Risk-based versus alternative algorithms for antibiotic prophylaxis among women seeking early suction abortion: a cost-effectiveness simulation

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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
The use of algorithms for antibiotic prophylaxis in women seeking early suction abortion. The alternatives examined were:

- World Health Organization (WHO) risk assessment (risk assessment alone);
- WHO examination (risk assessment and speculum examination); WHO microscopy (risk assessment, speculum examination and microscopy);
- risk-based algorithm; universal pH screening (treatment based on a vaginal pH of 4.7 or more);
- universal antibiotic prophylaxis (treatment of all infected women); and
- universal etiologic screening (treatment based on the results of etiologic tests).

The risk-based algorithm provided prophylaxis for cervical infection to women with high-risk scores (2, 3 or 4), regardless of pH test results, and to women with a middle-risk score (1) if the pH was 4.7 or higher. Women with a low-risk score (0) were not treated. Further, treatment for bacterial vaginosis and trichomoniasis was provided if the vaginal pH was at least 4.7, regardless of the risk index score. The risk factors considered were symptoms (score 1), education beyond high school (score 1), partner with symptoms (score 2), and age of 25 years or younger and a previous birth (score 1).

Type of intervention
Primary prevention, diagnosis, and screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women presenting for menstrual regulation, regardless of symptoms. Women were excluded if they reported the use of antimicrobial therapy in the last 14 days, or had undergone menstrual regulation during the preceding 6 weeks. Those who had attempted self-induced abortion using intrauterine methods during the preceding 6 weeks, or were more than 12 weeks pregnant (ineligible for menstrual regulation), were also excluded.

Setting
The setting was a community clinic. The economic study was conducted in Bali, Indonesia.

Dates to which data relate
The effectiveness and resource use data were gathered from June 1988 to August 1989. The price year was 1998.
Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was conducted prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
The use of power calculations was not reported. A single group of eligible women presenting to the study clinic and residing in Bali were considered. A total of 971 women presented to the clinic, of which 241 were ineligible. Reasons for ineligibility were pregnant for more than 12 weeks (126), could not return to the clinic (34), had already undergone menstrual regulation (9), had attempted self-induced abortion (1), presented with incomplete abortion (5), used antimicrobial therapy in the preceding 14 days (1), and non-Bali residents (65). Of the remaining women, 47 refused to participate, 14 continued their pregnancy, and 5 had other reasons that precluded study participation. Therefore, the final sample comprised 664 women (90% of those initially eligible). The participants were more likely to live in urban areas than non-participants who were excluded for reasons other than non-Bali residence (63% of 644 versus 51% of 241). In addition, they were younger (mean age 22 years, 95% confidence interval, CI: 21.7 - 22.4) than non-participants (mean age 23 years, 95% CI: 22.3 - 23.5). The participants were predominantly unmarried (68%) and well educated (26% beyond high school).

Study design
This was a diagnostic study that was conducted at the Caturwarga clinic of the Indonesian Planned Parenthood Association. The women completed a questionnaire to provide baseline data. Further investigations were conducted by performing several diagnostic tests (e.g. blood sample, standard examinations, vaginal specimen collection and etiologic tests). The length of follow-up was not reported. No loss to follow-up appears to have occurred.

Analysis of effectiveness
It appears that all the patients initially included in the study sample have been accounted for in the analysis of effectiveness. The outcome measures used were:

the prevalence of RTI;

the number of asymptomatic and asymptomatic women;

the predictive ability of symptoms, physical signs and clinic-based tests, as assessed by calculating the likelihood ratio (LR) and the corresponding 95% CIs.

A logistic regression analysis with cervical infection as the dependent variable was carried out to assess the risk factors. Data-based simulations permitted the calculation of the hypothetical sensitivity, specificity, positive predictive value (PPV), total number of women treated, and the number of cases detected and treated, for each algorithm under evaluation in the actual sample of women considered in the study.

Effectiveness results
The prevalence rates were 16.3% for bacterial vaginosis, 15.5% for candidiasis, 7.1% for trichomoniasis, 5.5% for Chlamidia trachomatis, 0.9% for Neisseria gonorrhoeae, 0.5% for Treponema pallidum and 0% for human immunodeficiency virus.

