



What is the effectiveness of antenatal care? (Supplement)

December 2005



ABSTRACT

This is a Health Evidence Network (HEN) evidence report on antenatal care (ANC). This report is a supplement to the 2003 HEN report on the same subject (<http://www.euro.who.int/Document/e82996.pdf>). It is a review of the best available evidence in the scientific literature regarding ANC interventions. It identifies evidence on effective ANC interventions, as well as on those that are not effective but still used, perhaps because of tradition. Additionally, it identifies interventions whose effectiveness is still unknown.

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Summary

The issue

Antenatal Care (ANC) means “care before birth”, and includes education, counselling, screening and treatment to monitor and to promote the well-being of the mother and foetus. The current challenge is to find out which type of care and in what quantity is considered sufficient to ensure good quality of care for low-risk pregnant women. Only interventions of proven effectiveness, for which benefits largely overcome possible harms, and those acceptable to pregnant women and their families, should be offered.

This report is a supplement to the 2003 HEN synthesis report. It is a review of the best available evidence in the scientific literature regarding ANC interventions. It identifies evidence on effective ANC interventions, as well as on those that are not effective but still used, perhaps because of tradition. Additionally, it identifies interventions whose effectiveness is still unknown.

The findings

Evidence-based effective interventions for ANC include:

- antenatal education for breast feeding;
- energy/protein supplementation in women at risk for low birth weight;
- folic acid supplementation to all women before conception and up to 12 weeks of gestation to avoid neural tube defects in the foetus;
- iodine supplementation in populations with high levels of cretinism;
- calcium supplementation in women at high risk of gestational hypertension and in communities with low dietary calcium intake;
- smoking and alcohol consumption cessation for reducing low birth weight and preterm delivery;
- acupressure (sea bands) and ginger for nausea control;
- bran or wheat fibre supplementation for constipation;
- exercise in water, massages and back care classes for backache;
- screening for pre-eclampsia with a comprehensive strategy including an individual risk assessment at first visit, accurate blood pressure measurement, urine test for proteinuria and education on recognition of advanced pre-eclampsia symptoms;
- anti-D given during 72 hours postpartum to Rh-negative women who have had a Rh-positive baby;
- Down's syndrome screening;
- screening and treatment of asymptomatic bacteriuria during pregnancy;
- screening of hepatitis B infection for all pregnant women and delivery of hepatitis B vaccine and immunoglobulin to babies of infected mothers;
- screening for HIV in early pregnancy, a short course of antiretroviral drugs, and caesarean section for infected mothers at 38 weeks, to reduce vertical transmission;
- screening for rubella antibody in pregnant women and postpartum vaccination for those with negative antigen;
- screening and treatment of syphilis;
- routine ultrasound early in pregnancy (before 24 weeks);
- external cephalic version at term (36 weeks) by skilled professionals, for women who have an uncomplicated singleton breech pregnancy; and
- a course of corticosteroids given to women at risk of preterm delivery to reduce respiratory distress syndrome in the baby and neonatal mortality.

Sexual intercourse and moderate aerobic exercise have been found safe during pregnancy.

Antenatal care from midwives or general practitioners in low-risk pregnancies is cost-effective. A model of ANC with a restricted number of visits for low-risk women has been shown to be safe, more sustainable, and possibly as effective as models with higher number of visits.

While for some interventions there is clear evidence of effectiveness or ineffectiveness, for many there is still uncertainty due to a lack of well-conducted randomized trials.

Policy considerations

- ANC is a right for any pregnant women. Therefore interventions proved effective in the scientific literature should be provided universally, free of charge.
- The package of interventions included in routine ANC should be based on effectiveness; local epidemiology of specific diseases in each country, local priorities and resources; and the preferences and values of recipients.
- The model of care developed by WHO seems the best evidence-based package for low-risk pregnant women. Continuous ANC from a midwife seems to be the most cost-effective way to provide this type of care.
- There are still interventions of unproven effectiveness in use. More research in these areas is needed.

Type of evidence

Interventions whose effectiveness has been assessed through systematic reviews (SR) of randomized or quasi-randomized controlled trials (RCT) were included. Priority was given to RCT, but observational studies were also included when needed. This document is a technical supplement to the 2003 HEN report.

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Introduction

The aim of Antenatal care (ANC) is to assist women to remain healthy, finding and correcting adverse conditions when present, and thus aid the health of the unborn (1–3). ANC should also provide support and guidance to the woman and her partner or family, to help them in their transition to parenthood. This implies that both health care and health education are required from health services. This broad definition of ANC is endorsed by national labour laws (4) and by evidence-based clinical guideline (5). Moreover, it introduces the needed holistic approach (biological care and concern with intellectual, emotional, social and cultural needs of women, babies and families) (2) during pregnancy. Care during pregnancy should enable a woman to make informed decisions, based on her needs, after discussing matters fully with the professionals involved. Any interventions offered in the antenatal period should be of proven effectiveness and be acceptable to the recipients. Both the individual components and the full package of ANC should conform to these criteria.

