AdViSHE

Assessment of the Validation Status of Health-Economic decision models

AdViSHE is a questionnaire that modellers can complete to report on the efforts performed to improve the validation status of their health-economic (HE) decision model. It is not intended to replace validation by model users but rather to inform the direction of validation efforts and to provide a baseline for replication of the results. In addition to using it after a model is finished, the modellers can use AdViSHE to guide validation efforts during the modelling process.

The modellers are asked to comment on the validation efforts performed while building the underlying HE decision model and afterwards. Many of the questions simply refer to the model documentation. AdViSHE is divided into five parts, each covering an aspect of validation:

- Part A: Validation of the conceptual model (2 questions)
- Part B: Input data validation (2 questions)
- Part C: Validation of the computerized model (4 questions)
- Part D: Operational validation (4 questions)
- Part E: Other validation techniques (1 question)

No final validation score is calculated, as the assessment of the answers and the overall validation effort is left to the model users. It is assumed that the model has been built according to prevailing modelling and reporting guidelines. For instance, the model builders would presumably adhere to the ISPOR-SMDM’ Modeling Good Research Practices (Caro et al., 2010) and/or CHEERS’ Statement (Husereau et al., 2013). Some questions may not be applicable to a particular model. If this is the case, the model builder should take the opt-out option and provide a justification of why this item is not deemed applicable.

Part A: Validation of the conceptual model (2 questions)

Part A discusses techniques for validating the conceptual model. A conceptual model describes the underlying system (e.g., progression of disease) using a mathematical, logical, verbal, or graphical representation. Please indicate where the conceptual model and its underlying assumptions are described and justified.

†: ISPOR: International Society For Pharmacoeconomics and Outcomes Research, SMDM: Society for Medical Decision making, CHEERS: Consolidated Health Economic Evaluation Reporting Standards
A1/ Face validity testing (conceptual model): Have experts been asked to judge the appropriateness of the conceptual model? 
If yes, please provide information on the following aspects:
- Who are these experts?
- What is your justification for considering them experts?
- To what extent do they agree that the conceptual model is appropriate?
If no, please indicate why not.

During the development of the economic model we consulted two medical practitioners (Dr Virginia Mumford and Dr Deborah Bateson) and a pharmacist (Dr Natalie Gauld).

Dr Virginia Mumford (MBBS, MBA, MHA, PhD) is an applied health economist working as a post-doctoral fellow at Macquarie University’s Australian Institute of Health Innovation (AIHI) at Macquarie University. She originally qualified as a medical doctor and worked as a general physician and paediatrician. She also plays a key role in conducting evaluations for the Pharmaceutical Benefits Advisory Committee – the pharmaceutical funding decision making body in Australia.

Dr Deborah Bateson is a Clinical Associate Professor in Gynecology and Neonatology at the University of Sydney, and the Medical Director at Family Planning NSW. She has an undergraduate degree in Biochemistry from Oxford University (MA Oxon), a Masters degree in Human Nutrition from the London School of Hygiene and Tropical Medicine and a medical degree from the University of Hong Kong. She was Chair, then Co-chair, of the Australasian Sexual Health Alliance from 2015 to 2017. At the time of writing she has published 64 articles, including in the area of contraception and unintended pregnancies. She also continues to practice as a GP providing family planning advice to patients.

Dr Natalie Gauld (DipPharm MPPharm PhD FPS RegPharmNZ MRPharmS) is a pharmacist and an Honorary Research Fellow at the Department of General Practice and Primary Health Care, University of Auckland, New Zealand. She was a member of the Medicines Classification Committee in New Zealand (2004–2009). She led the work and created the screening tools and patient information sheets for the reclassification of the oral contraceptive pill (OCP) in New Zealand with input from experts. She is also a member of the OCP Over the counter (OTC) research working group, an international group based in the US at Ibis Reproductive Healthcare. At the time of writing she has published 29 articles, including in the area of reclassification of medicines both in New Zealand and worldwide. She has also conducted a research project in New Zealand on oral contraceptive access (not yet published) and has written a chapter for a Pharmacy textbook on contraception (in press).

The experts initially considered the model to be missing certain aspects, including depression, ovarian cancer, deaths from pregnancy, and the costs of training of pharmacists. They also suggested that the intervention to be changed to include the need for an initial GP consultation. All of these aspects were included in the final model.

Aspects to judge include: appropriateness to represent the underlying clinical process/disease (disease stages, physiological processes, etc.); and appropriateness for economic evaluation (comparators, perspective, cost covered, etc.).

A2/ Cross validity testing (conceptual model): Has this model been compared to other conceptual models found in the literature or clinical textbooks?
If yes, please indicate where this comparison is reported.
If no, please indicate why not.