There were 154 symptomatic women and 500 asymptomatic women.

Of the 40 women with cervical infection, 40% presented with any of these symptoms, compared with 22% of women
without a diagnosis.

In asymptomatic women, the LRs for signs were: 3.4 (95% CI: 1.3 - 9.2) for yellow, green, or bloody cervical or vaginal discharge; 1.2 (95% CI: 0.6 - 2.3) for ectopy; 1.6 (95% CI: 1.2 - 2.2) for friability; and 1.4 (95% CI: 1.1 - 1.9) for erosion.

In asymptomatic women, the LRs for clinic-based tests were: 1.6 (95% CI: 1.0 - 2.5) for more than 30 cervical polymorphonuclear lymphocytes (PMNs); 1.8 (95% CI: 1.1 - 2.8) for cervical leukocyte esterase (LE) of at least 1; 1.4 (95% CI: 1.0 - 1.8) for vaginal LE of at least 2; 1.5 (95% CI: 1.2 - 1.9) for vaginal pH of at least 4.7; and 1.4 (95% CI: 0.9 - 2.2) for potassium hydroxide (KOH) whiff test.

In symptomatic women, the LRs for symptoms were: 0.9 (95% CI: 0.6 - 1.3) for yellow, green, or bloody vaginal discharge; 1.7 (95% CI: 0.4 - 7.2) for vaginal bleeding; and 0.8 (95% CI: 0.3 - 2.0) for lower abdominal pain.

In symptomatic women, the LRs for signs were: 1.6 (95% CI: 0.4 - 6.4) for yellow, green, or bloody cervical or vaginal discharge; 0.8 (95% CI: 0.3 - 1.9) for ectopy; 0.9 (95% CI: 0.5 - 1.8) for friability; and 1.0 (95% CI: 0.6 - 1.6) for erosion.

In symptomatic women, the LRs for clinic-based tests were: 1.3 (95% CI: 0.7 - 2.4) for more than 30 cervical PMNs; 2.0 (95% CI: 1.2 - 3.2) for cervical LE of at least 1; 1.3 (95% CI: 0.9 - 1.8) for vaginal LE of at least 2; 1.6 (95% CI: 1.2 - 2.1) for vaginal pH of at least 4.7; and 1.5 (95% CI: 0.7 - 3.0) for KOH whiff test.

The logistic regression analysis revealed that more than a high school education, age of 25 years or older, and partner with symptoms were significant predictors of cervical infection. These were included in the risk-based algorithm.

The analysis of complete data suggested that pH testing permitted the identification of a sub-group of women who could benefit from prophylaxis.

When considering chlamydial or gonococcal infection (40 cases in the sample of 655 women), the results were as follows.

With WHO risk assessment, the sensitivity was 0.3, the specificity was 0.790, the PPV was 0.085, the total number of women treated was 141, and the number of cases detected and treated was 12.

With WHO examination, the sensitivity was 0.55, the specificity was 0.566, the PPV was 0.76, the total number of women treated was 289, and the number of cases detected and treated was 22.

With WHO microscopy, the sensitivity was 0.55, the specificity was 0.566, the PPV was 0.076, the total number of women treated was 289, and the number of cases detected and treated was 22.

With the risk-based algorithm, the sensitivity was 0.7, the specificity was 0.706, the PPV was 0.134, the total number of women treated was 209, and the number of cases detected and treated was 28.

With universal pH screening, the sensitivity was 0.8, the specificity was 0.475, the PPV was 0.09, the total number of women treated was 355, and the number of cases detected and treated was 32.

With universal prophylaxis, the sensitivity was 1, the specificity was 0, the PPV was 0.061, the total number of women treated was 655, and the number of cases detected and treated was 40.

With universal etiologic screening, the sensitivity was 1, the specificity was 1, the PPV was 1, the total number of women treated was 40, and the number of cases detected and treated was 40.

When considering bacterial vaginosis (95 cases in the sample of 595 women), the results were as follows.