Complex examinations and a variety of combination of interventions are part of modern ANC. Nevertheless, there is a huge variety of tests and medical procedures included in routine ANC worldwide (6). Some of these interventions are based on evidence, but many of them are only based on long-held traditions. The state of the scientific evidence of risks and benefits of ANC interventions is a concern of health policy-makers. Another important concern is the level of care sufficient to delivering high-quality care for pregnant women.

Assessment of ANC should be carried out by well designed clinical trials for each intervention (7). The best evidence comes from randomized controlled trials (RCT), in which pregnant women are randomly assigned to either an experimental group that receives the intervention, or a control group that does not. Differences in results are then compared. Observational studies may also shed some light on the utility of these interventions. Other types of studies from social science (qualitative research) may provide other relevant evidence. Evidence-based clinical guidelines for clinical practice have been derived from the best of such evidence.

This document is a technical supplement to the HEN report published in 2003 (8). It is a review of the best available evidence in the scientific literature regarding ANC interventions. It identifies evidence on effective ANC interventions, as well as on those that are not effective but still used, perhaps because of tradition. Additionally, it identifies interventions whose effectiveness is still unknown. This supplement includes new information on:

- provision and organization of care
- lifestyle considerations
- management of common symptoms
- screening for foetal anomalies
- screening for infections
- foetal growth and well-being diagnosis
- management of breech presentation at term.

Additionally, an extension of some interventions described in the previous assessment are also included (screening for asymptomatic bacteriuria, diagnosis and management of HIV and syphilis).

This review focuses on interventions used routinely in everyday clinical practice, intended to monitor and promote the well-being of the mother and the foetus. The management of specific condition such as external cephalic version and corticosteroids for preterm delivery are included due to their potential high impact on maternal and neonatal outcomes. Finally, evidence on costs and cost-effectiveness of some interventions is presented at the end of the report. However, extrapolation of cost-effectiveness results from one country to another should be made with caution, due to the many variables among countries (e.g. organization of care and costs of interventions) that might affect the results of any cost-effectiveness study.

Sources for this review

Interventions whose effectiveness has been assessed through systematic reviews of randomized or quasi-randomized controlled trials (RCT) were included. Whenever strong evidence on important topics was lacking, a search of primary papers through medical databases (Medline, PubMed) was performed. Priority was given to RCTs, but observational studies were also included when needed.

The present review has relied in particular in the United Kingdom's National Collaborating Centre for Women's and Children's Health (NCC-WCH), Antenatal care clinical guideline (5). Additionally, updated systematic reviews from the Cochrane Library up to 2005 have been used. Finally, other relevant primary papers have been included. See Annex 1 for details of the literature search strategy and methods.

Findings

Provision and organization of care

Midwife and General Practitioner-led models of care for low-risk women (with uncomplicated pregnancies) improve positive outcomes and are appreciated by women (9). Routine involvement of obstetricians in the care of low-risk women at scheduled times does not appear to improve perinatal outcomes compared to involving obstetricians only when complications arise (9). ANC provided by a small group of carers with whom the woman feels comfortable improves the maternal feeling of preparedness for labour and child care as well as neonatal and maternal clinical outcomes (10).

Home-like settings for childbirth are associated with reduced likelihood of medical intervention. The evidence shows that the number of spontaneous vaginal births is higher, breastfeeding initiation more common and maternal satisfaction better in home-like institutional birth settings compared to conventional institutional settings. However, the evidence shows an increased risk of perinatal mortality, the reasons of which are not fully established. Thus, there is an increased need for monitoring early signs of complications in these home-like settings (10).

Based on a study supported by WHO (11), it has been suggested that a reduced scheme based on four goal-oriented antenatal visits could be as effective, in terms of maternal and neonatal mortality and morbidity, as schemes based on a higher number of visits. A systematic review assessing patterns of routine ANC for low-risk women concludes that the WHO scheme can be safely implemented (9), although women are less satisfied with it.

A system in place whereby women keep their own obstetric notes improves clinical safety (12,13). Additionally, the availability of antenatal records improves the women's sense of control and satisfaction (14).

Antenatal education

Antenatal education, especially when combined with postnatal education using a set of different interventions, is effective for increasing the breastfeeding initiation rate and prolonging exclusive breastfeeding (15-17). However, there is little and weak evidence of the effectiveness of antenatal classes (on, for example, mechanisms of labour and birth and relaxation techniques) and delivering written information about ANC. Therefore, it is not possible to give conclusive recommendations on these interventions (18). Moreover, the evidence shows that individualized prenatal education directed toward avoidance of caesarean births does not increase the rate of vaginal birth after a previous caesarean section (18,19). There is not enough evidence to evaluate the use of a specific set of criteria for self-diagnosis of active labour (20). The effects of general antenatal education for childbirth and/or parenthood remain unknown (18).