In the development of the model structure we conducted a review of studies estimating the cost-effectiveness of multiple contraceptive methods (1-5). This was because previous evaluations of reclassifying the OCP did not use an economic model and only considered the impact over a one year time horizon or did not report a time horizon (6-9).

The final model was influenced by Sonnenberg et al (2), although with some necessary differences due to the different aim of the economic evaluation. In particular, Sonnenberg et al:
- Included women aged 15 to 50 years;
- Considered 13 methods of contraception (but not consider condoms in combination with another form of contraception);
- Included different pregnancy outcomes (ectopic pregnancy, miscarriage, abortion, birth, death, but not stillbirth);
- Included some adverse events (myocardial infarction, stroke, venous thromboembolism, but not depression), sexually transmitted infections, STIs (human HIV and pelvic inflammatory disease caused by chlamydia, but not other STIs), and ovarian cancer.
- Varied risk of pregnancy over time, but only for copper intrauterine devices (IUDs) and tubal sterilisation.
- Assumed that after a pregnancy, we assume that a woman will select a different method of contraception.

- Assumed that menopause occurs at 51 years, they discontinue any contraceptive method and have a zero risk of pregnancy subsequently.

Sonnenberg et al used data from the US National Survey of Family Growth, which was also used in our model, and the disutilities associated with pregnancy outcomes estimated by Sonnenberg et al were also used in our model.


Part B: Input data validation (2 questions)

Part B discusses techniques to validate the data serving as input in the model. These techniques are applicable to all types of models commonly used in HE modelling.

Please indicate where the description and justification of the following aspects are given:

- search strategy;
- data sources, including descriptive statistics;
- reasons for inclusion of these data sources;
- reasons for exclusion of other available data sources;
- assumptions that have been made to assign values to parameters for which no data was available;
- distributions and parameters to represent uncertainty;
- data adjustments: mathematical transformations (e.g., logarithms, squares); treatment of outliers; treatment of missing data; data synthesis (indirect treatment comparison, network meta-analysis); calibration; etc.

B1/ Face validity testing (input data): Have experts been asked to judge the appropriateness of the input data?

If yes, please provide information on the following aspects:
- Who are these experts?
- What is your justification for considering them experts?
- To what extent do they agree that appropriate data has been used?

If no, please indicate why not.

During the development of the economic model we consulted two medical practitioners (Dr Virginia Mumford and Dr Deborah Bateson) and a pharmacist (Dr Natalie Gauld). See Question A1.

In general the experts agreed that the model inputs were reasonable and provide suggestions regarding some key model inputs, including appropriate sources for pregnancy rates, discontinuations, and parameters relating to the use of the OCP questionnaire.
Aspects to judge may include but are not limited to: potential for bias; generalizability to the target population; availability of alternative data sources; any adjustments made to the data.
**B2/ Model fit testing:** When input parameters are based on regression models, have statistical tests been performed?  
If yes, please indicate where the description, the justification and the outcomes of these tests are reported.  
If no, please indicate why not.

Not relevant.

Examples of regression models include but are not limited to: disease progression based on survival curves; risk profiles using regression analysis on a cohort; local cost estimates based on multi-level models; meta-regression; quality-of-life weights estimated using discrete choice analysis; mapping of disease-specific quality-of-life weights to utility values.  
Examples of tests include but are not limited to: comparing model fit parameters (R², Akaike information criterion (AIC), Bayesian information criterion (BIC)); comparing alternative model specifications (covariates, distributional assumptions); comparing alternative distributions for survival curves (Weibull, lognormal, logit); testing the numerical stability of the outcomes (sufficient number of iterations); testing the convergence of the regression model; visually testing model fit and/or regression residuals.

**Part C: Validation of the computerized model (4 questions)**

Part C discusses various techniques for validating the model as it is implemented in a software program. If there are any differences between the conceptual model (Part A) and the final computerized model, please indicate where these differences are reported and justified.

**C1/ External review:** Has the computerized model been examined by modelling experts?  
If yes, please provide information on the following aspects:  
- Who are these experts?  
- What is your justification for considering them experts?  
- Can these experts be qualified as independent?  
- Please indicate where the results of this review are reported, including a discussion of any unresolved issues.  
If no, please indicate why not.

The computerised model was not examined by modelling experts outside of the authors of the articles. However, the computerized model was provided as supplementary material to reviewers as part of the submission process, and it is expected will be publicly available if accepted.

Aspects to judge may include but are not limited to: absence of apparent bugs; logical code structure optimized for speed and accuracy; appropriate translation of the conceptual model.

**C2/ Extreme value testing:** Has the model been run for specific, extreme sets of parameter values in order to detect any coding errors?  
If yes, please indicate where these tests and their outcomes are reported.  
If no, please indicate why not.

