Costs and net health effects of contraceptive methods
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Thirteen different methods of contraception were compared with the non-use of contraception. The 13 methods investigated were combined oral contraceptives (OCs), transdermal contraceptive patch (patch), vaginal ring, male condom, diaphragm, copper intrauterine device (IUD), levonorgestrel-releasing IUD, depot medroxyprogesterone acetate (DMPA), estrogen-progestin monthly injection, periodic abstinence, withdrawal, tubal sterilisation, and vasectomy.

Type of intervention
Other: Contraception.

Economic study type
Cost-utility analysis.

Study population
The study population comprised women in average health, who were in a long-term mutually monogamous heterosexual relationship, with an age distribution similar to that observed in an insured population and with smoking rates observed in women of reproductive age.

Setting
The setting was the community. The study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies dating from 1986 to 2004. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a review of published sources, with an expert panel convened to review the literature on contraception. The authors also incorporated several assumptions into their model.

Modelling
The consequences and cost of each method were evaluated using Markov simulation modelling. The model was evaluated by Monte Carlo simulation. The base-case analysis simulated a 2-year time horizon. The effect of varying the time horizon from 1 to 5 years was examined in a sensitivity analysis.

Outcomes assessed in the review
The outcomes assessed were:
the annual probability of acquiring human immunodeficiency virus (HIV) from a seropositive male partner;

the efficacy of male condoms in preventing HIV transmission from male to female;

the annual probability of developing acquired immune deficiency syndrome (AIDS) in women with asymptomatic HIV infection;

the prevalence of HIV in the general male population;

the annual probability of pelvic inflammatory disease (PID);

the relative risk of PID in people using the barrier method, IUDs, or combination hormonal methods;

the annual probability of a urinary tract infection (UTI);

the relative risk of a UTI with diaphragm use;

the relationship between years on combinational hormonal method and the risk of ovarian cancer;

the relative risk of breast cancer with combinational hormonal methods;

the relative risk of myocardial infarction (MI) in combination hormone users who smoke and who do not smoke;

the relative risk of MI in smokers;

the relative risk of stroke in combination hormone users who smoke and who do not smoke;

the relative risk of stroke in smokers;

the relative risk of venous thromboembolic disease (VTE) in combination hormone users;

the fraction of mistimed pregnancies;

the annual probability of ectopic pregnancy;

the relative risk of ectopic pregnancy in copper IUD users, DMPA users, levonorgestrel-releasing IUD users, and after tubal sterilisation;

the age-specific probability of outpatient menstrual-related disorders (MRDs);

the age-specific efficacy of combination hormonal methods in improving MRDs;

the age-specific annual incidence of MRDs following tubal sterilisation;

the age-specific probability of a Caesarean-section;

the age-specific probability of elective abortion;

the age-specific probability of having a premature delivery;

the age-specific probability of spontaneous abortion;

the relative risk of cervical cancer incidence based on the cumulative years of use of barrier methods;

the relative risk of endometrial cancer based on the cumulative years of combination hormone use;

the relative risk of ectopic pregnancy by the number of prior ectopic pregnancies;
the relative risk of ectopic pregnancy by the number of prior episodes of PID;

the age-specific annual probability of pregnancy with levonorgestrel-releasing IUD, vasectomy, monthly injection, DMPA, diaphragm, male condoms, OCs, patch, vaginal ring, periodic abstinence, and withdrawal;

the annual probability of pregnancy based on years since initiation of method using copper IUD and tubal sterilisation;

the excess mortality rate after diagnosis of MI, stroke and VTE;

the case-fatality rate of MI, stroke, VTE, PID, and ectopic pregnancy;

the excess mortality rate due to AIDS;

the mortality rate of tubal sterilisation;

the mortality rate of Caesarean section;

the mortality rate of elective abortion and vaginal delivery;

the excess mortality after diagnosis of breast, cervical, endometrial and ovarian cancer; and

the age-specific mortality of spontaneous abortion.

Study designs and other criteria for inclusion in the review
The effectiveness data and other outcome data were derived from a number of cohort and population-based studies, clinical trials, US vital statistics, and other published material.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Approximately 38 studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The annual probability of acquiring HIV from a seropositive male partner was 0.072.
The efficacy of male condoms in preventing HIV transmission from male to female was 0.85.

The annual probability of developing AIDS in women with asymptomatic HIV infection was 0.006111.

The prevalence of HIV in the general male population was 0.00131.

The annual probability of PID was 0.01.

The relative risk of PID was 0.6 in barrier method users, 1.5 in IUD users, and 0.3 in combination hormonal method users.

The annual probability of a UTI was 0.108.

The relative risk of a UTI with diaphragm use was 2.83.

The slope of the relationship between years on combination hormonal method and risk of ovarian cancer was -0.122.

The relative risk of breast cancer with combination hormonal methods was 1.