In settings with limited resources, WHO supports the implementation of “birth preparedness” or “birth plans”, which are thought to reduce maternal and perinatal mortality. These actions prepare for emergencies and assist women and their families in ensuring that they have what they need for the birth. They aim at increasing awareness of danger signs, reducing the delays in receiving skilled care and improving intra-family communications and relations with providers (21). “Birth and emergency preparedness cards” are used, along with establishing close collaboration with community health workers and traditional birth attendants for additional social support (22). Birth preparedness may also include identification of the closest appropriate care facility, funds for birth-related and emergency expenses and identifying compatible blood donors in case of emergency (23). Little empirical evidence exists to examine the effectiveness of these interventions, and existing studies are flawed due to small scale and sample design (24); nevertheless, a recent cluster-randomized trial in Nepal showed a 30% reduction in neonatal mortality and a 75% reduction in maternal mortality in communities where some components of the birth preparedness plan (e.g., local female facilitators to activate, strengthen and support community groups of pregnant women, community generated funds for maternal or infant care, production and distribution of clean delivery kits, home visits by community group members to newly pregnant mothers, and information about perinatal health) were implemented (25).

Lifestyle considerations

Diet and supplementation

Balanced energy/protein supplementation improves foetal growth and may reduce the risk of foetal and neonatal death in nutritionally vulnerable women or those at risk for low birth weight children (26). High-protein supplementation alone is not beneficial and it is associated with an increased risk of small for gestational age (SGA) (26). Energy/protein restriction for pregnant women who are overweight or exhibit high weight gain is unlikely to be beneficial and may be harmful to the infant (26).

Dietary supplementation with folic acid, before conception and up to 12 weeks of gestation, reduces the risk of neural tube defects (anencephaly, spina bifida). The recommended dose is 400 micrograms per day (27). Some specific supplementations have found to be effective in selected circumstances. Iodine supplementation in a population with high levels of endemic cretinism results in an important reduction in the incidence of the condition with no apparent adverse effects (28). Calcium supplementation appears to reduce the risk of high blood pressure in pregnancy, particularly for women at high-risk and in communities with low calcium intake. Optimum dosage and the effect on more substantive outcomes require further investigation (29). Based on the possible association between maternal anaemia and negative perinatal outcome (30), it is assumed that iron supplementing in anaemic pregnant women may reduce the incidence of low birth weight and perinatal mortality, as well as adverse maternal outcomes. However, while there is clear evidence of a positive effect of iron supplementation during pregnancy in preventing low blood count at delivery or at six weeks post-partum, there is no evidence of any effect, beneficial or harmful, for the mother or the baby (31–33). Finally, routine iron supplementation for pregnant women may have unpleasant side effects like gastro-intestinal irritation, nausea and epigastric pain, exacerbation of diarrhoea in patients with inflammatory bowel disease, and constipation (31,34). There is insufficient evidence to evaluate the maternal and neonatal health effectiveness of either vitamin D (35) or magnesium supplementation (36). The possible beneficial effects on preterm delivery of zinc or pyridoxine supplementation during pregnancy need to be further evaluated (37); a single trial showed that the latter may have a beneficial effect on dental decay in pregnant women (38).

A low salt diet is often unpalatable. There is no evidence that advice to reduce salt intake during pregnancy has any beneficial effect in the prevention or treatment of pre-eclampsia, or any other outcome. Therefore, salt consumption during pregnancy should remain a matter of personal preference (39).

Other lifestyle factors

Neither beginning nor continuing a moderate course of aerobic exercise during pregnancy has been associated with any adverse outcomes (40), nor has sexual intercourse in pregnancy (41, 42). Smoking cessation programs in pregnancy are effective in smoking cessation and reducing low birth weights and preterm births (43). Heavy alcohol consumption during pregnancy is associated with low birth weights, preterm delivery (44), and brain injury (45). Moderate alcohol consumption (one standard unit per day: 2 cl of spirits, one small glass of wine, or a half pint of ordinary strength beer, lager or cider) is not dangerous for the foetus (46). An observational study suggests that motivational intervention is effective in reducing alcohol consumption in pregnancy (47).