Extreme value testing was conducted to detect coding errors during the building of the model. In general these results were not reported, however some scenario analysis involves extreme value testing.

Examples include but are not limited to: zero and extremely high (background) mortality; extremely beneficial, extremely detrimental, or no treatment effect; zero or extremely high treatment or healthcare costs.
C3/ Testing of traces: Have patients been tracked through the model to determine whether its logic is correct?  
If yes, please indicate where these tests and their outcomes are reported.  
If no, please indicate why not.  
Not reported. However, this information is available in the computerized model, which was provided as supplementary material to reviewers as part of the submission process, and it is expected will be publicly available if accepted.

In cohort models, this would involve listing the number of patients in each disease stage at one, several, or all time points (e.g., Markov traces). In individual patient simulation models, this would involve following several patients throughout their natural disease progression.

C4/ Unit testing: Have individual sub-modules of the computerized model been tested?  
If yes, please provide information on the following aspects:  
- Was a protocol that describes the tests, criteria, and acceptance norms defined beforehand?  
- Please indicate where these tests and their outcomes are reported.  
If no, please indicate why not.  
Not conducted.

Examples include but are not limited to: turning sub-modules of the program on and off; altering global parameters; testing messages (e.g., warning against illegal or illogical inputs), drop-down menus, named areas, switches, labelling, formulas and macros; removing redundant elements.

Part D: Operational validation (4 questions)

Part D discusses techniques used to validate the model outcomes.

D1/ Face validity testing (model outcomes): Have experts been asked to judge the appropriateness of the model outcomes?  
If yes, please provide information on the following aspects:  
- Who are these experts?  
- What is your justification for considering them experts?  
- To what extent did they conclude that the model outcomes are reasonable?  
If no, please indicate why not.  
During the development of the economic model we consulted two medical practitioners (Dr Virginia Mumford and Dr Deborah Bateson) and a pharmacist (Dr Natalie Gauld). See Question A1.  
In general, the experts agreed that the model outcomes were reasonable.  
Outcomes may include but are not limited to: (quality-adjusted) life years; deaths; hospitalizations; total costs.

D2/ Cross validation testing (model outcomes): Have the model outcomes been compared to the outcomes of other models that address similar problems?  
If yes, please provide information on the following aspects:  
- Are these comparisons based on published outcomes only, or did you have access to the alternative model?  
- Can the differences in outcomes between your model and other models be explained?  
- Please indicate where this comparison is reported, including a discussion of the comparability with your model.  
If no, please indicate why not.  
Section 4 compares the results of the model to other economic evaluations of reclassifying OCPs. The comparison were based on published outcomes only.  
Other models may include models that describe the same disease, the same intervention, and/or the same population.
**D3/ Validation against outcomes using alternative input data:** Have the model outcomes been compared to the outcomes obtained when using alternative input data? If yes, please indicate where these tests and their outcomes are reported. If no, please indicate why not.

*Scenario analysis was conducted on using utilities based on EQ-5D population norms. The results were not sensitive to the application of this data.*

Alternative input data can be obtained by using different literature sources or datasets, but can also be constructed by splitting the original data set in two parts, and using one part to calculate the model outcomes and the other part to validate against.

**D4/ Validation against empirical data:** Have the model outcomes been compared to empirical data? If yes, please provide information on the following aspects:
- Are these comparisons based on summary statistics, or patient-level datasets?
- Have you been able to explain any difference between the model outcomes and empirical data?
- Please indicate where this comparison is reported.
If no, please indicate why not.

**D4.A/ Comparison against the data sources on which the model is based (dependent validation).**

*The number of births per woman with prescription-only OCPs equalled that from the ABS (1.789)(1).*

(1) Australian Bureau of Statistics, Births Australia, 2016, Cat. no. 3301.0. 2016, ABS: Canberra

**D4.B/ Comparison against a data source that was not used to build the model (independent validation).**

*The predicted age of mothers in the model with prescription-only OCPs (30.45 years) was similar to that in Australia (31.2 years) (1).*

(1) Australian Bureau of Statistics, Births Australia, 2016, Cat. no. 3301.0. 2016, ABS: Canberra

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**Part E: Other validation techniques (1 question)**

**E1/ Other validation techniques:** Have any other validation techniques been performed? If yes, indicate where the application and outcomes are reported, or else provide a short summary here.

*No.*

Examples of other validation techniques: structured “walk-throughs” (guiding others through the conceptual model or computerized program step-by-step); naïve benchmarking (“back-of-the-envelope” calculations); heterogeneity tests; double programming (two model developers program components independently and/or the model is programmed in two different software packages to determine if the same results are obtained).