Incorporating calibrated model parameters into sensitivity analyses: deterministic and probabilistic approaches
Taylor DC, Pawar V, Kruzikas DT, Gilmore KE, Sanon M, Weinstein MC

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.

CRD summary
This study assessed the cost-effectiveness of a hypothetical vaccine against human papillomavirus, as a case study, to examine how uncertainty in calibration could affect the outcomes of a mathematical model. The authors concluded that compared with usual probabilistic sensitivity analysis, the calibration analysis revealed more uncertainty in the cost-effectiveness results, but this did not alter the conclusions. The methods were appropriate and the assessment of uncertainty was valid. Vaccination was cost-effective, and the authors’ conclusions seem valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of a hypothetical vaccine against human papillomavirus (HPV), as a case study, to examine how the uncertainty in calibration could affect the outcomes of a mathematical model; particularly, the drivers of uncertainty in calibration were evaluated.

Interventions
The two strategies were a hypothetical HPV vaccine and no vaccination.

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The model had been developed for the UK and was adapted to the US setting. A key step in the analysis was model calibration, which focused on multiple end points, including the age-specific and overall age-adjusted cervical cancer incidence, cancer-related mortality, and cervical intraepithelial neoplasia (CIN) prevalence. Calibration was based on the Nelder-Mead mathematical search algorithm. The perspective for the analysis was not clearly stated.

Effectiveness data:
Most of the input data were from published sources, such as the National Cancer Institute’s Surveillance Epidemiology and End Results database. The risks of infection in vaccinated or unvaccinated individuals were the key inputs for the model.

Monetary benefit and utility valuations:
The utility values associated with cancer, were estimated in the original model.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure, and were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of HPV screening, the diagnostic tests, and the treatment of various cancer stages. The costs were those used in the original model. They were in US $ and the price year was 2005. A 3% annual
discount rate was applied.

Analysis of uncertainty:
A probabilistic sensitivity analysis (PSA) was carried out, using conventional distributions, for the groups of inputs. A calibration PSA was performed, using the methods of the original PSA, while bootstrapping from 25 additional calibrated parameter sets, plus the original calibrated parameter set. A deterministic sensitivity analysis was carried out to examine the impact of using the optimal inputs from each of the 25 additional calibrations.

Results
The incremental cost per QALY gained with HPV vaccination, over no vaccination, was $4,300.

The basic PSA produced a 95% credible interval of dominant (where vaccination was less expensive and more effective) to $9,800 per QALY gained, with vaccination.

The calibration PSA produced a 95% credible interval of $1,000 to $37,700 per QALY gained.

The incremental cost per QALY gained using the optimal inputs, from the 25 additional calibrations, while keeping all other parameters at their original values, ranged from $1,500 to $39,100.

Authors' conclusions
The authors concluded that compared with usual PSA, the calibration analysis revealed more uncertainty in the cost-effectiveness results. This did not alter the cost-effectiveness conclusions, in this case, but could do so in other cases.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the proposed vaccination, was compared with no vaccination.

Effectiveness/benefits:
Limited information on the data sources was reported; most of the data were from the original model. The US epidemiological inputs were from nationally representative databases or other publications. Extensive sensitivity analysis was conducted on all the model parameters. QALYs were an appropriate benefit measure, given the impact of cervical cancer, from HPV, on both survival and quality of life. The utility values were reported, but their sources were not described.

Costs:
The cost categories could reflect the perspective of the third-party payer, but this was not explicitly stated. Little information on the data sources was provided, but the estimates were from published studies, conducted in the USA. The costs were presented as category totals, in an online appendix; the unit costs were not presented separately from the resource use. The price year was reported, allowing refolation exercises.

Analysis and results:
The results were selectively reported, as the expected costs and QALYs were not given, but the incremental cost-utility ratios were. The uncertainty was satisfactorily investigated, as this was the focus of the study: comparing an alternative approach to the usual one. Extensive details of the calibration method were given. The study focused on the methods for the calibration process, and few details of the sources of data were provided, as this was not the objective of the analysis.

Concluding remarks:
The methods were appropriate and the assessment of uncertainty was valid. Vaccination was cost-effective, and the authors' conclusions appear to be valid.

Funding
Funded by GlaxoSmithKline, USA.