Management of common symptoms

Women with persistent vomiting may need to be given extra fluids. Nausea can be controlled with acupressure (sea bands) or consumption of ginger (48); both seem to be effective and show no side effects. Antihistamines also work well for nausea but are likely to make women feel sleepy. There is not enough evidence to recommend vitamin B6 (pyridoxine) (48). Diet modification, such as bran or wheat fibre supplementation, is effective for constipation, and pregnant women should receive information on this topic (49). Exercising in water, massage therapy, and group or individual back care classes might help to ease backache during pregnancy. Women should be informed on these options (50).

Clinical examination of pregnant women

Routine breast examination during antenatal care does not increase the chances of successful breastfeeding (51). Routine antenatal pelvic examination does not accurately assess gestational age, nor does it accurately predict preterm birth or cephalopelvic disproportion, while it increases the risk of premature rupture of membranes (52). Routine vaginal examination to assess the cervix is not effective to predict preterm birth (53). Pelvimetry (X-ray) increases the risk of caesarean section and does not have any benefit for the pregnant woman, foetus or neonate (54).

Routine antenatal screening for the detection of postnatal depression with the Edinburgh Postnatal Depression Scale, has poor sensitivity (55). Antenatal educational interventions do not reduce postnatal depression (56), which is more frequent in women with previous episodes of puerperal (post-delivery) illness (with a 33–50% chance of recurrence). Moreover, the women who have had a previous puerperal illness have also the highest risk for suicide (57). A careful monitoring and referral system for women with previous psychosis should therefore put in place. However, there are no clear data on the best interventions to offer.

A comprehensive strategy to detect pre-eclampsia includes an individual risk assessment for pre-eclampsia at first visit, accurate blood pressure measurement, urine test for proteinuria and education on recognition of advanced pre-eclampsia symptoms. At least one-third of pre-eclampsia cases develop in women with normal blood pressure. Women presenting risk factors for pre-eclampsia, as established in the first prenatal visit, should be assessed more frequently. Since blood pressure measurement is prone to inaccuracy, standardized equipment, as well as standardized techniques and conditions for blood-pressure measurement, should be used by all personnel in order to have valid comparisons of measurement (58). When measuring blood pressure, a urine sample should be tested for proteinuria (5). Pregnant women should be informed of the symptoms of advanced pre-eclampsia, as they may be associated with poorer pregnancy outcomes for the mother or baby (5).

Screening for haematological conditions

All pregnant women should undergo blood grouping determination. Anti-D (formerly Rh), given to pregnant women within 72 hours after childbirth, reduces the risk of RhD alloimmunization in Rh-negative women who have given birth to an Rh-positive infant. However evidence of the optimal dose is limited. Higher doses (up to 200 micrograms) have been shown to be more effective than lower doses (up to 50 micrograms) in preventing RhD alloimmunization in a subsequent pregnancy (59).

Routine administration of 100 micrograms (500 IU) anti-D at 28 weeks and 34 weeks gestation to Rh-negative women in their first pregnancy can safely reduce the risk of RhD alloimmunization from 1.5% to about 0.2%. Although such a policy is unlikely to confer benefit or improve outcome in the present pregnancy, fewer women will have Rh-D antibodies in their next pregnancy. However, the costs of prophylaxis should be weighed against the costs of care for women who become sensitized and their infants. Additionally, local availability of anti-D gamma globulin must be taken into account (60).

Screening for gestational diabetes

Untreated gestational diabetes (GDM, an abnormal, pregnancy-related glucose level in the mother) can lead to serious problems for mother and foetus. At present, GDM screening appears to be hampered by the lack of a clear definition of risk, and agreed diagnostic criteria. Risk factors for GDM are neither selective nor specific enough, and are therefore useless (61). However, there is good evidence showing that interventions and treatments, like dietary counselling, blood glucose monitoring, and insulin (if appropriate), lead to improved outcomes for mother and foetus (62–64). The best test at present is probably the glucose challenge test, preferably combined with a fasting plasma glucose (65).

Screening for foetal anomalies

Screening for Down's syndrome is effective, but a woman's decision not to be tested should be accepted equanimously. The test should be offered only in health care services that can provide pre-test and post-test counselling (where the benefits and risks of the screening programme as well as the consequences of a positive test result are explained to the women), high quality standardized ultrasound equipment with an experienced ultrasonographer and monitoring of screening performance. When these conditions are met, the best set of tests to offer is an integrated test, which includes nuchal translucency – assessed through ultrasonography at 10–14 weeks gestation – plus serological tests conducted at 11–14 weeks and at 14–20 weeks. Women testing positive in the integrated test could undergo amniocentesis. However, the integrated test has a detection rate (sensitivity) of 90%, and a false positive rate of 2.8%. This data mean that for every nine foetuses affected by Down's syndrome detected, one unaffected foetus will die due to amniocentesis (66).

