

Guidelines Take-home exam HEVAL5130 – Fall 2024

General requirements

A take-home exam gives the student an opportunity to show the student's analytical skills, and ability to synthesize information and marshal facts for a clearly articulated argument. Furthermore, a take-home exam tests if the student knows where and how to look up information and what to do with it. A take-home exam requires that references to literature and materials used in the text are correct and consistent.

Assessment guidelines

The report should be no more than 2500 words (not including tables, figures and reference list).

The grading will be based on two main categories (40%/60% valuation split):

1. Structure (understand what should be included in each section) **(40%)**
 - Follow the recommended structure
 - Content within each section was correctly placed (for example, introduction did not include methods, results did not methods or theoretical framework, discussion did not present new results)
 - Comprehensive tables and figures with legends that include necessary information for “stand-alone” exhibits
2. Content and interpretation (show understanding of the theoretical frameworks, application, correct interpretation of methods and findings, and assessment of the limitations with potential implications of assumptions) **(60%)**

The take-home exam will be assessed on the following guidelines:

- The take-home exam addresses the problem stated in a clear and consistent manner; Choices and assumptions made are clarified and substantiated, and the method chosen is presented, justified, and discussed;
- The application of methods meets scientific criteria (is methodologically correct);
- Discussion and analysis: Relevant empirical evidence is presented and critical discussed against the theoretical framework;
- The take-home exam should include reference to relevant peer-reviewed literature;
- Format: the take-home exam fulfill format requirements, meets the academic standards with regard to style, structure and deepening of the subject.

What determines the grade?

- Structure and length of the take-home exam must meet the formal requirements;
- The application of methods must be methodologically sound;
- Concepts, theoretical frameworks and empirical knowledge are presented correctly, and used in the discussion of the stated problem;
- The student must be capable of arguing in a logical and clear manner;
- There must be originality and critical reflection: the student must be able to indicate what he or she has learned or what he or she would do differently in a next study (note: this is not a matter of personal experiences but of academic insights);
- The student uses an approved reference style, without any errors;
- Layout of exam in academic style (appropriated titled figures and tables, and use of complete sentences and paragraphs);
- Unformatted result tables should not be copied directly from output files from statistical programs (e.g., STATA, R), or other statistical programs.

Special requirements and evaluation criteria:

All reports **MUST** include the following sections; sub-sections may vary by exam topic (see pages 6 and 7 for example Table of Contents):

1. Introduction/motivation that describes that economic evaluation is required in Far Far Away prior to implementation of Progression-stopper 2.0, and the evidence gap that one has not been completed. Elaborate on the need for analyses in 1A or 1B should also be included.
2. Objective
 - Topic 1A: The objective needs to capture both evaluation of the cost-effectiveness of Progression-stopper 2.0 (CEA) as well assessment of the decision uncertainty and potential need for further research using VOI.
 - Topic 1B: The objective needs to capture both evaluation of the cost-effectiveness of Progression-stopper 2.0 (CEA) but also the need to identify potential limited use criterion and the monetary value of a LUC.
3. Theoretical framework (presentation of the theory relevant for the chosen topic; peer-reviewed papers and/or book citations required)
 - Importantly, a smooth structure that logically flowed from one theoretical topic to the next strengthened the evaluation of the exam.
 - Methods should not be presented here (no sentences such as, “in this analysis I assumed...”).
 - All methods/approaches used in the analysis should be explained generally in this section from a theoretical perspective.
 - Inclusion of formulas (e.g., ICER, NMB, EVPPI, etc) strengthened the evaluation (linked to transparency best-practices)
 - Both topics: Theoretical framework on economic evaluation (and ICERs and Net Monetary Benefits) and decision-analytic modeling to estimate outcomes should also be included, including the need for transparency and validation (debugging using checklists) of decision-analytic models (e.g., citing Sanders et al), and uncertainty in decision modeling (i.e., probabilistic analysis and preferably the other types of uncertainty should be mentioned). Transition to model input estimation using survival analysis (for both topics) also require a presentation of survival- and hazard functions, censoring, time-dependency, non-parametric versus parametric models. The student should include the importance of smoothed hazard plots, visual inspection and goodness of fit (AIC and BIC) with references, e.g., Latimer et al.
 - Topic 1A: Theory on value of information, define and explain the theoretical step-wise approach to conducting VOI: EVPI, EVPPI and EVSI (and scaling to population). Importantly, how these values are theoretical maximum values of collecting additional research and why you might need EVSI. Distinguish between gold standard method to estimate EVPPI and the approximation methods. Theory on how to scale to population level, and design of trials (e.g., grouping parameters for EVPPI). Mention why probabilistic draws often need to utilize Cholesky decomposition to capture correlated input parameters.
 - Topic 1B: Theoretical framework for calibration approaches (e.g., citing Vanni’s 7-step approach) as well as on stratified analysis/heterogeneity, LUC and incremental net benefits from stratification (citing Coyle et al). For the probabilistic component of this topic, mention why probabilistic draws often need to utilize Cholesky decomposition and how individual EVPPI can also be used as a type of sensitivity analysis.
4. Methods