The relative risk of MI in combination hormone users was 41.3 for those who smoke and 4.47 for those who do not smoke.

The relative risk of MI in smokers was 8.02.

The relative risk of stroke in combination hormone users was 2.7 for those who smoke and 1 for those who do not smoke.

The relative risk of stroke in smokers was 2.7.

The relative risk of venous VTE in combination hormone users was 4.15.

The fraction of mistimed pregnancies was 0.634.

The annual probability of ectopic pregnancy was 0.005.

The relative risk of ectopic pregnancy was 7.4 in copper IUD users, 1 in DMPA users, 50 in levonorgestrel-releasing IUD users, and 32 after tubal sterilisation.

The age-specific probability of outpatient MRDs was 0.0029 in women aged 15 - 49 years.

The age-specific efficacy of combination hormonal methods in improving MRD was 0.8 in women aged 15 - 49 years.

The age-specific annual incidence of MRD following tubal sterilisation ranged from 0.002 in women aged 20 - 29 to 0.006 in women aged 40 - 44.

The age-specific probability of a Caesarean section ranged from 0.150 in women aged 15 - 19 to 0.347 in women aged 40 - 49.

The age-specific probability of elective abortion ranged from 0.146 in women aged 30 - 34 to 0.292 in women aged 15 - 19.

The age-specific probability of having a premature delivery ranged from 0.067 in women aged 25 - 29 to 0.183 in women aged 45 - 49.

The age-specific probability of spontaneous abortion ranged from 0.1226 in women aged 20 - 24 to 0.183 in women aged 45 - 49.
The relative risk of cervical cancer incidence based on the cumulative years of using barrier methods ranged from 0.2 (used for more than 10 years) to 1 (never used them).

The relative risk of endometrial cancer based on the cumulative years of using combination hormonal methods ranged from 0.4 (used for more than 2 years) to 1 (used for less than one year).

The relative risk of ectopic pregnancy by number of prior ectopic pregnancies ranged from 1 (no prior episode) to 610 (2 prior episodes).

The relative risk of ectopic pregnancy by number of prior episodes of PID ranged from 1 (no prior episodes) to 125 (3 prior episodes).

The age-specific annual probability of pregnancy with:

- levonorgestrel-releasing IUD was 0.1% in women aged 15 - 44;
- vasectomy was 0.2 in women aged 15 - 44;
- monthly injection was 0.6 in women aged 15 - 44;
- DMPA was 0.4 in women aged 15 - 44;
- diaphragm ranged from 22.5 in women aged 35 - 44 to 38.2 in women aged 20 - 24;
- male condoms ranged from 5.1 in women aged 35 - 44 to 27.9 in women aged 20 - 24;
- OCs ranged from 3.2 in women aged 35 - 44 to 13.1 in women aged 15 - 19;
- patch ranged from 2.5 in women aged 40 - 44 to 7.5 in women aged 15 - 19;
- vaginal ring ranged from 2.6 in women aged 35 - 39 to 5.8 in women aged 15 - 19;
- periodic abstinence ranged from 7.6 in women aged 35 - 44 to 29.6 in women aged 15 - 19; and
- withdrawal ranged from 7.6 in women aged 35 - 44 to 41.8 in women aged 20 - 24.

The annual probability of pregnancy based on years since initiation of the method was 0.8 in the first year of using a copper IUD and 0.2 subsequently. The corresponding values for tubal sterilisation were 0.6 in the first year, 0.2 in the second and third year after, and 0.1 subsequently.

The excess mortality rate after diagnosis was 0.0998 for MI, 0.0336 for stroke and 0 for VTE.

The case-fatality rate was 0.223 for MI, 0.41 for stroke, 0.01 for VTE, 0.0005 for PID, and 0.00038 for ectopic pregnancy.

The excess mortality rate due to AIDS was 0.285.

The mortality rate was 0.00004 for tubal sterilisation, 0.00037 for Caesarean section, 0.00008 for elective abortion, and 0.0000896 for vaginal delivery.

The excess mortality after diagnosis was 0.0297 for breast cancer, 0.0693 for cervical cancer, 0.0323 for endometrial cancer, and 0.127 for ovarian cancer.

The age-specific mortality of spontaneous abortion ranged from 0.000011 in women aged 15 - 19 to 0.000080 in women aged 40 - 44.
Methods used to derive estimates of effectiveness
The authors used an expert panel, including the co-authors, to review the literature on contraception and to determine which methods to include. They also determined which health factors were considered important in making a choice of contraceptive method.

Estimates of effectiveness and key assumptions
The assumptions used in constructing the Markov model were as follows.

The analysis applied only to women who were sexually active and not attempting to become pregnant during the time horizon of the analysis.