Screening for infections

Asymptomatic bacteriuria

Antibiotics are effective in clearing asymptomatic bacteriuria (bacteria in the urine) and in preventing symptomatic kidney infection in the mother. The incidence of preterm delivery or low birth weight is also reduced when bacteriuria is treated with antibiotics (67). There is not enough evidence to evaluate whether single dose (lower cost and better compliance) or longer duration doses are equivalent.

Hepatitis B virus

Mother-to-child transmission of the hepatitis B (HB) virus is preventable in 95% of cases through administration of vaccine and immunoglobulin to the baby at birth (68,69). To prevent mother-to-child transmission, all pregnant women who are carriers of HB virus need to be identified. Blood sample screening is the accepted standard for antenatal screening for HB virus. It consists of three stages: screening for HBs Antigen, confirmatory testing of a new sample upon a positive result and, where infection is confirmed, testing for HBe Antigen in order to determine whether the baby will need immunoglobulin in addition to vaccine (70).

Asymptomatic bacterial vaginosis

Evidence from randomized controlled trials (RCTs) indicates that screening and treating healthy pregnant women for asymptomatic bacterial vaginosis does not lower the risk for preterm birth, nor for other adverse reproductive outcomes like the risk of preterm prelabour rupture of membranes. In women with a previous preterm birth, treatment did not affect the risk of subsequent preterm birth; however, it may decrease the risk of preterm prelabour rupture of membranes and low birthweight (71).

Human Immunodeficiency Virus (HIV)

Early diagnosis of HIV infection in pregnant women optimizes their medical and psychosocial care, decreases the incidence of mother-to-child transmission, and decreases the risk of horizontal transmission to sexual partners. New, third-generation HIV tests have reduced false-positive rates (72).

Short-course zidovudine and single-dose nevirapine are effective therapies for reducing mother-to-child transmission of HIV. The challenge for low and middle income countries will be to institutionalize this therapy in practice. In industrialized countries, antiretroviral therapy aimed primarily at preventing disease progression in the mother is the standard of care (73).

Results coming from a single multicentric trial show that compared with vaginal delivery, there is a significant reduction in the risk of mother-to-child transmission of HIV infection with elective caesarean at 38 weeks of gestational age (74). The trade-off between benefits and harms in countries with high risk of intra-operative infection or limited resources should be considered when deciding whether to implement this policy. The addition of hyperimmune immunoglobulin to zidovudine does not appear to have any additional effect on the risk of mother-to-child transmission (74).

Rubella

Screening for the rubella antibody in pregnancy helps to identify women at risk, so that rubella vaccination can be offered postpartum to protect future pregnancies (75). Risk of congenital rubella syndrome depends on the availability of local national immunization programs. A recent review conducted in the WHO European Region Member States (76) confirms the wide heterogeneity of policies regarding rubella vaccination. These differences are due both to contextual and economical reasons. However, all economic analysis are consistent on the positive cost/benefit ratio programs that implement rubella eradication (77–79).

Toxoplasmosis

Pregnant women should be informed that simple and feasible primary prevention measures are effective against toxoplasmosis infection (80). It is not clear if routine toxoplasmosis screening in pregnant women is effective in reducing the prevalence of congenital toxoplasmosis. The serological test has a high percentage of false positive results, that may lead to unneeded anxiety and termination of healthy foetuses (81). Screening of toxoplasmosis during pregnancy is a routine practice in some countries, like Italy, while it is not recommended in others, like the United Kingdom. The difference in policies is due to different prevalence of toxoplasmosis infections (10–40%). Despite the availability of a large number of studies, it is still not clear whether antenatal treatment in women with presumed toxoplasmosis reduces the vertical transmission of infection (82,83).

Screening for toxoplasmosis is expensive, and there is not good evidence regarding the impact of screening and treatment on clinical outcomes for the foetus. Therefore, evaluation studies of good quality are necessary. Moreover, in countries where screening or treatment is not currently a routine practice, these technologies should not be available outside the context of a carefully controlled trial.

Syphilis

Antenatal screening and treatment of syphilis is a feasible and a cost-effective intervention (84,85). Non-treponemal tests – such as *rapid plasma reagin* (RPR) test and *venereal diseases research laboratory* (VDRL) test – are as effective and cheaper and easier to perform than treponemal tests. However, the former tests have low sensitivity (i.e. the proportion of correct results among women who have the disease) and specificity (i.e. the proportion of correct results among women who are actually free of the disease). In developed countries positive non-treponemal tests are usually confirmed by a treponemal test. Treponemal tests like *Treponema pallidum haemagglutination assay* (TPHA) have high sensitivity and specificity, but they are expensive. Therefore, when a country has a

lack of resources along with a high prevalence of syphilis, it is advisable to treat all, at non-treponemal tests seropositive pregnant women (86).