With WHO risk assessment, the sensitivity was 0.463, the specificity was 0.514, the PPV was 0.153, the total number of women treated was 287, and the number of cases detected and treated was 44.
With WHO examination, the sensitivity was 0.463, the specificity was 0.514, the PPV was 0.153, the total number of women treated was 287, and the number of cases detected and treated was 44.

With WHO microscopy, the sensitivity was 0.168, the specificity was 0.912, the PPV was 0.267, the total number of women treated was 60, and the number of cases detected and treated was 16.

With the risk-based algorithm, the sensitivity was 0.926, the specificity was 0.536, the PPV was 0.275, the total number of women treated was 320, and the number of cases detected and treated was 88.

With universal pH screening, the sensitivity was 0.926, the specificity was 0.536, the PPV was 0.275, the total number of women treated was 320, and the number of cases detected and treated was 88.

With universal prophylaxis, the sensitivity was 1, the specificity was 0, the PPV was 0.160, the total number of women treated was 595, and the number of cases detected and treated was 95.

With universal etiologic screening, the sensitivity was 1, the specificity was 1, the PPV was 1, the total number of women treated was 95, and the number of cases detected and treated was 95.

When considering bacterial trichomoniasis (47 cases in the sample of 655 women), the results were as follows.

With WHO risk assessment, the sensitivity was 0.830, the specificity was 0.541, the PPV was 0.123, the total number of women treated was 318, and the number of cases detected and treated was 39.

With WHO examination, the sensitivity was 0.830, the specificity was 0.541, the PPV was 0.123, the total number of women treated was 318, and the number of cases detected and treated was 39.

With WHO microscopy, the sensitivity was 0.745, the specificity was 1, the PPV was 1, the total number of women treated was 35, and the number of cases detected and treated was 35.

With the risk-based algorithm, the sensitivity was 0.872, the specificity was 0.483, the PPV was 0.115, the total number of women treated was 355, and the number of cases detected and treated was 41.

With universal pH screening, the sensitivity was 0.872, the specificity was 0.483, the PPV was 0.115, the total number of women treated was 355, and the number of cases detected and treated was 41.

With universal prophylaxis, the sensitivity was 1, the specificity was 0, the PPV was 0.072, the total number of women treated was 655, and the number of cases detected and treated was 47.

With universal etiologic screening, the sensitivity was 1, the specificity was 1, the PPV was 1, the total number of women treated was 47, and the number of cases detected and treated was 47.

**Clinical conclusions**

As expected, universal screening and prophylaxis led to the highest detection-and-treatment rates. Acceptable results were obtained with the risk-based algorithm, while all WHO strategies led to low detection rates.

**Measure of benefits used in the economic analysis**

The summary benefit measure was the number of cases detected and treated, as associated with each strategy under evaluation. It was derived directly from the effectiveness analysis.

**Direct costs**

Discounting was not relevant since the costs were incurred during a short time. The unit costs were reported only for the tests. The quantities of resources used were not reported in detail. The health services included in the analysis were those related to tests and treatments. These covered materials as well as clinician and technician time. The costs of
averted cases of PID and their sequelae, travel and pelvic examination (assumed to be offered routinely to all women presenting at the clinic) were not considered. Only the costs relevant to the clinic and the patients were considered. The costs of materials were derived from the study clinic. Wages came from data provided by the World Bank. The costs of the tests and treatments were, presumably, obtained from the clinic. The resource use data were estimated from the sample of women involved in the effectiveness study and from assumptions based on recommendations made by the Centers for Disease Control and the WHO. All costs were presented in 1998 values using the Consumer Price Index for Urban Consumers.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The cost per patient was:

- $2.00 with the WHO risk assessment algorithm,
- $4.03 with the WHO examination algorithm,
- $4.05 with the WHO microscopy algorithm,
- $3.04 with the risk-based algorithm,
- $5.04 with universal pH screening,
- $9.11 with universal prophylaxis, and
- $11.32 with universal etiologic screening.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits of the alternative prophylaxis strategies. Each strategy was compared with the immediate preceding option (i.e. the less effective strategy in terms of the number of chlamydial or gonococcal infections).

The ICER of WHO examination relative to WHO assessment was $132.61.

