charity dedicated to pregnancy problems

March of Dimes ([URL here](#))—Get ready for pregnancy: advice on preconception care from a global charitable organisation

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## Tables

**Table 1 | Prepregnancy lifestyle modification: evidence and recommendations**

Factors	Impact on pregnancy	Evidence for prepregnancy intervention and recommendations
Smoking	Smoking is associated with decreased fertility and delayed conception, <sup>w11</sup> congenital birth defects including heart defects, musculoskeletal defects and gastrointestinal defects, <sup>w12</sup> miscarriage, <sup>w13</sup> preterm delivery, <sup>w14</sup> low birth weight and fetal growth restriction (dose dependent, with infants born to smokers 170 g lighter on average), <sup>w15</sup> stillbirth, and sudden infant death syndrome <sup>w16</sup>	Offer advice on smoking cessation through pharmacological interventions, such as nicotine replacement therapy <sup>w17</sup> and nicotine receptor partial agonists, <sup>w18</sup> and internet based interventions. <sup>w19</sup> Counsel a woman to stop smoking before conception. <sup>w20</sup> Nicotine replacement therapy in pregnancy has not been shown to reduce adverse pregnancy or birth outcomes, <sup>w21 w22</sup> but women who stop by 15 weeks' gestation have rates of small for gestational age infants and preterm birth similar to non-smokers <sup>w23</sup>
Alcohol	Light to moderate alcohol consumption in pregnancy does not increase the risk of low birthweight infants, preterm birth, and small for gestational age infants. <sup>w24</sup> Heavy alcohol consumption (>10 g/day or more than 3 alcoholic drinks a day) increases risk of low birthweight infants, small for gestational age infants, and preterm birth. <sup>w25</sup> Binge drinking (defined as more than five standard drinks or 7.5 UK units on a single occasion) may affect neurodevelopmental outcomes in the baby <sup>w26</sup>	Advise a woman planning a pregnancy to avoid drinking alcohol (or to drink no more than one to two UK units once or twice a week) around conception and in the first three months of pregnancy because it may be associated with an increased risk of miscarriage <sup>w27</sup>
Caffeine	Caffeine is associated with delayed conception <sup>w28 w29</sup> but has no teratogenic effects in humans. <sup>w30</sup> There is a possible association between greater caffeine intake (>145 mg/day) and late miscarriages or stillbirths, <sup>w31</sup> but rigorous review of all studies found methodological limitations. <sup>w32</sup> A recent prospective cohort study reported no such association <sup>w33</sup>	Women trying to conceive should limit caffeine intake to no more than 200 mg caffeine (two cups of coffee or four cups of tea a day). <sup>w34</sup> There is insufficient evidence on birth weight and other pregnancy outcomes to recommend caffeine avoidance <sup>w35</sup>
Substance misuse	The likely neurobiological effects of cannabis include effects on the child's behaviour and mental health. <sup>w36</sup> Prenatal exposure to cocaine is significantly associated with preterm birth, low birthweight infants, and small for gestational age infants. <sup>w37</sup> Heroin is associated with miscarriage, fetal growth restriction, preterm labour, <sup>w38</sup> and increased risk of infections such as HIV, hepatitis B, and hepatitis C	Counsel a woman about the effects of illicit drugs on the fetus. If feasible, offer women interventions and multidisciplinary input before pregnancy to reduce the risks to maternal and fetal health. Offer methadone maintenance treatment and other interventions to women who are dependent on opiates to reduce the risks to the fetus and maternal health <sup>w39</sup>
Optimisation of weight and diet	Obesity is associated with increased risk of neural tube defects, cardiac defects, abdominal wall defects, orofacial defects, <sup>w40</sup> miscarriage, <sup>w41</sup> stillbirth, <sup>w42</sup> pre-eclampsia, <sup>w43</sup> and diabetes <sup>w44</sup>	Weight loss is associated with a decreased risk of type 2 diabetes and cardiovascular disease in epidemiological studies. <sup>w45</sup> Lifestyle interventions such as a low energy diet or diet with exercise are associated with a reduction in hypertension and type 2 diabetes. <sup>w46</sup> Advise women to maintain their body mass index at 19-25 through regular exercise (30 minutes a day on 5 days a week) and a nutritious diet <sup>w47</sup>
Blood pressure	Risk for subsequent pre-eclampsia significantly increases when blood pressure at booking is >130/80 mm Hg. <sup>w48</sup> Established risk factors for pre-eclampsia (such as obesity and nulliparity) are associated with higher blood pressure in early pregnancy <sup>w49</sup>	Physical exercise, weight reduction, limitation of sodium intake and alcohol consumption, and consumption of a healthy diet may lower blood pressure. <sup>w50</sup> Women with established hypertension need treatment (table 3). Start low dose aspirin for pre-eclampsia prophylaxis once pregnancy is confirmed <sup>w51</sup>
Oral health	Periodontal disease may be associated with adverse pregnancy outcomes such as preterm birth <sup>w52</sup>	Recommend annual dental check-ups
Vitamin D deficiency	Deficiency is associated with rickets (if severe) and suboptimal bone size and density in the infant (if less severe); there is an uncertain association with adverse maternal outcomes, including pre-eclampsia and gestational diabetes <sup>w53</sup>	Advise a woman at particular risk of vitamin D deficiency (South Asian, African, Caribbean, or Middle Eastern family origin; limited exposure to sunlight; diet particularly low in vitamin D; prepregnancy body mass index above 30) to take 10 µg of vitamin D a day routinely. All pregnant and breastfeeding women are advised to take 10 µg of vitamin D a day, <sup>w54</sup> but women who are deficient (or at high risk of deficiency) may need higher doses
Intimate partner violence	Consequences include unintended pregnancy, sexually transmitted infections, trauma, and death	In the US, doctors are recommended to screen all women of reproductive age and offer help to those who are affected. Intensive advocacy input may reduce subsequent physical abuse, but wider evidence for long term benefit is still lacking. <sup>w55</sup> The most recent National Institute for Health and Clinical Excellence guideline for antenatal care urged evaluations of appropriate interventions before universal screening is introduced <sup>w27 w56</sup>