Penicillin is an effective treatment for syphilis during pregnancy. However, more research is needed regarding the best dosage and duration of treatment (87).

Foetal growth and well-being diagnosis

Routine ultrasound in early pregnancy (before 24 weeks) is effective in assessing gestational age, early detection of multiple pregnancies and early detection of clinically unsuspected foetal malformation at a time when termination of pregnancy is possible (88,89).

Routine late pregnancy ultrasound in low-risk women or unselected populations, does not benefit the mother or the baby (90). There is a lack of data about both the potential psychological effects of routine ultrasound in late pregnancy (after 24 weeks) and the effects on both short and long-term neonatal and childhood outcomes (90). The use of uterine Doppler ultrasound for the prediction of pre-eclampsia, foetal growth restriction and perinatal death in low-risk populations has poor positive predictive value (91, 92). Routine foetal-movement counting is not effective for the prevention of late foetal death in normally formed singletons (93). Cervical shortening, identified by transvaginal ultrasound examination (94), and increased levels of foetal fibronectin (95) are associated with increased risk for preterm birth. This information does not improve outcomes in healthy pregnant women (94,95). There is too little evidence to show whether measuring symphysis-fundal height at antenatal visits leads to better perinatal outcomes (96), and antenatal cardiotocography for foetal assessment has no effect on perinatal outcomes (97).

Management of specific conditions

Breech presentation at term

External cephalic version (ECV) in women who have an uncomplicated singleton breech pregnancy at term (36 weeks) reduces the chance of breech birth and caesarean section (98). The chances of success increase when ECV is associated with administration of tocolytic drugs, to relax uterine muscles (99). However, there are some contraindications, including women in labour or with a uterine scar or abnormality, foetal compromise, ruptured membranes, vaginal bleeding or some conditions like severe hypertension.. ECV before term, for babies in the breech position, does not lead to cephalic presentation at term (100). Moxibustion of acupoint BL67 in primigravidae (women in their first pregnancy) with breech presentation at 33 weeks of gestation, increases cephalic presentation at delivery (101).

One review has found insufficient evidence from well-controlled trials to support the routine use in clinical practice of certain postures to change the foetus's position to head down (102).

Corticosteroids for preterm newborns

Corticosteroids given to women prior to preterm delivery (as a result of either preterm labour or elective preterm delivery) are effective in preventing both respiratory distress syndrome in the baby and neonatal mortality (103). There is insufficient evidence to recommend repeat doses of corticosteroids for women at risk of preterm delivery (104). Moreover, there is not enough evidence to recommend the use of repeated doses of corticosteroids in women who remain undelivered, but are at continued risk of preterm delivery (103).

Annexes 2, 3 and 4 summarize the interventions found to be effective, not effective or of unknown effectiveness, respectively.

Cost considerations

This section presents results from economic studies for some of the interventions previously described. The data reported should be interpreted with caution. Transferability of economic evaluation to countries with different health care contexts (epidemiology of diseases, organization of care, etc.) and resources may be limited. However, experiencing a safe pregnancy, labour and delivery is a right in itself, therefore health care policy decisions should not be driven by exclusively economic considerations.

Anti-D administration to Rh-negative women

Economic evaluations (performed mainly in United Kingdom) show that routine anti-D prophylaxis, added to postpartum prophylaxis, for Rh-negative pregnant women is cost-effective when there is a moderate or high probability of subsequent pregnancies (105).

Gestational diabetes mellitus (GDM) screening

In the absence of adequate evidence to determine whether selective or universal screening is effective in improving health outcomes for pregnant women and babies, reliable estimates of the cost-effectiveness of screening are not possible. The available studies do not include all relevant information related to screening for GDM (the costs of screening, diagnostic tests, various treatments and complications) and data on the extent to which the entire screening process reduces adverse outcomes (caesarean sections and other birth trauma, and morbidity such as hypoglycaemia among neonates and later diabetes among mothers), and on the net cost per adverse event prevented. Reliable estimates of the costs of GDM for women who are not screened are not available (61,65).

Down's syndrome screening

Two cost-effectiveness evaluations of Down's syndrome screening performed in the United Kingdom have been identified (66, 106). The integrated test mentioned above seems to be more cost-effective than other screening strategies, since additional costs due to the screening tend to be offset by savings in the cost of diagnosis arising from the low false-positive rate with the integrated approach (66). However, both studies conclude with caution, and recommend further sensitivity analysis (examination of the extent to which the results of an analysis are affected by changes in methods or assumptions).

Asymptomatic bacteriuria

A cost-effectiveness analysis conducted by the National Collaborating Centre for Women's and Children's Health (NCC-WCH) (5), favours urine culture screening over leucocyte esterase-nitrite dipstick screening.