Each clinical strategy was defined as initiating a contraceptive method and continuing that method unless a clinical event (i.e. contraceptive failure, development of cancer or a cardiovascular event) necessitated discontinuation. Subsequent to discontinuation, women selected either another method or no method according to observed frequencies of use for women of the corresponding age.

After a pregnancy, the authors assumed a woman would select a different method from among highly effective methods (excluding withdrawal, periodic abstinence, condoms and diaphragm) based on usage prevalence for her age.

Menopause was assumed to occur at a mean age of 51 years with a normal distribution. Women were assumed to discontinue any contraceptive method at that time and to have a zero risk of subsequent pregnancy.

Following a diagnosis of ovarian, cervical or endometrial cancer, it was assumed that the patient would undergo total abdominal hysterectomy with bilateral salpingo-oophorectomy. All contraceptive methods would be stopped and the subsequent risk of pregnancy was assumed to be zero.

Following diagnosis of breast cancer, stroke, VTE or MI, patients were assumed to stop use of all hormonal contraceptive methods and to use of a non-hormonal contraceptive method until the menopause.

The authors assumed that the relative risks of breast cancer, ovarian cancer, endometrial cancer, stroke, VTE, and MI were the same for all combination hormonal methods (i.e. patch, vaginal ring and monthly injection) as for the use of OCs.

The authors assumed that women were at low risk for sexually transmitted infections. In addition, the rates of PID for all combination hormonal methods were the same as those observed for OCs.

Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs). The utilities for most morbid health states were elicited from a convenience sample of female members of the research team and advisory panel using the time trade-off technique. The utility of symptomatic AIDS was obtained from a study by Tsevat et al. (2003). For temporary morbidity, the utility values were subtracted directly to calculate the contribution towards the QALYs. For long-term morbidity, the utility value was converted to a utility factor (fraction of life expectancy) that multiplied time spent in the clinical condition to calculate its contribution towards the QALYs gained.

The short-term disutility values were:

0.99 for breast cancer,

0.16667 for cervical and endometrial cancer,

0.99 for ovarian cancer,

0.16667 for MI,
0.5 for stroke,
0.08333 for VTE and PID,
0.0193 for UTI,
0.21 for HIV,
0.0385 for MRDs,
0.0375 for the pregnancy itself,
0.08333 for vaginal delivery,
0.1154 for Caesarean section,
0.08333 for ectopic pregnancy,
0.0385 for elective induced abortion, and
0.0577 for spontaneous abortion.

The long-term disutility values were 0.15 for breast cancer, 0.2 for ovarian cancer, 0.05 for MI, 0.2 for stroke, and 0.01 for VTE.

**Direct costs**
The costs and the quantities were not reported separately. The direct costs included in the analysis were those of the health service and the patient. These comprised the costs of the contraceptive methods and the costs of medical events and complications. The contraception costs covered the annual cost of medication, supplies, professional fees for visits, fitting or insertion costs for some methods (e.g. IUDs, diaphragm), surgical and facility costs associated with sterilisation methods, and the costs of removal for IUD users discontinuing or replacing this method. The costs of medical events and complications included average payments on claims for both ambulatory and hospitalised patients with each of the clinical conditions in the model.

The costs of the contraceptive methods were derived from two databases (PriceProbe and MarketScan). The costs of medical events related to hospitalisation and subsequent care were determined using data from a large administrative health claims database representing inpatient and outpatient health care service use for a nationwide sample of privately insured individuals. All the costs were adjusted to 2002 prices using figures for medical inflation published by the National Bureau of Labor Statistics. All future costs were discounted by 3% annually, although this was not strictly necessary as the time horizon was 2 years in the base-case scenario. Evidence showed that 63.4% of unintended pregnancies were considered mistimed rather than truly unwanted (i.e. women wanted to become pregnant eventually). In this case, the authors decided that the costs of pregnancy and delivery were discounted by 63.4% for analyses in which the time horizon exceeded 2 years. The authors reported the mean costs.

**Statistical analysis of costs**
The costs were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).
Sensitivity analysis
In the sensitivity analysis, the authors examined the potential impact of increasing the use of effective methods beyond the rates of use observed in the general population. Scenario 1 considered increasing patch use and decreasing the use of other methods and no methods. Scenario 2 considered increasing the use of both the patch and vaginal ring at the expense of other methods and no method.

The authors also investigated non-smokers and smokers separately to determine the effects of smoking on the cost and QALY savings of combination hormonal methods. The assumption that women were not in a mutually monogamous relationship, thus exposing them to increased risks of sexually transmitted diseases was also examined. However, the authors assumed that women would use condoms in combination with all other methods. Also varied in the sensitivity analysis was the time horizon of the analysis, omitting the quality of life adjustments, and the discount rate.