- Both topics: Theoretical framework, definitions and results should not be in this section (general equations should be in the theoretical framework section). In general, the text should NOT reflect the mechanistic detailed tasks that were performed, e.g., “I copied and pasted worksheet x”, but rather described methodological assumptions and approach in a “report-based” methods format, e.g., “we adapted the baseline model to reflect x, y, and z”; or, “we assumed that there were x number of patients over a y year period.”
- Topics 1A and 1B: In this section, it is required that the candidate describes the structure of the decision-analytic model including health states and important assumptions (e.g., assumptions associated with transitions between health states, strategies considered, model outcomes), and presents the data used for the analysis, defines the variables used in the analysis. All other assumptions made in the analysis must be specified, including time horizon, discount rate and perspective (analysis transparency). Need to describe approach model and analysis validation. Exams were strengthened by including impact inventory/CHEERs/TECH-VER in appendix. Describe Chloriplasma dataset, and the variables used in the analysis. Analysis needed to convert monthly observational data to annual time step (to align with model cycle length (or adapt model to monthly cycle)). Methods should include a presentation of estimating preferred parametric distribution, e.g., using the smoothed plot of overall hazard over time to choose between distributional forms that captures the hazards rates over time, AIC/BIC, and visual inspection.

- A case should likely be made for the Weibull distribution when all factors are considered simultaneously. The shape / scale for an annual time step assuming Weibull distribution should be approximately:

\$weibullPH	est	L95%	U95%	se	shape	scale
shape	-0.3237389	-0.6857234	0.0382455	0.184689	0.03411	-0.01087
scale	-1.2977472	-1.7223868	-0.8731076	0.216657	-0.01087	0.04694

- Model should be adapted for cycle-dependent transition probabilities that decrease over time (no longer constant)
- Detection of at least two bugs: 1) background mortality rates to probabilities, and 2) continuity correction, e.g., ½ cycle correction. Could mention the discrepancy of the probability of dying at the oldest ages compared with the severe-only state death probability.
- Topic 1A: Present input parameters and the assumed probability distributions (report transparency). Provide all assumptions made in VOI analysis, including data used to inform input parameters, estimation of the population to benefit from research, discount rate, threshold, proposed research studies and assumed expected costs of research studies. The grouping of input parameters to perform EVPPI should be presented and justified in this section, e.g., Weibull parameters can be collected in a new observation trial, while relative treatment effect would often require an RCT (could simultaneously collect HRQoL parameters). Preferably a table outlining these assumptions. Report approach to calculate 95% credible intervals, i.e., lower and upper 2.5% of simulations, (and do not refer to them confidence intervals).
- Topic 1B: Describe calibration approach used, preferably using Vanni’s 7-steps. E.g., using Excel Goal Seek or manual calibration to identify the comorbidity-specific relative risk (RR) that fit to the targets provided for cycle 4 (you would need to change the starting cohort size for each comorbidity group to match the ‘trial’ sample size). Adapt model for treatment effect (RRs) for the comorbidity groups. Describe the LUC criteria assumptions (patient

population proportion, number of patients, thresholds evaluated). Explain the motivation of EVPPI as a way to evaluate decision uncertainty (could touch on research priorities, but for 1B, the motivation was more about using EVPPI as a type of sensitivity analysis to assess parameter contributions).