Rubella

The implementation of a rubella eradication program has a positive cost-effectiveness ratio (77–79). Strategies include mass campaign immunization (107), female adolescent immunization and children of both sexes immunization (108). Nevertheless, it is not clear which strategy show the best cost-effectiveness ratio.

Syphilis

A cost-effectiveness analysis conducted by the NCC-WCH (5) concludes that universal screening (as currently performed in UK) is more cost effective than either screening high-risk groups or no screening at all. Screening for syphilis is also considered cost effective both in developed and developing countries in a recent WHO review (85).

Conclusions

Effective and appropriate antenatal care should be offered to all pregnant women. However, different countries offer different sets of routine ANC, which are hardly based on explicit effectiveness criteria, being mainly linked with long-term tradition or other inexplicit criteria. Some interventions still provided to women with normal pregnancies are not effective, and many of them have not been evaluated. These interventions should be eliminated from basic health care packages, and more research is needed on those interventions of unknown effectiveness.

As pointed out in the previous HEN ANC review (8), debate today is still over the extent of services that should be offered to women with low-risk pregnancies and which is the best service package. The WHO model for low-risk women seems to be the most cost-effective (a restricted number of visits, evidence-based effective interventions) (11). As for the best package, this review has included many interventions, some essential for ANC, and others optional, depending on the health care context and resources available. In an ideal setting, with unlimited resources, all sets of effective interventions described above would be accessible by all pregnant women or women who intend to become pregnant. However, at present it is not possible to establish a common package of routine ANC for WHO European Region Member States. Differences in epidemiology of given conditions, investment priorities, and cultural and social values preclude implementation of a homogeneous ANC package. However, in countries with scarce resources, attention should be primarily focused on a limited set of essential interventions that are effective in reducing relevant adverse outcomes for mothers and babies. These interventions, based on the available evidence and in line with the WHO model for ANC (11) are:

- a strategy for early detection and proper treatment of pre-eclampsia;
- screening for HIV infection and implementation of a strategy to reduce mother to child transmission;
- screening for syphilis and treatment of positive pregnant women;
- screening for rubella and postpartum immunization of susceptible women;
- hepatitis B screening and immunization of babies born of recently infected women;
- administration of corticosteroids to women at risk of preterm birth;
- anti-D administration in Rh-negative women who deliver Rh-positive babies;
- multifaceted intervention aimed to give the woman and the family a positive experience of the pregnancy, labour and delivery, along with parenting and breastfeeding skills.

These interventions should be provided free of charge to all pregnant women to ensure their universal access and utilization.

Annex 1. Literature search strategy and methods

The database of the National Guideline Clearinghouseⁱ was searched. Two guidelines on routine antenatal care were found. One was excludedⁱⁱ since no description of the methodology and literature search strategy was available. Therefore the National Collaborating Centre for Women's and Children's Health (NCC-WCH) clinical guidelineⁱⁱⁱ was the unique guideline included, since it is based on the results of systematic reviews (SRs), presents a full description of the search strategy, has been elaborated by a multidisciplinary panel and has a grading system for the quality of evidence.

Among the full sets of interventions proposed by the NCC-WCH, only those assessed through SRs, RCTs, controlled trials (without randomization) and well designed quasi-experimental studies were included for this review. The NCC-WCH recommendations are updated to 2003. If an SR reported by the NCC-WCH guideline was withdrawn or updated since then, the corresponding information was accordingly changed or deleted.

All newly published or updated SRs from The Cochrane Library^{iv}, starting from the *Cochrane Database of Systematic Reviews*, 4, 2003 to the *Cochrane Database of Systematic Reviews*, 1, 2005, were also included in this review.

Whenever strong evidence on important topics was lacking, a search of primary papers through PubMed Medline^v was performed. Priority was given to RCT, but observational studies were also included when needed. Any additional reference known by the author and suggested by the WHO Regional Office for Europe have been appraised for the level of evidence and included as appropriate.

For cost analysis consideration the National Health Service Economic Evaluation Database (NHS EED)^{vi} was searched and relevant studies were reported, in addition to some cost considerations founded in the NCC-WCH clinical guidelineⁱⁱⁱ.

ⁱ National Guideline Clearinghouse. Rockville, MD, United States Agency for Healthcare Research and Quality (<http://www.guideline.gov/>, accessed 29 September 2005).

ⁱⁱ Institute for Clinical Systems Improvement (ICSI). *Routine prenatal care*. Bloomington, MN, Institute for Clinical Systems Improvement, 2005 (<http://www.icsi.org/knowledge/detail.asp?catID=29&itemID=191>, accessed 29 September 2005).

ⁱⁱⁱ National Collaborating Centre for Women's and Children's Health. *Antenatal care. Routine care for the healthy pregnant woman*. Clinical guideline. London, RCOG Press, 2003 (http://www.rcog.org.uk/resources/Public/pdf/Antenatal_Care.pdf, accessed 29 September 2005).