The ICER of WHO microscopy relative to WHO examination was not calculated because they had comparable effectiveness, but the WHO examination algorithm had slightly lower costs.
The ICER of risk-based algorithm over both WHO examination and WHO microscopy was not calculated because the risk-based algorithm was dominant (both more effective and less costly).

The ICER of universal pH screening over the risk-based algorithm was $327.04.

The ICER of universal prophylaxis over universal pH screening was $333.28.

The ICER of universal etiologic screening over universal prophylaxis was not calculated because they had comparable effectiveness, but universal etiologic screening had slightly lower costs.

**Authors' conclusions**
The risk-based algorithm proved to be a cost-effective strategy in resource-poor settings that might not be able to fund universal strategies for the prophylaxis of post-abortion pelvic inflammatory disease (PID).

**CRD COMMENTARY - Selection of comparators**
The choice of the comparators was appropriate. The range of interventions considered in the study covered all possible strategies for the antibiotic prophylaxis of post-abortion PID. The authors provided a detailed description of each option, as well as a rationale for the choice of each strategy. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was based on a diagnostic study, which was used to assess the prevalence of disease and the predictive ability of the risk-based algorithm. Hypothetical calculations were then made to assess the predictive ability of the other strategies on the basis of the results of the sample of patients considered in the study. Thus, a possible limitation of the analysis, as the authors acknowledged, was that the risk-based algorithm was assessed using the same data set from which it was created. It should have been tested in a different study sample to ensure its generalisability. It would also have been more appropriate had the authors applied each strategy to a real sample of patients. The method used to select the sample was reported clearly. The patients were not followed after the diagnosis was made and the actual outcomes associated with treating women with infection were not assessed.

**Validity of estimate of measure of benefit**
The summary benefit measure was specific to the disease considered in the study. It would be difficult to compare it with the benefits of other health care interventions. The measure assessed the efficacy of the prevention options, rather than the actual impact of the strategies under evaluation on the patients' health.

**Validity of estimate of costs**
The authors stated that only those costs relevant to the clinic and the patients were included in the analysis. Some cost items were not considered in the study and the authors did not justify all such exclusions. The unit costs were provided for the tests only and the information relating to resource use was unclear. The price year was given, which facilitates reflation exercises in other settings. The source of the data was reported for almost all items. The costs were specific to the study setting and no sensitivity analyses were conducted to address variability in the data. No statistical analyses of the costs or quantities were performed. Overall, it appears that it would be difficult to replicate the study in other settings. In addition, the exclusion of important categories of costs limits the validity of the analysis.

**Other issues**
The authors did not compare their findings with those from other studies. In terms of the generalisability of the study results, the authors stated that caution is required when interpreting the results of the analysis, or when extrapolating the conclusions of the analysis to other settings. The study involved the general population of women presenting for menstrual regulation, and this was reflected in the conclusions of the analysis. The authors noted that disease prevalence
is likely to represent a key factor in the analysis. Finally, the authors pointed out that, if the averted medical costs for PID had been included, the risk-based algorithm would have remained more cost-effective than any WHO algorithm, and the cost-difference between the risk-based algorithm and the three algorithms with higher sensitivity would have been reduced.

**Implications of the study**
The authors suggested that the risk-based algorithm should be tested in different study samples. They also stated that the addition of recently introduced, rapid, inexpensive, clinic-based tests for bacterial vaginosis could further improve the cost-effectiveness of the risk-based algorithm.

**Source of funding**
Supported by a grant from the International Women's Health Coalition.

**Bibliographic details**

**PubMedID**
11725227

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Abortion, Induced /adverse effects; Adult; Algorithms; Antibiotic Prophylaxis /economics; Cost-Benefit Analysis; Cross-Sectional Studies; Decision Trees; Female; Humans; Indonesia /epidemiology; Medically Underserved Area; Odds Ratio; Pelvic Inflammatory Disease /etiology /prevention & control; Pregnancy; Pregnancy Trimester, First; Prevalence; Risk Factors; Surveys and Questionnaires; Trichomonas Vaginitis /epidemiology; Uterine Cervical Diseases /epidemiology; Vaginosis, Bacterial /epidemiology

**AccessionNumber**
22002000004

**Date bibliographic record published**
31/01/2005

**Date abstract record published**
31/01/2005