Estimated benefits used in the economic analysis
The QALYs gained with each contraception method were:

1.923 with vasectomy,
1.930 with DMPA,
1.921 with copper IUD,
1.929 with levonorgestrel-releasing IUD,
1.924 with patch and vaginal ring,
1.903 with condom,
1.921 with OCs,
1.929 with monthly injection,
1.898 with periodic abstinence,
1.892 with withdrawal,
1.870 with diaphragm,
1.922 with tubal sterilisation, and
1.783 with no method.

Cost results
The costs for each contraception method were:

$902 with vasectomy,
$1,022 with DMPA,
$1,072 with copper IUD,
$1,075 with levonorgestrel-releasing IUD,
$1,742 with patch,
$1,842 with vaginal ring,
$1,939 with condom,
$2,011 with OCs,
$2,067 with monthly injection,
$2,190 with periodic abstinence,
$2,597 with withdrawal,
$4,126 with diaphragm,
$4,931 with tubal sterilisation, and
$10,838 with no method.

**Synthesis of costs and benefits**
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the extra cost per QALY gained). When DMPA was compared with vasectomy, the incremental cost-utility ratio was $18,406 per QALY gained. All other methods were dominated by DMPA (they were both more expensive and less effective than DMPA).

Increasing the use of effective methods resulted in significant savings of $780 (scenario 1) and $751 (scenario 2). Even when the time horizon was restricted to a single year, all methods were still cost-saving when compared with no method. The results did not differ significantly when women were assumed not to be in a mutually monogamous relationship.

Omitting quality of life adjustment and altering the discount rate from 0 to 5% did not have material effects on the results of the analysis.

**Authors' conclusions**
Every method of contraception dominated non-use in the base-case scenario and in most clinical settings. The authors also concluded that increasing the use of more effective methods (i.e. patch and vaginal ring) even modestly at the expense of less effective methods would improve health and reduce costs. It was also reported that methods requiring action by the user less frequently than daily were both less costly and more effective than methods requiring action on a daily basis.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator was clear. Non-use of contraception was chosen because it represents the only comparator to use of contraception, which in the authors’ case also included periodic abstinence. You should consider if this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not state that a systematic review of the literature had been undertaken to identify relevant research and minimise biases. However, due to the large number of outcome and effectiveness measures used in their model, a systematic review to identify relevant research for each particular area would not appear to be feasible, owing to the time it would take. The authors derived their estimates from a wide array of sources, reflecting the large number of outcomes to assess, which included population-based studies, vital statistics, and clinical trials. An expert panel was appropriately convened, not only to review the literature but also to determine which contraceptive methods to include and the health factors of importance when choosing a contraceptive method. For the majority of outcome measures, one study was used to derive each outcome, so it was not particularly necessary for the authors to report how the estimates of effectiveness from primary studies were combined, nor if differences between them were investigated.
However, even though the authors performed a sensitivity analysis, many of the outcome measures derived from the literature and several of the assumptions made in the model were not varied.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The utility weights were derived mainly from a convenience sample using a time trade-off approach. The benefits were discounted at a rate of 3% per annum.

**Validity of estimate of costs**
Although the authors reported that the costs were estimated from a societal perspective, the productivity costs associated with mortality and morbidity were not included in the analysis. However, for all other categories of cost, it would appear that all the relevant costs were included in the analysis. The costs and the quantities were not reported separately, which will limit the generalisability of the authors’ results to other settings. The costs were derived from several databases. Even though the authors varied the time horizon over which the costs were incurred, a sensitivity analysis of the costs was not performed. The costs were discounted at 3% per annum, although this was not strictly necessary as all the costs were incurred during 2 years. Hence, it is not surprising that varying the discount rate in the sensitivity analysis did not alter the results. The price year was reported, which will assist any possible inflation exercises. The cost data for medical complications were obtained from a medical claims database, with the assumption that payment reflects costs. However, as these do not reflect true costs, the actual costs of care may have been mis-estimated.

**Other issues**
The authors made appropriate comparisons with a study that found that contraception saved health care costs and that all methods saved costs in comparison with no method. However, the authors reported that their analysis was the first one that examined contraception in a cost-utility framework. The issue of generalisability to other settings was not addressed because the sensitivity analysis was not sufficiently comprehensive. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported a number of further limitations to their study. First, they assumed that women would use the same method of contraception continuously and, although this was consistent with a published analysis, this might have resulted in an overestimation of the benefits and cost-savings compared with switching methods. Second, a convenience sample was used to derive utilities for the health states, but the results from the sensitivity analysis demonstrated that the results were not affected when utility was varied. Third, owing to limited data, the model did not address the extended-use OC regimen. Finally, the efficacy data for older contraceptive methods came from large-scale epidemiological observations and reflected typical use, whereas for newer methods, the efficacy data were derived from small clinical trials.

**Implications of the study**
The authors reported that it was advisable to cover the costs of contraception to uninsured populations, as this was sure to save money.

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