The cost effectiveness of patient-applied versus provider-administered intervention strategies for the treatment of external genital warts
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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
A two-stage switch therapy involving the use of patient-applied topical therapies (imiquimod or podofilox gel) as first-line therapy, and the use of provider-administered ablative therapies (podophyllin, laser surgery, cryotherapy, and trichloroacetic acid (TCA)) as second-line therapy for patients failing the patient-applied therapy, in the treatment of external genital warts.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with external genital warts.

Setting
Hospital. The economic study was carried out in the USA.

Dates to which data relate
Clinical probabilities were obtained from the literature published between 1987 and 1998. The dates of the resource use data, estimated by an expert panel of physicians, were not specified. Cost data were from 1991, 1992, and 1997. The price year was 1997.

Source of effectiveness data
Effectiveness data were derived from a review of the literature.

Modelling
A decision-analytic model was constructed to estimate the expected costs and effects associated with each strategy.

Outcomes assessed in the review
The review assessed the following outcomes: Clearance rates, recurrence rates, and sustained clearance rates.

Study designs and other criteria for inclusion in the review
Randomised controlled trials were selected from a collection of studies of monotherapy of genital warts published since
1978, by an expert panel consisting of an external genital wart clinician and internal 3M pharmaceutical personnel. Other criteria taken into account were patient populations, treatment regimens and techniques, and different manifestations of human papillomavirus (HPV) infection.

**Sources searched to identify primary studies**
Medline was searched to identify studies.

**Criteria used to ensure the validity of primary studies**
The principle used in the calculation of clearance and recurrence rates was intention to treat.

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

**Number of primary studies included**
16 studies were included in the review: 14 for the provider-administered ablative therapies and 2 for the patient-administered therapies.

**Methods of combining primary studies**
A weighted average method based on sample size (for values related to provider-administered ablative therapies) was used to combine data from the primary studies.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The results were:

- intention to treat clearance rate for podofilox gel at 4 weeks and at 8 weeks, 28.3% and 37%, respectively;
- recurrence rate for podofilox gel at 12 weeks of observation, 30.9%;
- calculated sustained clearance rate at 4 weeks for podofilox gel, was 19.6% (95% CI: 16.9% - 22.3%) and at 8 weeks (2 courses) was 25.6% (95% CI: 22.7% - 28.5%);
- intention to treat clearance rate with imiquimod cream at 16 weeks, 49.5%;
- recurrence rate with imiquimod at 12 weeks, 11.1%;
- the corresponding sustained clearance rate for imiquimod, 44% (95% CI: 35% - 53%);
- clearance rate for podophyllin was 41.5%, for laser surgery was 100%, for cryotherapy was 61.7%, and for trichloroacetic acid was 65.7%. An average of 67.2% for provider-administered ablative therapies;
- recurrence rates were: podophyllin 55.4%, laser surgery 59.9%, cryotherapy 56.3%, and trichloroacetic acid 45.7%. An average of 54.3% for provider-administered ablative therapies;
- sustained clearance rates were: 18.5% (podophyllin), 40.1% (laser surgery), 26.9% (cryotherapy), and 35.7% (trichloroacetic acid). An average of 30.3% for provider-administered ablative therapies.
Measure of benefits used in the economic analysis
Sustained clearance rates was the measure of benefits.

Direct costs
Costs were not discounted due to the short time frame of the study (apparently up to 16 weeks). Some quantities were reported separately from the costs. Cost items were reported separately. Cost analysis covered the costs of first- and second-line therapies consisting of drug costs, initial office visit, follow-up visits, and office-based procedures. The perspective adopted in the cost analysis was that of the typical private insurer. The resource use data (for the number and extent of initial and follow-up visits and procedures) were estimated by an expert panel of physicians. The source of cost data on provider-administered ablative therapies and podofilox was a study by Strauss et al published in 1996. The source of the wholesale price for imiquimod was an official report published in 1997. The simple average of the costs of using common ablative therapies was attributed to the cost of provider-administered ablative therapies. Cost data were from 1991, 1992, and 1997. 1997 price data were used. The Consumer Price Index (CPI-U) was used to adjust the cost data to 1997 prices.

Indirect Costs
Not considered.

Currency
US dollars ($).

Sensitivity analysis
A set of one-way sensitivity analyses was performed on the assumed clearance rate for ablative treatment, and the scenario of two courses of therapy with podofilox gel or imiquimod before provider-administered ablative treatments.

Estimated benefits used in the economic analysis
The total two-stage sustained clearance rate for imiquimod cream was 60.8% (based on a 40% sustained clearance rate for imiquimod as first-line therapy and 30% average sustained clearance rate for second-line provider-administered ablative therapies) versus 43.7% for podofilox gel (based on a 19.6% sustained clearance rate for podofilox gel as first-line therapy and 30% average sustained clearance rate for second-line provider-administered ablative therapies).

Cost results
The average total two-stage treatment cost for imiquimod was $768 ($506 for initial imiquimod therapy and $468*0.56 average cost for second-line provider-administered ablative therapies. This was based on treatment costs of $464 for podophyllin, $449 for laser surgery, $493 for cryotherapy, and $464 for trichloroacetic acid. This compares to $570 for podofilox gel (based on $194 for initial imiquimod therapy and $468*0.56 average cost for second-line provider-administered ablative therapies).

Synthesis of costs and benefits
The two-stage cost per sustained cleared patient was calculated as the measure of cost-effectiveness. This produced a cost of $1,263 for imiquimod cream versus $1,304 for podofilox gel. The sensitivity analyses produced corresponding values of $1,390, $1,547, and $1,158 for imiquimod cream versus $1,601, $2,067, and $1,304 for podofilox gel.

Authors' conclusions
Initial treatment with imiquimod is the preferred intervention option as it yields a 39% greater sustained clearance rate than podofilox gel while being 3% less costly per successful outcome.
CRD COMMENTARY - Selection of comparators
No specific strategy was regarded as the comparator since both of the patient-applied products (imiquimod or podofilox gel) were introduced into the US market around mid-1997.

Validity of estimate of measure of benefit
The internal validity of the estimate of benefit for provider-administered therapies is likely to be high due to a systematic literature review, quality assessment of the primary studies and inclusion of randomised studies in the review. However, in assessing the effectiveness of the patient-administered therapies, only two studies were used and it is not clear whether other relevant clinical trials with differing results were available. As the authors noted, the effects of ablative therapies on quality of life (they can be painful and can impact on social and sexual activities because of their side effects) were not reflected in the estimate of benefit.

Validity of estimate of costs
Some quantities were reported separately from the costs and adequate details of the methods of cost estimation were given. Cost results may not be generalisable to other settings. As the authors mentioned, the cost analysis did not consider the effects of ablative therapies on indirect costs which may be important because they are time intensive and can lead to time off work.

Other issues
The authors’ conclusions seem to be reasonably justified given the heavy reliance on studies with randomised design. The issue of generalisability to other settings or countries was addressed by performing extensive sensitivity analyses on all parameters of the model. Appropriate comparisons were made with other studies.

Implications of the study
The findings of the study suggest treatment with imiquimod is the preferred intervention as it produces greater sustained clearance rates than podofilox gel while being marginally less costly per successful outcome.

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3M Pharmaceuticals, St Paul, MN, USA.

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Other publications of related interest

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