5. Results (assessment includes review of calculations/coding in Excel file/R code)

- Both topics: Clear presentation of the findings in a logical order, and according to questions asked in the home-exam (if statistical analysis/methods were defined in this section, it is a negative with regard to structure, but not to content).
- Topic 1A: No need to present deterministic results; if exam presented both, justification of why should have been stated. Results should have focused on presentation of the probabilistic results including: QALYs (mean of probabilistic outcomes with 95% credible intervals), costs (mean of probabilistic outcomes with 95% credible intervals), incremental QALYs, other descriptive health outcomes such as death by year 5 (mean of probabilistic outcomes with 95% credible intervals). The additional model outcomes should have been simulated in the PA (analysis transparency requires all presented). The incremental cost-effectiveness ratio (ICER) should not have 95% CIs (for reasons mentioned in class about negative ICERs). Interpretation of the results assuming that your cost-effectiveness threshold of £25,000 per QALY. Visualization of the CEAF results and interpretation of these results (cannot say this is simply the strategy with the highest probability of being cost-effective). Explicit step-wise interpretation of VOI results, i.e., the population EVPI results, assuming that the expected research costs are between £0.5-10 million depending on the research study design, and that your WTP threshold is £25,000 per QALY. Interpretation of the population EVPPI results with justified study designed (here drug effectiveness was a major driver of EVPI, which would, in most cases, require an RCT). Exam evaluation was weakened if parameter groupings were not justified by a study design. Visualization of all VOI results and/or presentation in form of a table. There should be no statements that further research is definitively worthwhile based on pEVPI or pEVPPI alone, only that it is potentially worthwhile / might be worthwhile (if EVPPI > study cost, though we cannot know for sure without EVSI).
- Topic 1B: Model should have correctly incorporated sub-group-specific calibrated treatment effects, and presented descriptive health outcomes from the model by comorbidity group (cumulative death, death by cycle x, etc) compared with the 'population' outcomes based on the weighted average of the three groups. Present the group(s) for which Progression-stopper was considered cost-effective for the varying thresholds, as well as the weighted population ICER. Exam should describe the optimal LUC and the value of the LUC by threshold. Present the individual-level EVPPI for C1 to show which parameters contributed to decision uncertainty at the threshold (shape and scale should have been grouped).

6. Discussion

- Both topics: Discuss summary of results, refer to other literature when relevant was a bonus, how general are the findings, etc. Limitations and potential biases of assumptions.
- Topic 1A: Elaboration on whether the decision maker should make an immediate decision or collect additional evidence and explain the next steps,

such as EVSI and ENBS (briefly that EVSI and ENBS would be needed to determine whether further research is worthwhile).

- Topic 1B: could have discussed ethical implications of LUCs.

7. Conclusion

- Both topics: Should be in line with the objective, defined in the introduction of the home exam.
- Topic 1A: Conclusions should comment on the cost-effectiveness of Progression-stopper 2.0 compared with standard of care, the robustness of this conclusion across the thresholds, and, depending on the assumed cost of the research, whether a decision should be made today (because research costs would exceed EVPPI group value) or the next steps of VOI (i.e., EVSI and ENSB) should be evaluated. Insufficient conclusion to only comment on the CEA portion of the exam.
- Topic 1B: Conclusions should comment on the cost-effectiveness of Progression-stopper 2.0 compared with standard of care (based on the weighted average the groups' costs and QALYs, then calculate ICER), and how it differed between the sub-groups at the cost-effectiveness threshold(s). Insufficient conclusion to only comment on the CEA portion of the exam.

8. References

- Consistently referenced and styled.

9. Appendix

- Must include R/do file script (Topic 1) as an appendix, and completed Excel model (both topics) as the additional file.

Example outline for a comprehensive exam (1A), note checklists and extensive documentation of theoretical framework equations in the appendix:

- 1. Introduction**
- 2. Theoretical Framework**
 - 2.1. Economic evaluation, ICER, cost-effectiveness threshold, NMB
 - 2.2. Decision-analytic models
 - 2.2.1. Validation and model transparency
 - 2.3. Survival analysis
 - 2.4. Uncertainty
 - 2.4.1. Probabilistic analysis
 - 2.4.2. Value of Information (EVPI, EVPPI, EVSI and ENBS; scaling to population)
- 3. Methods**
 - 3.1. Analytic overview
 - 3.2. Model structure
 - 3.3. Model inputs
 - 3.3.1. Survival analysis and extrapolation
 - 3.3.2. Transition probabilities, HRQoL, costs
 - 3.3.3. Probabilistic analysis
 - 3.4. VOI assumptions and approach
- 4. Results**
- 5. Discussion**
- 6. Conclusions**
- 7. References**
- 8. Appendices**
 - Appendix A: Theoretical framework formulas
 - Appendix B: Model input parameters and distributions
 - Appendix C: Checklists (CHEERS, TECH-VER)

Example outline for a comprehensive exam (1B), note checklists and extensive documentation of theoretical framework equations in the appendix:

1. Introduction

2. Theoretical Framework

2.1. Economic evaluation, ICER, cost-effectiveness threshold, NMB

2.2. Decision-analytic models

2.2.1. Validation and model transparency

2.3. Survival analysis

2.4. Calibration

2.5. Stratified analysis and LUC

2.6. Uncertainty

2.6.1. Probabilistic analysis and EVPPI

3. Methods

3.1. Analytic overview

3.2. Model structure

3.2.1. Validation checks

3.3. Model inputs

3.3.1. Survival analysis and extrapolation

3.3.2. Transition probabilities, HRQoL, costs

3.3.3. Calibration approach

3.4. Stratified analysis approach

3.5. EVPPI sensitivity analysis

4. Results

5. Discussion

6. Conclusions

7. References

8. Appendices

Appendix A: Theoretical framework formulas

Appendix B: Model input parameters and distributions

Appendix C: Checklists (CHEERS, TECH-VER)