^{iv} The Cochrane Library [database on the Internet and CD-ROM]. London, John Wiley & Sons Ltd., 2005 (http://www3.interscience.wiley.com/aboutus/sharedfiles/cochrane_transition/, accessed 29 September 2005).

^v PubMed Medline. Bethesda MD, United States National Library of Medicine (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>, accessed 29 September 2005).

^{vi} National Health Service Economic Evaluation Database (NHS EED). York, Centre for Reviews and Dissemination (<http://www.york.ac.uk/inst/crd/nhsdhp.htm>, accessed 29 September 2005).

Annex 2. ANC interventions of proven safety and effectiveness

- antenatal care from midwives or general practitioner in low-risk pregnancies;
- home-like institutional births, when resources, organizational skills and monitoring systems are adequate;
- a model of care with a restricted number of visits for low-risk women;
- giving women their own obstetric notes to carry (including all the essential information on obstetric history, current pregnancy and general medical conditions), and making the antenatal records available for the pregnant women;
- antenatal education for breastfeeding;
- energy/protein supplementation in women at risk for low birth weight;
- folic acid supplementation to all women before conception and up to 12 weeks of gestation to avoid neural tube defects in the foetus;
- iodine supplementation in populations with high levels of cretinism;
- calcium supplementation in women at high risk of gestational hypertension and in communities with low dietary calcium intake;
- sexual intercourse during pregnancy is safe
- moderate aerobic exercise during pregnancy is safe
- smoking and alcohol consumption cessation for reducing low birth weight and preterm delivery;
- acupressure (sea bands), ginger or antihistamines for nausea control, though the last may induce drowsiness;
- bran or wheat fibre supplementation for constipation:
- exercising in water, massages and back care classes for backache;
- screening for pre-eclampsia with blood pressure measurements at first visit and periodically through the remainder of pregnancy;
- urine testing for proteinuria and education on recognition of advanced pre-eclampsia symptoms (women showing risk for pre-eclampsia should be controlled more frequently.);
- anti-D given to Rh-negative women who have had an Rh-positive baby, during the 72 hours postpartum (different policies can be implemented depending on availability of resources);
- Down's syndrome screening;
- screening and treatment of asymptomatic bacteriuria during pregnancy;
- screening of all pregnant women for hepatitis B infection to all pregnant women and delivery of hepatitis B vaccine and immunoglobulin to babies of infected mothers;
- screening for HIV in early pregnancy, short course of antiretroviral drugs, and caesarean section at 38 weeks for infected mothers for the reduction of vertical transmission;
- screening for rubella antibodies in pregnant women and postpartum vaccination to those women with negative antigen;
- screening and treatment for syphilis;
- ultrasound performed routine before 24 weeks of pregnancy;
- external cephalic version at term (36 weeks) by skilled professionals, for women with uncomplicated singleton breech pregnancy (the success rate of external cephalic version increases with administration of tocolytic drugs);
- a course of corticosteroids given to women at risk of preterm delivery to reduce respiratory distress syndrome in the baby and neonatal mortality.

Annex 3. Ineffective ANC interventions:

- high protein supplementation (harmful);
- energy/protein restriction in overweight pregnant women (may be harmful to the foetus);
- iron supplementation (may have unpleasant maternal side effects);
- vitamin B6 (pyridoxine) to control nausea;
- breast examination for increasing chances of breastfeeding;
- routine antenatal pelvic examination to predict preterm labour or cephalopelvic disproportion (increases the chance of premature membrane rupture);
- vaginal examination to predict preterm labour;
- pelvimetry (increases the chances of caesarean section);
- screening and education for postpartum depression;
- screening and treatment of asymptomatic bacterial vaginosis in healthy pregnant women;
- routine third-trimester ultrasound;
- uterine Doppler ultrasound for prediction of pre-eclampsia;
- routine formal foetus movement counting for the prevention of late foetal death in normally formed singletons;
- transvaginal ultrasound monitoring for cervical shortening to avoid preterm birth;
- antenatal cardiotocography for foetal assessment.

Annex 4. ANC interventions of unknown effectiveness

- antenatal education for childbirth and/or parenthood
- use of specific sets of criteria for self-diagnosis delivery
- attending antenatal classes for maternal attachment behaviours and reduction of caesarean births
- vitamin D supplementation
- magnesium supplementation
- zinc supplementation
- pyridoxine supplementation
- reduction of salt intake during pregnancy
- interventions for postnatal depression
- routine screening for gestational diabetes mellitus
- antenatal treatment of pregnant women with suspected toxoplasmosis
- routine second-trimester ultrasound in low-risk pregnant women.

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