**Table 2| Infections with particular impact on the fetus**

Infection	Effects of congenital infection	Prevention
Rubella <sup>w57</sup>	Sensorineural deafness, ocular abnormalities including glaucoma or cataracts, cardiovascular defects such as patent ductus arteriosus or septal defects, brain damage including mental retardation, microcephaly, or spastic diplegia	Routine vaccination
Varicella zoster <sup>w58</sup>	Skin lesions in dermatomal distribution (76%), neurological defects (60%), eye diseases (51%), and skeletal anomalies (49%)	Vaccination is available in many countries but is not routinely given in the UK
Toxoplasmosis <sup>w59</sup>	Chorioretinitis, hydrocephalus and intracranial calcifications; neurological problems such as microcephaly, learning difficulties, and mental disability	Avoidance of cat litter, undercooked meat, and raw cured meat
Cytomegalovirus <sup>w60</sup>	10-15% present with manifestations at birth including petechiae; hepatomegaly; splenomegaly; hepatitis; or neurological signs such as microcephaly, chorioretinitis, and intracranial calcification. 40-58% of these infants develop adverse outcomes including neurological problems, sensorineural deafness, and cerebral palsy	Hand washing with soap and water, especially if handling items used by young children

Table 3| Drugs that need review

Drug	Potential teratogenic risk <sup>w61</sup>	Alternative to consider
Angiotensin converting enzyme inhibitors and angiotensin receptor blockers	Increase risk of neurological and cardiac congenital abnormalities. Affect fetal renal function; skull defects and oligohydramnios have also been reported	Nifedipine, labetalol, or methyldopa. <sup>w51</sup> Consider prepregnancy conversion to amlodipine in women with prepregnancy hypertension (once daily, well tolerated, safe in pregnancy)
Antidepressants: selective serotonin reuptake inhibitors (SSRIs) and lithium	The main cardiovascular defects associated with SSRIs are septal defects and neural tube defects; the absolute risk is low and benefit usually outweighs risk for major depression. Risk is highest for paroxetine and lower for sertraline. <sup>w61</sup> Lithium is associated with cardiac abnormalities but the absolute risk is low	Discuss the benefit to risk ratio for each woman. <sup>w62</sup> For many women already on a SSRI, sertraline may be the best option, but alternatives (tricyclic antidepressants) can be considered
Antibiotics	Tetracycline can cause dental discoloration. There is a theoretical risk of malformations with trimethoprim (folate antagonist)	Consider penicillin or cephalosporins for long term prevention of urinary tract infection
Non-steroidal anti-inflammatory drugs	These drugs can cause premature closure of ductus arteriosus if used in the 3rd trimester	Avoid use in 3rd trimester unless benefit outweighs the risks and consider other analgesics, such as paracetamol or codeine
Warfarin	Associated with cartilage defects, skeletal defects, brain defects, and eye anomalies in the 1st and 2nd trimesters; associated with intracranial haemorrhage in the 3rd trimester	Consider low molecular weight heparin—liaise with a secondary care specialist before conversion
Antiepileptics	Valproate carries the highest risk of impaired neurocognitive development and fetal malformations such as neural tube defects. Phenytoin can cause fetal hydantoin syndrome (microcephaly, intrauterine growth restriction, and mental disability)	Liaise with a secondary care specialist before conversion. Consider lamotrigine or levetiracetam for women with epilepsy or alternative mood stabilisers for women with bipolar disorder
Cytotoxics	Alkylating drugs, anthracyclines, cytotoxic antibiotics, vinca alkaloids (such as etoposide) have been shown to be teratogenic and mutagenic in animal studies. Antimetabolites (such as methotrexate) have been shown to be toxic in animal studies	Effective contraception is needed during treatment; ensure adequate folic acid supplementation. Advise a woman planning to conceive to stop these drugs only after discussion with her hospital specialist
Immunosuppressants	Mycophenolate mofetil is teratogenic; it causes microtia, low set ears, and other congenital malformations	Effective contraception is needed before treatment, during treatment, and for six weeks after discontinuation of treatment
Isotretinoin	Has a teratogenic effect in animal studies	Effective contraception is needed for at least one month before starting treatment, during treatment, and for at least one month after stopping treatment
Statins	Congenital anomalies have been reported in animal studies; decreased synthesis of cholesterol possibly affects fetal development	Avoid in pregnancy; effective contraception is needed during treatment and for one month afterwards